

# Bacterium can reverse autism-like behaviour in mice

Findings support idea that gut microbiome has a role in disorder.

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Mice displaying symptoms of autism are less social and more anxious than control animals.

Doses of a human gut microbe helped to reverse behavioural problems in mice with autism-like symptoms, researchers report today in *Cell*<sup>1</sup>. The treatment also reduced gastrointestinal problems in the animals that were similar to those that often accompany autism in humans.

The work builds on previous research by Paul Patterson, a neurobiologist at the California Institute of Technology (Caltech) in Pasadena. In 2012, he and his team created mice with autism-like symptoms by injecting a chemical that mimics viral infection into pregnant mice; those animals then bore offspring that were less sociable and more anxious than wild-type animals<sup>2</sup>. The autistic mice also had 'leaky guts', in which the walls of the intestine break down and allow substances to leak through. Several studies have found that humans with autism are also more likely to have gastrointestinal disorders, suggesting that the two problems may be linked<sup>3</sup>.

To investigate what role the gut might play in the animals' symptoms, Patterson and his Caltech colleagues — microbiologist Sarkis Mazmanian and neuroscientist Elaine Hsiao — took a census of the bacteria living in the guts of the mice. They found that mice with symptoms of autism had lower levels of a bacterium called *Bacteroides fragilis* that is normally present in the mouse gut. When the researchers fed *B. fragilis* to these mice, the animals began behaving more normally and their gastrointestinal symptoms improved.

## Chemical imbalance

Next, the researchers tried to determine how the bacteria 'talk' to the brain by examining the blood of autistic and wild-type mice for chemicals that indicate how cells are working in the body. They found that the blood of mice with autism symptoms had levels of a chemical called 4-ethylphenylsulphate (4EPS) that were 46 times higher than that of the control group. This substance is structurally similar to a chemical called para-cresol that is elevated in people with autism<sup>4</sup>.

When the researchers injected 4EPS into wild-type mice, they started behaving like the untreated autistic mice — obsessively repeating some behaviours and squeaking differently when greeting other mice. Hsiao says that although it is still unclear whether 4EPS is made by *B. fragilis*, it does seem to be made by gut bacteria.

"It's incredible that putting this one bacteria back can reverse all these widespread changes," says John Cryan, a pharmacologist at

University College Cork in Ireland. Although many anecdotal reports and small studies have suggested that ‘probiotic’ bacteria, such as those found in yoghurt, and antibiotics can help with the symptoms of autism, Cryan says more research needs to be done. Because there are a number of types of autism in humans, it will be important to look at how different symptoms might be affected by different microbes. Another question is whether the microbiomes of the mice — whose symptoms result from maternal infection — differ from those of mice that are genetically predisposed to autism-like symptoms, Cryan adds.

“I think there is now sufficient proof of concept where people can start to look at probiotic bacteria to improve brain function in humans,” says gastroenterologist Stephen Collins of McMaster University in Ontario, Canada. The next step, he says, will be to determine more precisely how different bacteria use the immune, metabolic and nervous systems to influence the brain.

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## References

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