

OPINION

# Ritalin reaction

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Hyperactive drive: About half of children with autism and hyperactivity respond to Ritalin, according to ratings from parent and teacher surveys.

The stimulant **methylphenidate**, commonly marketed as Ritalin, can quiet hyperactive behavior and increase focus among children who have both autism and attention deficit hyperactivity disorder (ADHD).

But some hyperactive children with autism can't tolerate the drug and suffer side effects such as nausea, mood swings and appetite loss after just a few doses. These children may have a **genetic intolerance to the drug**, suggests a new study published 16 July in *Pharmacogenomics*.

**Up to 75 percent** of children with autism have characteristics of ADHD, including inattention and impulsivity. About **one-third of these children** take stimulants such as Ritalin for their ADHD symptoms.

In a 2005 study of 72 children with autism, hyperactivity and inattention, **35 children responded well to Ritalin**, 14 dropped out after experiencing strong side effects and the rest showed little or no improvement. The children, who were 5 to 14 years of age, were not taking other medications.

The new study examined variants in the genes of 58 of these children. The researchers focused on several genes coding for receptors and transporters of dopamine, norepinephrine and serotonin — chemical signals that regulate mood and higher-order cognitive function.

During the first week of the five-week study in 2005, the children took first a placebo and then increasing doses of Ritalin to test their response to the drug. Over the following four weeks, they received varying doses of Ritalin in a random order, or a placebo, but were unaware which they were taking.

The researchers then asked those who responded well to the Ritalin to continue taking it for the following eight weeks.

The children's parents and teachers filled out surveys at the start of the study and while it was underway, rating the children's day-to-day ability to cope and their levels of hyperactivity. Among those who responded to Ritalin, the surveys reported the greatest improvement on higher doses, **confirming results** from other studies.

Among the 14 children who could not tolerate Ritalin, many carry certain variants in the dopamine receptors **DRD2** and **DRD3**, the researchers found.

Some who respond well to Ritalin tend to have other variants in the genes DRD1, DRD3 and DRD4, which code for dopamine receptors, and in the COMT gene, which codes for a chemical that breaks down **neurotransmitters** and hormones, such as dopamine and norepinephrine.

Others carry variants in the genes for two transporters of dopamine and serotonin (SLC6A3 and SLC6A4) or ADRA2A, a receptor for norepinephrine.

The study is small, and 90 percent of the participants are male. Also, some of genetic variants identified may not be associated with Ritalin response.

Still, if larger studies confirm that certain genetic variants improve the response to Ritalin, it would help doctors decide whom to treat and how.

**Correction:** *This article has been modified from the original. The previous version incorrectly stated that the journal's title is Pharmacogenetics. It is Pharmacogenomics.*