

NEWS

Probiotic curbs autism features in mouse model

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Beneficial bugs: Treatment with *Bacteroides fragilis*, a bacterial species found in the human gut, improves some behaviors in mice whose mothers were exposed to an infection during pregnancy.

Treatment with a single bacterial species curbs anxiety and **repetitive behaviors** and boosts vocalizations in a mouse model of autism, according to a poster presented Monday at the **2012 Society for Neuroscience annual meeting** in New Orleans.

These mice were born to mothers exposed to an infection during their pregnancy. This *in utero* exposure alters the offspring's immune system and leads to behaviors reminiscent of autism.

The so-called probiotic treatment does not improve the animals' social behaviors. Still, the study fuels the **long-standing hypothesis** that the immune system affects the brain and contributes to some aspects of autism, the researchers say.

The study provides proof of principle that changes to even one of the slew of bacterial species in the gut can affect behavior, says **Paul Patterson**, professor of biological sciences at the California Institute of Technology. "Now, how does that work? Where it is acting? We don't know."

Many children with autism are picky eaters and have **gastrointestinal troubles** such as stomach pain and constipation. Some researchers have reported that individuals with the disorder have **an atypical composition of gut microbiota** — the vast ecosystem of bacteria that live in the human gastrointestinal tract¹.

The link is far from understood, however. For instance, some studies of people with autism suggest that antibiotic treatments **worsen symptoms**, whereas others find they **provide relief**.

Patterson's team studies the '**maternal infection**' model of autism. Injecting pregnant mice with a mock flu virus triggers an immune response that affects the brains and behaviors of their offspring. The offspring show anxiety, **few social interactions**, abnormal vocalizations and repetitive burying of marbles.

In August, Patterson's team reported that **a bone marrow transplant can reverse** some of these symptoms, implicating an **immune system gone awry**.

In the new work, the researchers report that the offspring show a host of abnormalities in the gut. They have unusually permeable intestinal membranes, for instance, which may allow metabolites of gut bacteria to leak into the bloodstream.

One such metabolite, 4-ethylphenylsulfate, shows a 40-fold increase in the blood of offspring born to infected mice compared with controls. When the researchers injected this small molecule into healthy mice, it induced anxious behavior and an abnormal startle response. These dramatic changes in blood could serve as **biomarkers for autism**, Patterson says.

Most provocatively, feeding young mice *Bacteroides fragilis*, a bacterial species that's common in the healthy human gut, makes the intestinal barriers less permeable and normalizes levels of 4-ethylphenylsulfate in the blood. "[It] completely blocks leaky gut," Patterson says. The treated mice also show less anxiety and marble-burying, and vocalize more.

In preliminary experiments, the researchers have given similar probiotic treatments to three other mouse models of autism: the **BTBR inbred strain**, the **valproic acid model** and mice **lacking the CNTNAP2 gene**. They saw "some promise" in all three models but not effects as dramatic as those in the maternal infection model, notes Elaine Hsiao, a graduate student in Patterson's lab who presented the work.

The findings raise the intriguing possibility that children with autism who have stomach troubles could benefit from **probiotic treatment**. These treatments are appealing because they have no harmful side effects and would be easy to take. In the mouse experiments, Patterson notes, the researchers simply mixed the bugs into applesauce.

The trouble is that, for now, scientists know little about the more than 1,000 bacterial species that can populate the healthy human gut — nor how similar the ecosystem is in mice and people. "We don't know which changes in the microbiota are the most important," Patterson says.

For more reports from the 2012 Society for Neuroscience annual meeting, please [click here](#).

References:

1: Williams B.L. *et al. PLoS One* **6**, e24585 (2011) [PubMed](#)