

A Genomic Copy Number Variation Study in Autism Spectrum Disorder

Abstract

Autism spectrum disorder (ASD) is a severe neurodevelopmental disorder characterized by deficits in social, communicative, and behavioral function. Despite the high heritability of the disorder, significant levels of genetic and phenotypic heterogeneity have hindered the identification of susceptibility genes by traditional linkage screens. In this study, we introduced the use of the high-density, Affymetrix 500k SNP array in consanguineous families to confront this challenge. Using the SNP array, we investigated the role of submicroscopic copy number variation (duplications or deletions of chromosomal regions) in the etiology of ASD in 97 affected individuals from the Middle East, Turkey, Pakistan, and India where there is a high rate of consanguineous marriages. Six homozygous deletions and 19 de novo copy number variants of clinical relevance were identified. In accordance with recent studies, we also implicated NRXN1 in our screen and further investigated the region through a novel application of homozygosity mapping in ASD. This study reveals the potential of high-resolution array methods to identify ASD susceptibility regions in the face of extreme genetic complexity