

# Autistic mice act a lot like human patients

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UCLA scientists have created a mouse model for autism that opens a window into the biological mechanisms that underlie the disease and offers a promising way to test new treatment approaches.

Published in the Sept. 30 edition of *Cell*, the research found that autistic mice display remarkably similar symptoms and behavior as children and adults on the autism spectrum. The animals also responded well to an FDA-approved drug prescribed to autism patients to treat [repetitive behaviors](#) often associated with the disease.

"Though many genes have been linked to autism, it remains unclear what goes awry to increase a person's susceptibility to the disorder," explained Dr. Daniel Geschwind, who holds the Gordon and Virginia MacDonald Distinguished Chair in [Human Genetics](#) and is a professor of neurology at the David Geffen School of Medicine at UCLA and director of the Center for [Autism Research](#) and Treatment at the Semel Institute for Neuroscience and Human Behavior at UCLA. "We developed a [mouse model](#) to observe how a gene variant commonly linked to human autism reveals itself in mice."

The UCLA team focused on a gene called CNTNAP2 (contactin associated protein-like 2), which scientists believe plays an important role in [brain circuits](#) responsible for language and speech. Previous research has linked common CNTNAP2 variants to heightened autism risk in the general population, while rare variants can lead to an inherited form of autism called cortical dysplasia-focal epilepsy syndrome (CDFE).

UCLA researchers studied mice lacking CNTNAP2 and found that the animals demonstrated many features of human autism, including abnormal [vocal communication](#), irregular social interaction and repetitive behaviors. The animals were hyperactive and suffered [epileptic seizures](#) like patients with CDFE.

A closer look at the animals' brains before their seizures set in revealed abnormal development of brain-cell circuitry. The problems included irregularities in how neurons travel from their site of origin to their final position in the brain and in how groups of neurons communicate with each other.

The animals also possessed fewer nerve cells that connect the neurons that carry impulses into the central nervous system with those that transmit impulses out to the rest of the body.

This finding dovetails with Geschwind's earlier research, which found that children carrying the CNTNAP2 variant possess a disjointed brain. Their frontal lobe is over-connected to itself and poorly connected to the rest of the brain. Communication with the back of the brain was particularly diminished.

"Our observations are consistent with theories suggesting that autism rewires the brain to reduce long-range connections and boost short-range connections," said Geschwind. "The front of the brain talks mostly with itself. It doesn't communicate as much with other parts of the brain and lacks long-range connections to the back of the brain."

Geschwind admits that he initially had low expectations of the mouse model and was surprised by its findings. He never expected the behaviors of autistic mice and autistic persons to so closely resemble each other.

"I did not expect to see the same behaviors in mice as in humans because we don't know how many neural pathways are shared between the two species," said Geschwind. "This suggests the pathways are very similar – surprisingly so."

The mice also responded well to treatment with risperidone, an antipsychotic drug that was the first to win FDA approval for treating symptoms of autism spectrum disorder.

Animals given the drug grew less hyperactive, showed less repetitive grooming behavior and were better at building nests. Consistent with previous observations in human patients, however, the mice did not show improvement in social interactions.

"Our findings suggest that evolution has maintained the repetitive behaviors related to autism across species," Geschwind said. "If the same is true of social behaviors, we will use the mouse model to study potential therapies that may one day help people with [autism](#)."

His lab next aims to develop drug treatments to improve social skills and use the mouse model to explore the different brain-cell pathways that influence core autistic behaviors.

Provided by University of California - Los Angeles

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