

Science News

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When kids' autistic brains can't calm down

Mutation is linked for first time to seizures in autism and is new drug target

Date: April 5, 2018

Source: Northwestern University

Summary: One third of children who have autism spectrum disorder also have epilepsy. It's related to an autism risk gene. But scientists didn't know why the mutation, *catnap2*, caused seizures. Now scientists have discovered the mutation shrinks the neurons' dendrite arbors and synapses that enable brain cells to relay vital messages. The 'Calm down!' message gets lost in the brain, causing neurons to spin out of control. Drugs could soon be tested to reverse seizures, language delay and intellectual disability.

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FULL STORY



Autism risk gene: The important message to calm down can get lost in the brain.

Credit: © Lori Werhane / Fotolia

One third of children who have autism spectrum disorder also have epilepsy. It's related to a major autism risk gene, which is mutated in patients with autism. But scientists didn't know why the mutation, *catnap2*, caused seizures.

Now Northwestern Medicine scientists have discovered the mutation acts like a bad gardener in the brain. It shrinks the neurons' tiny branches and leaves -- its dendrite arbors and synapses -- that enable brain cells to relay vital messages and control the brain's activity. The shrinkage causes a breakdown in message delivery.

An important message that gets lost? Calm Down!

In people with the mutation, inhibitory neurons -- whose job is to keep things tranquil in the brain and slam the brake on excitatory neurons -- don't grow enough branches and leaves to communicate their Zen-like message, the scientists found. That leads to seizures.

The mutation, *CNTNAP2* or "*catnap2*," works as a team with another mutated gene, *CASK*, implicated in mental retardation. As a result, scientists have a new target for drugs to treat the disorder.

The paper was published April 2 in *Molecular Psychiatry*.

"Now we can start testing drugs to treat the seizures as well as other problems in autism," said lead author Peter Penzes, the Ruth and Evelyn Dunbar Professor of Psychiatry and Behavioral Sciences at Northwestern University Feinberg School of Medicine. "Patients with the mutation also have language delay and intellectual disability. So a drug targeting the mutation could have multiple benefits."

Next Penzes's team will do high-throughput screening of molecules with the goal of reversing these abnormalities in patients with autism.

Catnap2 is an adhesive molecule that helps cells stick together, in this case helping the synapses adhere to the dendrites. It's a difficult molecule to target with drugs, Penzes said.

But *catnap2*'s partner, *CASK*, is a social butterfly enzyme that interacts with many other molecules. It can more easily be inhibited or activated with drugs. Penzes's team will screen drugs to activate it because that appears to maintain healthy dendrite branches. When scientists blocked *CASK* in the study, dendrites didn't grow.

Story Source:

Materials provided by **Northwestern University**. Original written by Marla Paul. *Note: Content may be edited for style and length.*

Journal Reference:

1. Ruoqi Gao, Nicolas H. Piguel, Alexandria E. Melendez-Zaidi, Maria Dolores Martin-de-Saavedra, Sehyoun Yoon, Marc P. Forrest, Kristoffer Myczek, Gefei Zhang, Theron A. Russell, John G. Csernansky, D. James Surmeier, Peter Penzes. **CNTNAP2 stabilizes interneuron dendritic arbors through CASK**. *Molecular Psychiatry*, 2018; DOI: 10.1038/s41380-018-0027-3

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