Scientists identify new gene linked to autism risk, especially in boys

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(PhysOrg.com) -- UCLA scientists have discovered a variant of a gene called CACNA1G that may increase a child's risk of developing autism, particularly in boys. The journal *Molecular Psychiatry* publishes the findings in its May 19 advance online edition.

Classic autism strikes boys four times more often than girls. When including the entire spectrum of autism disorders, such as the milder Asperger syndrome, boys are diagnosed 10 times more often than girls.

"This is a strong finding," said Dr. Stanley Nelson, professor of human genetics at the David Geffen School of Medicine at UCLA. "No one has scrutinized the role that CACNA1G plays in autism.

"We found that a common form of the gene occurs more frequently in the DNA of families that have two or more sons affected by autism, but no affected daughters," he explained. "Our study may explain why boys are more susceptible to the disorder than girls."

Nelson and his colleagues zeroed in on a region of Chromosome 17 that previous studies have tied to autism. The research team scoured the DNA of 1,046 members of families with at least two sons affected by autism for common gene variants.

A variant is a gene that has undergone subtle changes from the normal DNA yet is shared by a significant portion of the population.

The researchers used tools of the Human Genome Project to scan thousands of variants across all genes in the suspicious region of the chromosome and to pluck out the most common forms.

"We wanted to identify what was happening in this region of Chromosome 17 that boosts autism risk," said Nelson. "When the same genetic markers kept cropping up in a single region of the DNA, we knew we had uncovered a big clue."

The researchers traced the genetic markers to CACNA1G, which helps move calcium between the cells. They discovered that the gene has a common variant that appears in the DNA of nearly 40 percent of the population.

"This alternate form of CACNA1G consistently increased the correlation to autism spectrum disorder, suggesting that inheriting the gene may heighten a child's risk of developing autism," observed Nelson.

How the gene contributes to higher autism risk remains unclear, but Nelson emphasized that it cannot be considered a risk factor on its own.

"This variant is a single piece of the puzzle," he said. "We need a larger sample size to identify all of the genes involved in autism and to solve the whole puzzle of this disease."

The UCLA team's next step will be to sequence the gene in people who possess the altered variant in order to identify the exact change that increases autism risk. These subtle variations offer potential markers for the real mutation causing greater susceptibility to the disease.

Nelson's coauthors included Samuel Strom, Jennifer Stone, John ten Bosch, Barry Merriman, Rita Cantor and Daniel Geschwind, all of UCLA. The study was funded by the National Institute of Mental Health and Cure Autism Now, which has since merged with Autism Speaks.

The DNA samples and clinical data were provided by families who donated blood to the Los Angeles-based Autism Genetic Resource Exchange (AGRE), a program created and funded by Cure Autism Now.

"When parents like me first formed AGRE, this was our dream, that talented scientists would use our gene bank to collaborate and bring us closer to understanding autism," said Jon Shestack, co-founder of Cure Autism Now and a board member of Autism Speaks. "AGRE has played an important role in almost every major autism genetics paper in the past five years."

Autism is a complex brain disorder that strikes in early childhood. The condition disrupts a child's ability to communicate and develop social relationships and is often accompanied by acute behavioral challenges. The Centers for Disease Control and Prevention report that one in 150 American children is diagnosed with an autism spectrum disorder. The diagnosis of autism has expanded tenfold in the last decade.

Source: University of California - Los Angeles