Autism risk higher in people with gene variant

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Scientists have found a variation in a gene that may raise the risk of developing autism, especially when the variant is inherited from mothers rather than fathers. The research was funded by the National Institute of Mental Health (NIMH), part of the National Institutes of Health.

Inheriting the gene variant does not mean that a child will inevitably develop autism. It means that a child may be more vulnerable to developing the disease than are children without the variation.

The gene, CNTNAP2, makes a protein that enables brain cells to communicate with each other through chemical signals and appears to play a role in brain cell development. Previous studies have implicated the gene in autism, and in this study researchers were able to link a specific variation in its structure to the disease.

Results of the study were reported online January 10 in the *American Journal of Human Genetics*, by Aravinda Chakravarti, Ph.D., Dan E. Arking, Ph.D., and colleagues from the Johns Hopkins University School of Medicine, with Edwin Cook, M.D., and colleagues from the University of Illinois at Chicago.

“Autism is highly heritable. Identifying the genes involved is crucial to our ability to map out the pathology of this isolating and sometimes terribly disabling disease, which currently has no cure,” said NIMH Director Thomas R. Insel, M.D.

Autism is a developmental brain disorder that impairs basic behaviors needed for social interactions, such as eye contact and speech, and includes other symptoms, such as repetitive, obsessive behaviors. The symptoms sometimes cause profound disability, and they persist throughout life. Treatments may relieve some symptoms, but no treatment is fully effective in treating the core social deficits.

Although the cause of autism is not yet clear, studies of twins have shown that genes play a major role. It is likely that variations in many genes, influenced by environmental factors, interact during brain development to cause vulnerability to the disease. These genes have yet to be identified. Several candidates, including CNTNAP2, have been suggested.

The assertion that the CNTNAP2 gene appears to be involved is strengthened by the fact that each of the different analytical approaches the researchers used in this study led to the same conclusion. Results were replicated in a second, larger group of participants, further implicating the gene. Together, the two groups of participants comprised one of the largest autism studies reported to date.

The first part of the study included 145 children with autism and their parents, from families that had two or more children with autism. Using a technique called genome-wide linkage analysis, the researchers found that a chromosome, 7q35, appeared to be linked to the disease.

Looking deeper into that chromosome, they identified a gene – CNTNAP2 – that contained a variant relevant to autism. Where a single segment of the genetic code could contain either the chemical base adenine or thymine, children with autism tended to have inherited the thymine variant.

To validate these findings, the researchers studied a separate group of

participants; 1,295 children with autism and their healthy parents. The scientists again found that children with autism had higher rates of the thymine variant in the CNTNAP2 gene than would be expected to occur by chance.

When the researchers combined the data from the studies, they found that children with autism were about 20 percent more likely to have inherited the thymine variant from their mothers than from their fathers.

“This is a common variant. People inherit it all the time. Our finding that it’s associated with autism more often when it’s inherited from mothers is intriguing, but needs to replicated,” Chakravarti said.

The role of CNTNAP2 in brain-cell development suggested by earlier studies has to do with differentiation, the process by which precursor cells develop into the different kinds of cells of the body. CNTNAP2 carries the genetic code for a protein, part of a family called neurexins, that appears to enable the precursor cells to develop myelinated axons. These are projections through which brain cells send each other electrical impulses essential for normal brain function at especially high speeds.

“CNTNAP2 is an excellent candidate gene for autism,” Chakravarti said. “It encodes a protein that’s known to mediate interactions between brain cells and that appears to enable a crucial aspect of brain-cell development. A gene variant that altered either of these activities could have significant impact.”

Source: National Institute of Mental Health