

**NEWS**

# Shared genetic pathways underlie autism, attention deficit

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A trio of studies make the strongest case to date that autism and attention deficit hyperactivity disorder (ADHD) share similar genetic causes.

The findings could help explain why **up to 80 percent** of children with autism also meet the criteria for ADHD.

Several studies have shown that autism and ADHD **co-occur in families**, but researchers have yet to identify overlapping genes.

“It’s a conundrum,” says **Amir Miodovnik**, a pediatrician at Maimonides Medical Center in New York, who was not involved in the studies. “That’s why people are continuing to try to show the genetic linkage in different ways.”

One of the new studies explores the genetic basis of autism and ADHD traits in the general population, another examines how autism and ADHD co-occur in families, and the third reveals how features of autism relate to those of ADHD. Together, they show that the two conditions are closely related.

“The overlap is not a bias, it’s not an artifact; it’s real,” says **Jan Buitelaar**, professor of psychiatry at Radboud University in the Netherlands, who led one of the studies.

Understanding the nature of this overlap may help researchers reveal the causes of both conditions and point to new therapies.

## Population traits:

In the latest study, published in April in *Molecular Autism*, researchers looked for genetic variants associated with features of either condition in typical children<sup>1</sup>. They examined genetic and behavioral data from more than 5,000 children enrolled in the **Avon Longitudinal Study of Parents and Children**, which tracks children’s health and development in the United Kingdom.

The behavioral data came from parents, who reported on signs of autism, such as social-communication difficulties, and features of ADHD, such as hyperactivity and inattention, in their children. “We see quite often that psychiatric conditions are on a continuum, from very severely affected individuals to traits seen in general population,” says lead investigator **Beate St Pourcain**, researcher at the Max Planck Institute for Psycholinguistics in the Netherlands.

Normal variation across the genome can explain the range of autism- and ADHD-related traits among the typical children, the researchers found.

The researchers then looked for overlap in the genetic variation underlying the two sets of traits. They quantified the extent of this overlap using measure called a ‘genetic correlation.’

“If correlation is 100 percent, for example, it means there are identical genes behind the traits,” St Pourcain says.

The analysis revealed a strong genetic overlap between hyperactivity, inattention and social communication difficulties. The results vary based on the age of the children. But in late childhood and adolescence, the correlation ranges between 80 and 100 percent.

This type of analysis cannot pinpoint particular genes involved, but suggests that similar biological mechanisms contribute to features of both ADHD and autism, St Pourcain says.

## Twin tales:

In the second study, researchers analyzed medical records for 1,899,654 people born in Sweden between 1987 and 2006<sup>2</sup>. About 28,500 of the individuals have an autism diagnosis, and 82,400 have ADHD. The sample included 4,180 identical twin pairs and 12,655 fraternal twin pairs.

The association between the two conditions is strongest among identical twins, who share the same DNA: An identical twin is nearly 18 times more likely than average to have ADHD if her twin has autism. Fraternal twins and full siblings, who share half their DNA, have a fourfold increased risk of ADHD if their sibling has autism.

The results show a clear drop-off from identical to fraternal twins, says **Alan Brown**, professor of psychiatry and epidemiology at Columbia University, who was not involved in the study. “This is the kind of drop-off that you see with familial disorders.”

The association weakens as the relationship becomes more distant: A person stands a 30 percent increased risk of ADHD if his half-cousin has autism.

The study, published 28 February in *Molecular Psychiatry*, is unique in its ability to show a “dose-response” pattern of familial overlap between autism and ADHD, Miodovnik says.

Another strength of the study is its size, he says. But its reliance on medical records means the researchers can’t directly verify the **accuracy of diagnoses** made by various doctors over many years.

## Cause and effect:

In the third study, researchers sought to clarify whether certain autism features give rise to features of ADHD, or vice versa<sup>3</sup>.

Buitelaar and his colleagues used an algorithm to determine the likely direction of influence between the autism and ADHD features in 130 children with a diagnosis of autism, 317 children with ADHD, and 139 children with both conditions, as well as 393 unaffected siblings and 414 controls.

The algorithm works by identifying 'fixed' relationships between certain variables. For instance, being male increases autism risk, but not the other way around. From that point, the algorithm predicts the likely direction of associations between other variables.

The analysis, published 2 March in the *Journal of Autism and Developmental Disorders*, suggests impulsivity can lead to social problems, and hyperactivity may give rise to **repetitive behaviors**, another feature of autism. "Interventions that reduce impulsivity and hyperactivity would have some downstream beneficial effect on improving autism symptoms," Buitelaar says.

All three studies suggest a close relationship between autism and ADHD, but homing in on the genes they have in common may require genetic studies using large numbers of participants.

**REFERENCES:**

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