Single gene linked to host of abnormalities during neurodevelopment

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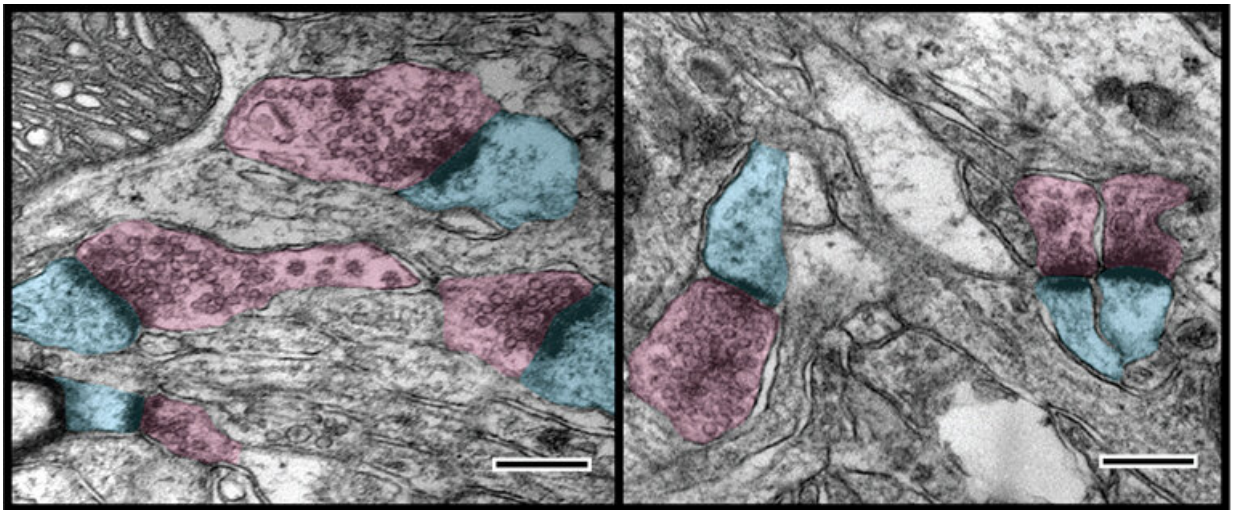

Pre- (pink) and post- (blue) synaptic compartments are smaller than normal in mice lacking TRIO gene, impairing normal brain function and causing disease-associated symptoms. A sample from a mouse with reduced TRIO levels is on the right in this figure. Credit: Yale University

Yale researchers have shown that mutations of a gene associated with autism, schizophrenia, bipolar disorder, and epilepsy cause some of the same structural and behavioral abnormalities that characterize those neurodevelopmental disorders, they report March 5 in the journal *Cell Reports*.

Whole genome sequencing has shown mutations of the TRIO gene, which plays a crucial role in shaping brain cells and orchestrating neural signals in the developing brain, are found in a significant number of people suffering from several neurodevelopmental disorders.

A Yale team headed by co-corresponding author Anthony Koleske, professor of molecular biophysics and biochemistry and of neuroscience, and Ph.D. candidate Sara (Katrancha) Sarnoski modeled these genetic mutations in mice to study their impact on the developing brain. Mice lacking even a single copy of the gene tended to be more anxious, showed deficits in motor coordination, and failed to develop social bonds with other mice. Brains of the mice were also small and lacked the normal synaptic and dendritic connections that enable neuronal signaling.

"TRIO mediates changes in the structure of neurons and the trafficking of proteins in response to developmental cues, while reducing TRIO function inhibits the ability of neurons to develop normally," Koleske said.

Researchers also found that drugs that remedy the biochemical abnormalities seen in mice lacking the TRIO gene can help restore normal synapses in these mice.

"We are hoping to use similar drugs to treat the structural and behavioral abnormalities associated with mutations in the TRIO gene and eventually improve the lives of patients," Sarnoski said.

Provided by Yale University