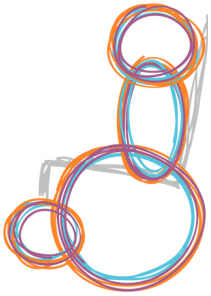
Identifying new genetic markers associated with autism spectrum disorders

childhood disability LINK



Summary

Autism spectrum disorders (ASD) cause a wide range of intellectual effects but are typically marked by impaired social communication, repetitive behaviors, and restricted interests. Although it is well established that ASDs are highly heritable within families, the genetic basis of this inheritance remains poorly defined.

Several rare genetic deletions or duplications, called copy number variants (CNVs), have been implicated is ASDs. However, common variants that explain multiple cases of ASD are hard to come by. Continuing genetic investigations of ASDs will hopefully illuminate variants that confer a high risk for disorders in the spectrum.

To identify genetic markers of autism, genome-wide analysis based on 1 million single nucleotide polymorphisms (SNP) was performed in 1369 families with at least one individual affected by ASD. All study subjects were recruited through the Autism Genome Project (AGP) Consortium, which represents several centers in Europe and North America. Analysis showed that mutations in one genetic locus, MACROD2, were significantly associated with ASD. However, the association fell below a significant level when analysis was repeated in a larger sample that included an additional 2179 families with ASD-affected members and a cohort of control families. Strong, though not significant, associations with ASDs were found for the KIAA0564, PLD5, POU6F2, ST8SIA2, and TAF1C loci.

What families should know

ASDs are extremely prevalent, affecting between 6 and 10 of every 1000 children. Symptoms range widely in type and severity, a phenomenon which is likely linked to the genetic variability associated with ASDs. This wide genetic variation makes it difficult to predict or test for ASDs. However, continuing elucidation of important genetic markers will facilitate earlier outcome prediction and therapeutic intervention in children with ASDs.

What practitioners should know

This study adds 6 potential target loci to the list of genetic mutations that are associated with ASD. Many genetic variations that have previously been implicated in ASD affect neuronal development, especially in synapses. The function of MACROD2 remains unknown, but the portion of this locus disrupted in this study also contains the FLRT3 locus, a gene important for cell adhesion and neuronal development. ST8SIA2 codes for a protein that modifies a neural cell adhesion molecule (NCAM1), and TAF1C is important for transcription initiation. This study also included an exploratory analysis of genetic associations based on ASD phenotype. The STA8SIA2 and PLD5 loci were significantly associated with verbal ASD, and the KIAA0564 locus was significantly associated with maternal inheritance pattern. Nonetheless, these findings are difficult to interpret because of the effects of multiple testing. Because this study only examined 1369 families, it has limited power to detect population-wide associations. As more individuals with ASD are genotyped, the understanding of the genetic bases and molecular pathways involved in ASD will become clearer, enabling targeted testing and therapies.

Reference

Anney, R., Klei, L., Pinto, D., Regan, R., Conroy, J., Magalhaes, T. (2010). A genome-wide scan for common alleles affecting risk for autism. Human Molecular Genetics, 19(20), 4072-4082.

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