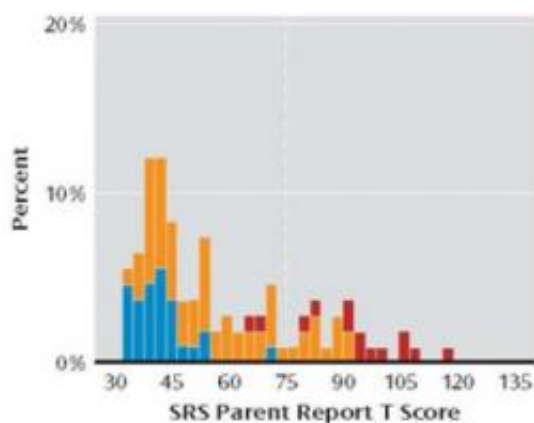


Language delays found in siblings of children with autism

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This graph tracks the symptoms of girls in one category of families affected by autism. Yellow denotes girls with histories of language delay and autistic traits who were never formally diagnosed as having an autism spectrum disorder (ASD). Blue represents unaffected girls, red represents those diagnosed with ASD. Credit: Image courtesy of *The American Journal of Psychiatry*. Copyright © 2010 American Psychiatric Association. Used with permission.

Siblings of children with autism have more frequent language delays and other subtle characteristics of the disorder than previously understood. Girls also may be mildly affected more often than recognized in the past.

A new study, led by researchers at Washington University School of Medicine in St. Louis, found mild traits, not strong enough to provoke a diagnosis of autism, seem to be present in the siblings of affected children at significantly higher rates than seen in the general population. The findings appear online and will be published in the November issue of *The American Journal of Psychiatry*.

"Mild symptoms, called quantitative traits, may be confounding studies that compare children with autism to their siblings," says first author John N.

Constantino, MD. "Researchers presume one child is affected, and the other is not, but our findings suggest that although one child may have autism while the other does not, it's very possible both children are affected to some degree by genes that contribute to autism."

[Genetic factors](#) exert their influence in different ways. Some families have only a single child with autism and no other affected children. But in other families, more than one child may be affected, or other siblings may have a number of autism characteristics.

The study found that approximately one in five siblings thought to be unaffected experienced language delays or speech problems early in life. The researchers also noticed many female siblings had subtle traits, but few had full-blown [autism spectrum disorders](#). Boys are thought to be affected four times more often than girls. But when the researchers used standardized methods to account for the presence of quantitative traits, the rate looked more like three affected boys for every two affected girls.

"The gender difference may not be as pronounced as we once thought it was," Constantino says. "If we rely only on a professional diagnosis of autism to determine who is affected, then boys vastly outnumber girls. But it may be that many girls are being missed."

The data comes from almost 3,000 U.S. children in 1,235 families who are part of the Interactive Autism Network, a national online research registry at www.IANproject.org. Developed by study co-author Paul Law, MD, director of medical informatics at Kennedy Krieger Institute in Baltimore, the network has more than 35,000 participants who share information to help advance autism research.

For this study, parents provided information about

their children using the Social Responsiveness Scale, a survey developed at Washington University that identifies traits associated with autism and autism spectrum disorders such as Asperger Syndrome and Pervasive Developmental Disorder.

About 10 percent of children with autism have genetic mutations believed to directly lead to the disorder. In others, common gene variations create small increases in susceptibility. When a child has an accumulation of quantitative traits, that child will be diagnosed with autism or a related disorder, but siblings can have subtle quantitative traits without reaching the threshold for a diagnosis.

"It's not an all-or-nothing condition," Constantino says. "When we look only at the full syndrome for inherited traits, we miss a lot of individuals who may have genetic susceptibility and subtle aspects of autism. In other words, many siblings of children on the spectrum have significant, subclinical traits of autism, but, for whatever reason, they never actually develop the disorder."

Constantino, the Blanche F. Ittleson Professor of Psychiatry and Pediatrics and director of the William Greenleaf Eliot Division of Child and Adolescent Psychiatry at Washington University, compares it to the difference between insulin resistance and diabetes. Not all people with insulin resistance are diabetic, and some never develop diabetes, but they are at a much higher risk for the disease. The same thing is true for autism, he says.

One striking finding was that among siblings, 20 percent had received a diagnosis of language delay or speech problems early in life. And half of them had particular qualities of speech that are autistic in nature. So the investigators believe that what is aggregating in these families is more than just the full syndrome of autism. In about 11 percent of families, more than one sibling has autism, and in many others, these subtle, quantitative signs and symptoms indicate many undiagnosed children are affected as well.

That's important, Constantino says, because in studies involving DNA tests, brain imaging or biological comparisons between affected children

and their unaffected siblings, researchers traditionally assume undiagnosed children are unaffected. But this study would suggest that's not necessarily the case.

The study also found quantitative traits of autism tended to occur more frequently in children from families with more than one fully affected child. In families with only one child with autism, it was much more common for that child's siblings not to have any evidence of quantitative traits. And the study also found that it was less common for [siblings](#) to be affected with those traits than for non-identical twins — a finding suggested by pooling the results of this study with a recent twin study from Law and his colleagues at Kennedy Krieger Institute that used exactly the same methods and the same family registry.

Law and Constantino say their findings provide insight into the inheritance patterns of autism and its associated traits. Although those severely affected with autism spectrum disorders seldom have their own children, those who are affected with quantitative traits of [autism](#) usually grow up to be parents themselves, and understanding how best to predict patterns of transmission in families and identifying the specific genetic and environmental factors underlying those patterns could offer hope for new, more effective interventions that could be used early in the lives of affected [children](#), Constantino says.

More information: Constantino JN, Zhang Y, Frazier T, Abbacchi AM, Law P. Sibling recurrence and the genetic epidemiology of autism. *The American Journal of Psychiatry*, vol. 167 (11), published online Oct. 1, 2010. ajp.psychiatryonline.org

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