

NEWS

Rare autism mutations linked to low intelligence

BY NICHOLETTE ZELIADT

20 OCTOBER 2017



People with autism who have rare, damaging mutations tend to have low scores on intelligence tests. The unpublished results, presented yesterday at the **2017 American Society of Human Genetics Annual Meeting** in Orlando, Florida, suggest that these mutations contribute to the risk

of autism with intellectual disability, rather than to autism alone.

“Sometimes variants may be more related to intellectual disability, or autism with intellectual disability, and not solely autism,” says **Matthew Jensen**, a graduate student in **Santhosh Girirajan**’s lab at Pennsylvania State University, who presented the findings.

To link a gene to autism, researchers look for damaging mutations that appear in multiple people with autism and rarely in people without the condition. But up to 40 percent of people with autism also have intellectual disability, making it difficult to distinguish true autism risk genes from those that influence intelligence.

In the new work, Jensen and his colleagues looked at the intelligence quotients (IQs) of nearly 2,300 children with autism. Of these children, 288 of have a single-letter mutation not found in their parents or siblings, and 81 lack a large chunk of DNA — a glitch known as a **copy number variant**.

They found that the children with autism who carry either type of mutation have a significantly lower IQ, on average, than do children without either type.

By contrast, they score similarly to the children without these mutations on a test of autism severity, called the Social Responsiveness Scale. Together, the findings suggest that the harmful mutations largely affect cognitive abilities.

Decoding diversity:

In addition, the 397 children with autism and high IQ (a score above 100) are less likely to carry harmful spontaneous mutations than the other children in the study. They are also less likely than those with an IQ below 70 to carry a mutation in any of the **top 76 autism genes** — those that have been found in at least three people with autism.

But mutations in any of those 76 genes may contribute to both autism and intellectual disability: The 54 children who have mutations in one of these genes have more severe autism features and a lower IQ than the children who don’t have such mutations, the researchers found.

“[The results are] a step towards lining up the genetic heterogeneity with the phenotypic heterogeneity,” says **Mark Daly**, associate professor of medicine at Massachusetts General Hospital in Boston, who was not involved in the new work.

The findings align with those from several previous studies, including a 2014 analysis from Daly’s team showing that boys with autism and a low IQ have a **higher-than-average rate** of spontaneous mutations.

Jensen and his colleagues also used **a tool called BrainSpan** to map the expression patterns of the top 76 autism genes in the developing brain, and those of 42 genes mutated in children with autism and a high IQ. Many of the top autism genes are expressed in the cerebral cortex, the brain's outer layer, during fetal development. By contrast, mutations found in the individuals with a high IQ do not show a consistent pattern of expression in the brain, suggesting they play a less specific role in brain development.

For more reports from the 2017 American Society of Human Genetics Annual Meeting, please [click here](#).