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Could ADHD be diagnosed genetically?

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Despite it being very common, ADHD is often missed until a child reaches age seven or older. By that time, they have likely been struggling socially and in school. Could early genetic testing be part of the solution?

Anne Arnett, Ph.D., in partnership with Ryan Doan, Ph.D., at Boston Children's Hospital, set out to see whether genetic diagnosis of ADHD is feasible. Experts have always assumed that ADHD is the product of multiple genes and therefore very hard to diagnose genetically. But to the

researchers' surprise, their pilot study showed that single-gene alterations could explain up to half of cases.

"Earlier diagnosis would allow us to support the child and family before secondary problems arise, such as academic problems, social rejection, and stress on the family," says Arnett, a researcher in the Division of Developmental Medicine.

A high rate of genetic diagnoses

As described November 20 in *JAMA Pediatrics*, Arnett and Doan analyzed clinical whole-genome sequencing data from 77 children aged 6 to 18, provided through the Children's Rare Disease Cohorts Initiative. All 77 children had a confirmed ADHD diagnosis.

To keep the results specific to ADHD, the researchers excluded children with autism, moderate to severe intellectual disability, or known genetic syndromes. They also obtained genetic test results from siblings and parents, with and without ADHD, giving added power to their search.

"We started finding genetic diagnoses in the children pretty quickly," says Doan, of the Division of Genetics and Genomics at Boston Children's. "That was a little surprising."

Forty families, or 52%, had genetic variants that were likely causative of ADHD. Some variants were inherited, and some were de novo, meaning they were not found in the parents.

Interestingly, many of the affected genes are also known to be involved in other neurodevelopmental disorders.

"We're finding that there's quite a bit of overlap," Arnett says. "It's just that in ADHD, the variants are milder. A more severe variant to the

same gene, causing it to lose its function, could result in autism or intellectual disability."

Other genes with detected variants are involved in methylation—chemically modifying other genes.

More to explore about ADHD genetics

Arnett and Doan speculate that the variety of genetic causes they found may explain why ADHD symptoms and severity vary so much from child to child. The genetic overlap with other conditions may explain why it is sometimes hard to distinguish ADHD from conditions like autism.

"Many kids don't fit into diagnostic 'boxes' very well," Arnett says.

Arnett stressed that genetic testing for ADHD isn't available to families right now. But she hopes that in the future, a genetic diagnosis could provide prognostic information. It might indicate, for example, whether ADHD will persist into adulthood or whether the child will have learning disorders, as well as strengths the child could lean into, like creativity or athleticism.

"Previous research shows that girls with ADHD tend to have a stronger family history of ADHD and more genetic risk factors," notes Arnett. "I think there may be other factors that protect girls with mild genetic risk for ADHD."

More information: Anne B. Arnett et al, Rare De Novo and Inherited Genes in Familial and Nonfamilial Pediatric Attention-Deficit/Hyperactivity Disorder, *JAMA Pediatrics* (2023). DOI: 10.1001/jamapediatrics.2023.4952

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