

NEWS

Gene linked to schizophrenia tied to autism-like behaviors

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Mice with mutations in a gene called DLG2 are anxious and asocial; they also sleep poorly and overgroom themselves, according to a new study¹. These characteristics resemble those seen in some people with autism.

The results offer the first evidence that mutations in DLG2 may account for some of the condition's behavioral traits.

"This study is a baby step indicating DLG2's implication in [autism's] core behavioral symptoms," says lead investigator **Soo Young Kim**, assistant professor of pharmacy at Yeungnam University in Gyeongsan, South Korea.

A 2013 study reported that mice and people with DLG2 mutations have differences in learning, attention and other cognitive processes². Last year, a study of nearly 500 families with two or more autistic children identified DLG2 as a candidate gene for autism³.

The new work offers "a more full picture" of DLG2's effect on behavior, says **Seth Grant**, professor of molecular neuroscience at the University of Edinburgh in Scotland. Grant led the 2013 work but was not involved in the new study. "It's a useful contribution."

Living in a box:

Kim and her colleagues bred male mice that have two mutant copies of DLG2. The animals lack the corresponding protein, which forms part of a neuron's scaffolding. DLG4, **another gene implicated in autism**, has a similar role.

The team put the DLG2 mice through a battery of behavioral tests. The mice explore a well-lit box

significantly less than controls, the team found. They groom themselves even at times when mice usually sleep, suggesting that they also have disrupted sleep patterns.

Overgrooming in mice is considered an analog to **repetitive behaviors** in autistic people. These behaviors are thought to be **rooted in the striatum**, a brain region that controls voluntary movement.

The researchers measured how electrical signals move through brain slices taken from the mutant mice. They found diminished excitatory activity in the animals' striatum. The results were published 12 March in *Molecular Autism*.

This finding is “a clue, but not a proof” of a mechanism, Grant says. The mice lack both working copies of DLG2, whereas autistic people would have mutations in only one copy, he adds.

Another limitation is that the study used **only male mice**, says **Holly Stessman**, assistant professor of pharmacology and neuroscience at Creighton University in Omaha, Nebraska, who was not involved in the study. **Schizophrenia**, which is also linked to DLG2, affects men and women equally, whereas autism is thought to **affect more men than women**.

“They really missed an opportunity to think about how sex might play a role here,” Stessman says.

Kim acknowledges the limitation but says it is common to use mice of a single sex in studies, to limit the influence of factors that vary between the sexes, such as hormones. Her team plans to investigate how mutations in DLG2 alter excitatory activity in the striatum of mutant mice.

REFERENCES:

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