A Genetic Clue to Why Autism Affects Boys More

By ALICE PARK Alice Park–Wed May 20, 6:20 am ET
Among the many mysteries that befuddle autism researchers: why the disorder affects boys four times more often than girls. But in new findings reported online today by the journal *Molecular Psychiatry,* researchers say they have found a genetic clue that may help explain the disparity.

The newly discovered autism-risk gene, identified by authors as CACNA1G, is more common in boys than in girls (why that's so is still not clear), and the authors suggest it plays a role in boys' increased risk of the developmental disorder. CACNA1G, which sits on chromosome 17, amid other genes that have been previously linked to autism, is responsible for regulating the flow of calcium into and out of cells. Nerve cells in the brain rely on calcium to become activated, and research suggests that imbalances in the mineral can result in the overstimulation of neural connections and create developmental problems, such as autism and even epilepsy, which is also a common feature of autism. (See six tips for traveling with an autistic child.)

"Our current theories about autism suggest that the disorder is related to over excitability at nerve endings," says Geri Dawson, chief science officer of Autism Speaks, an advocacy group that provided the genetic data used by the study's authors. "It's interesting to see that the gene they identified appears to modulate excitability of neurons."

For the new study, researchers at the University of California, Los Angeles (UCLA), combed the genetic database of the Autism Genetic Resource Exchange (AGRE), a resource of DNA from 2,000 families with at least one autistic child. The scientists focused on the more than 1,000 genetic samples of families in which at least one son was affected by the disorder, prompted by the results of an earlier study using the same database, which identified a rich autism-related genetic region on chromosome 17 that contained genetic variants more common in boys than in girls. While nearly 40% of the general population has the most common form of CACNA1G, one variant of the gene was more prevalent in autistic boys, researchers found. "There is a strong genetic signal in this region," says Dr. Daniel Geschwind, director of UCLA's Center for Autism Research and Treatment and one of the study's co-authors. "But this gene doesn't explain all of that signal or even half of it. What that means is that there are many more genes in this region contributing to autism." (See pictures of inside a school for autistic children.)

That's not surprising for a disorder as complex as autism - actually, a spectrum of developmental disorders involving impairment in language, social behavior and certain physical behaviors - with symptoms that range widely in number and severity. So far, studies have linked a handful of genes, all of which play a role in the way nerve cells connect and communicate, with autism spectrum disorders. It's likely not only that a large number of genes contribute to the disorder, but also that a different combination of genes - as well as unique interactions between genes and environment - are responsible for each individual case of autism.

So it's certainly a daunting challenge to begin teasing out the individual genes that may contribute to autism, as the UCLA team has with CACNA1G, but databases like AGRE make the job slightly easier. The next step will be to try to use known autism genes to help develop screening tools or early interventions. "We are going to have a much better understanding of the causes of autism over the next five to 10 years," says Dawson. "We're in a period of great discovery."