

Scientists reveal two paths to autism in the developing brain

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Two distinct neurodevelopmental abnormalities that arise just weeks after the start of brain development have been associated with the emergence of autism spectrum disorder, according to a new Yale-led

study in which researchers developed brain organoids from the stem cells of boys diagnosed with the disorder.

Researchers say, the specific abnormalities seem to be dictated by the size of the child's [brain](#), a finding that could help doctors and researchers to diagnosis and treat [autism](#) in the future. The findings were published in the journal *Nature Neuroscience*.

"It's amazing that children with the same symptoms end up with two distinct forms of altered [neural networks](#)," said Dr. Flora Vaccarino, the Harris Professor in the Child Study Center at Yale School of Medicine and co-senior author of the paper.

Using stem cells collected from 13 boys diagnosed with autism—including eight boys with macrocephaly, a condition in which the head is enlarged—a Yale team created [brain organoids](#) (small, three-dimensional replicas of the developing brain) in a lab dish that mimic neuronal growth in the fetus. They then compared [brain development](#) of these affected children with their fathers. (Patients were recruited from clinician colleagues at the Yale Child Study Center, which conducts research, service, and training to improve understanding of health issues facing children and their families.)

The study was co-led by Alexandre Jourdon, Feinan Wu, and Jessica Mariani, all from Vaccarino's lab at the Yale School of Medicine.

About 20% of autism cases involve individuals with macrocephaly, a condition in which a child's head size is in the 90th percentile or greater at birth. Among autism cases these tend to be more severe.

Intriguingly, the researchers found that children with autism and macrocephaly exhibited excessive growth of excitatory neurons compared with their fathers while organoids of other children with

autism showed a deficit of the same type of neurons.

The ability to track the growth of specific types of neurons could help doctors diagnose autism, symptoms of which generally appear 18 to 24 months after birth, the authors say.

The findings may also help identify autism cases that might benefit from existing drugs designed to ameliorate symptoms of disorders marked by excessive excitatory neuron activity, such as epilepsy, Vaccarino said. Autism patients with macrocephaly might benefit from such drugs while those without enlarged brains may not, she said.

Creating biobanks of patient-derived [stem cells](#) could be essential to tailor therapeutics to specific individuals, or personalized medicine.

Abyzov Alexej, an associate professor of biomedical informatics at the Mayo Clinic, is co-senior author of the paper.

Provided by Yale University

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