

Children with certain dopamine system gene variants respond better to ADHD drug

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Children with certain dopamine system gene variants have an improved response to methylphenidate - the most commonly prescribed medication for Attention Deficit Hyperactivity Disorder - in a finding that could help eliminate the guesswork from prescribing effective medications for children with ADHD.

Researchers reporting their results in the Oct. 21 *Journal of the American Academy of Child and Adolescent Psychiatry* tested 89 children with ADHD between ages 7 and 11. They found that children with specific variants of the dopamine transporter (DAT) and dopamine receptor D4 (DRD4) genes showed greater improvement in [hyperactivity](#) and [impulsivity](#) after taking methylphenidate compared to children with alternative DAT and DRD4 versions.

"Physicians don't have a good way of predicting who will experience great improvement in ADHD symptoms with a particular medication, so currently we use a trial-and-error approach. Unfortunately, as a result, finding an effective treatment can take a long time," explained Tanya Froehlich M.D., lead investigator on the study and a physician in the division of Developmental and [Behavioral Pediatrics](#) at Cincinnati Children's Hospital Medical Center.

"With more information about genes that may be involved in ADHD medication response, we may be able to predict treatment course, tailor our approach to each child, and improve symptom response while decreasing health care costs," she added.

The study is the first-ever placebo-controlled pharmacogenetic drug trial for ADHD in school age children to evaluate the effects of [dopamine system](#) genes variants using teacher as well as parent ratings of children's symptoms. Given the importance of academic functioning for children with ADHD, Dr. Froehlich said it is crucial to consider medication impact at school as well as at home. Children in the study were not already taking stimulant medications for their ADHD.

Participants were prescribed one week each of placebo and three different doses of methylphenidate for their ADHD. Parents and teachers assessed and scored the children's behavioral symptoms based on the Vanderbilt ADHD Parent and Teacher Rating Scales.

The researchers analyzed DNA from saliva samples to see which ADHD-related gene types the children carried. They looked initially at four genes frequently implicated in ADHD – DRD4, DAT, COMT and ADRA2A. DRD4 and DAT, the most well studied [genes](#) for ADHD, showed the strongest effects on methylphenidate dose-response in study participants, according to the researchers.

The DRD4 gene encodes the dopamine receptor protein, which helps control the synthesis and release of dopamine and the firing rate of neurons. The DAT gene encodes the dopamine transporter protein, which removes [dopamine](#) from the brain synapses.

Children who lack what is known as the DAT 10-repeat variant showed greater improvement after taking methylphenidate compared to those carrying the 10-repeat. [Children](#) without the DRD4 gene 4-repeat variant showed less symptomatic improvement with [methylphenidate](#) compared to 4-repeat carriers. A "repeat" is a short nucleotide coding sequences in a gene that is repeated.

Dr. Froehlich and her colleagues indicate in their study that although

findings are promising, additional research is needed in larger patient samples to confirm current study findings and their clinical relevance.

Provided by Cincinnati Children's Hospital Medical Center

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