

# Brain scans spot early signs of autism in high-risk babies

Experts say replication is needed and other hurdles must be surmounted to apply findings to the clinic.

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Researchers have no way to tell whether young babies may later be diagnosed with autism. But brain scans could help, a small study suggests.

By scanning the brains of babies whose siblings have autism, researchers say they have been able to make reasonably accurate forecasts about which of these high-risk infants will later develop autism themselves. The findings raise the prospect of diagnosing autism spectrum disorder (ASD) months before children develop symptoms, a goal that has proved elusive. *Nature* looks at the new study and its implications.

## Why has it been so tough to diagnose autism in infants?

Children typically show symptoms of ASD, such as difficulty making eye contact, after the age of 2. Researchers believe that the brain changes underlying ASD begin much earlier — possibly even in the womb. But behavioural assessments haven't been helpful in predicting who will get autism, says Joseph Piven, a psychiatrist at the University of North Carolina (UNC) in Chapel Hill, who co-led the study, published online in *Nature*<sup>1</sup>.

"Children who end up with autism at 2 or 3, they don't look like they have autism in the first year," he says.

## Are there genetic signatures or biomarkers that could help predict an autism diagnosis?

Certain rare mutations are linked to ASD, but the vast majority of cases cannot be pinned to a single or even a handful of genetic risk factors. Beginning in the 1990s, Piven and other researchers noticed that children with autism tended to have larger brains than developmentally normal children, suggesting that brain growth could be a biomarker for ASD. But Piven and colleague Heather Cody Hazlett, a psychologist at UNC-Chapel Hill, say it had not been clear when overgrowth occurred.

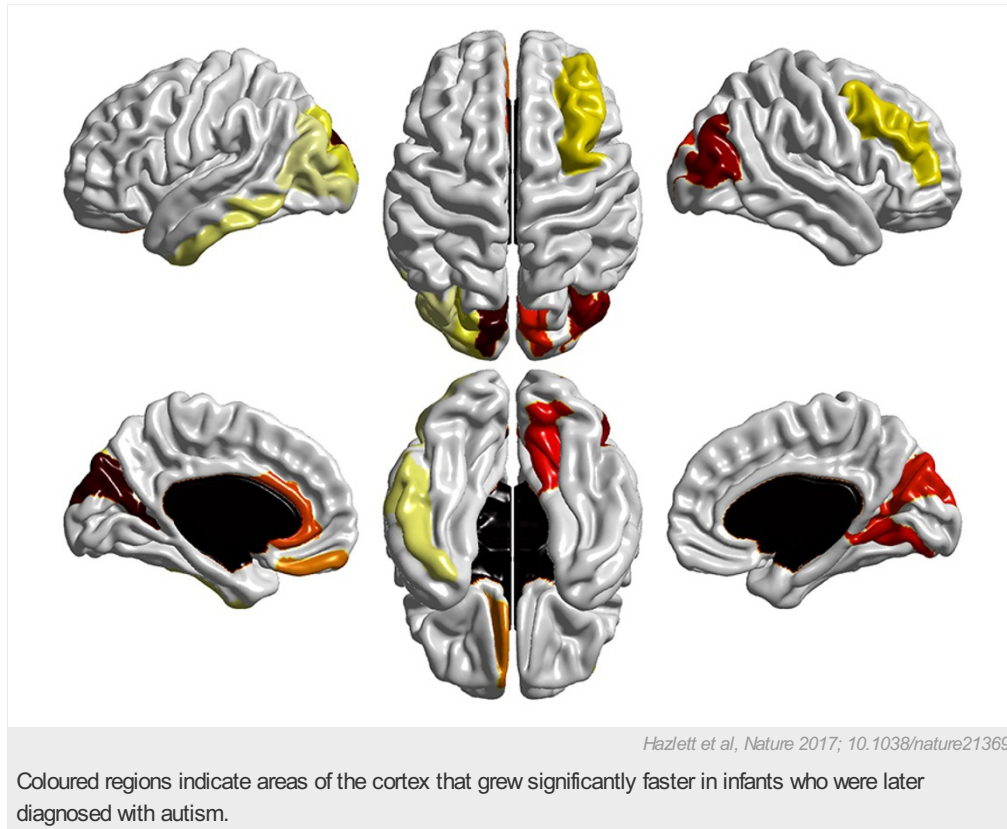
## What did their latest study look at?

Autism occurs in roughly 1 in 100 children in the general population, but infants with an older sibling with a diagnosis have about a 1 in 5 chance of developing ASD. As part of the US National Institutes of Health (NIH)-funded Infant Brain Imaging Study (IBIS), Piven and Hazlett's team scanned the brains of 106 of these 'high-risk' infants at age 6, 12 and 24 months using magnetic resonance imaging (MRI), to see if they could catch the brain overgrowth in the act. They also followed 42 low-risk infants.

### What did they find?

Fifteen of the high-risk infants were diagnosed with autism at 24 months. MRI scans revealed that the volume of these infants' brains grew faster between 12 and 24 months, compared with children who were not diagnosed with ASD, and that this accelerated growth occurred at the same time that behavioural signs of autism appeared.

The researchers also found brain changes between 6 and 12 months, before ASD symptoms appeared. The cortical surface area — a measure of the size of folds on the outside of the brain — grew faster in infants later diagnosed with autism, compared with those who did not receive a diagnosis.



### Could these brain changes be used to predict autism diagnosis in infants?

Hazlett and Piven's team then used a deep-learning neural network, a form of machine learning, to ask if MRI scans at 6 and 12 months in a larger set of high-risk infants could predict an autism diagnosis at age 2. The algorithm correctly predicted 30 out of the 37 autism diagnoses (81%), while producing false-positives in 4 out of the 142 infants who were not later diagnosed.

"We now have this finding in these high familial risk infants that we can predict 8 out of 10 that we think will get autism," says Piven, adding that behaviour-based predictions do no better than 50–50 at that age. "This has tremendous clinical implications."

### What will it take for these results to be used in the clinic?

A lot more research, agree Piven's team and other experts. In the first instance, the results need to be confirmed with a larger follow-up study of high-risk infants: Piven's team has applied for NIH funding for such a study. They are also looking at whether other brain-imaging techniques can detect the early brain changes.

"It's an excellent piece of science, but ultimately it's based on a few hundred individuals," says Armin Raznahan, a clinician-scientist at the National Institute of Mental Health in Bethesda, Maryland. "The key thing is going to be replicating this."

Even if the findings are robust, clinical applications could prove limited. Cynthia Schumann, an expert on autism brain imaging at the University of California, Davis, notes that the findings apply only to high-risk infants, and not to the general population. A large follow-up study would be needed to test whether autism can be predicted in the general population, she says.

Differences between MRI scanners and methods for extracting data could also swamp the subtle anatomical changes detected in the study, adds Raznahan. Widespread application would also depend on having a 'growth-chart for the brain' that is broadly applicable

across the general population — a huge challenge, he notes.

### **If autism could be predicted in infants, could doctors do anything about it?**

There is no evidence that the risk of developing autism can be reduced in infants, says Raznahan, and the immediate application of early diagnosis would be to inform families. Having a reliable tool for early diagnosis could help researchers to test interventions, because it would help them to determine whether a treatment is working or not, adds Piven.

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### **References**

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1. Hazlett, H. C. *et al.* *Nature* <http://dx.doi.org/10.1038/nature21369> (2017).