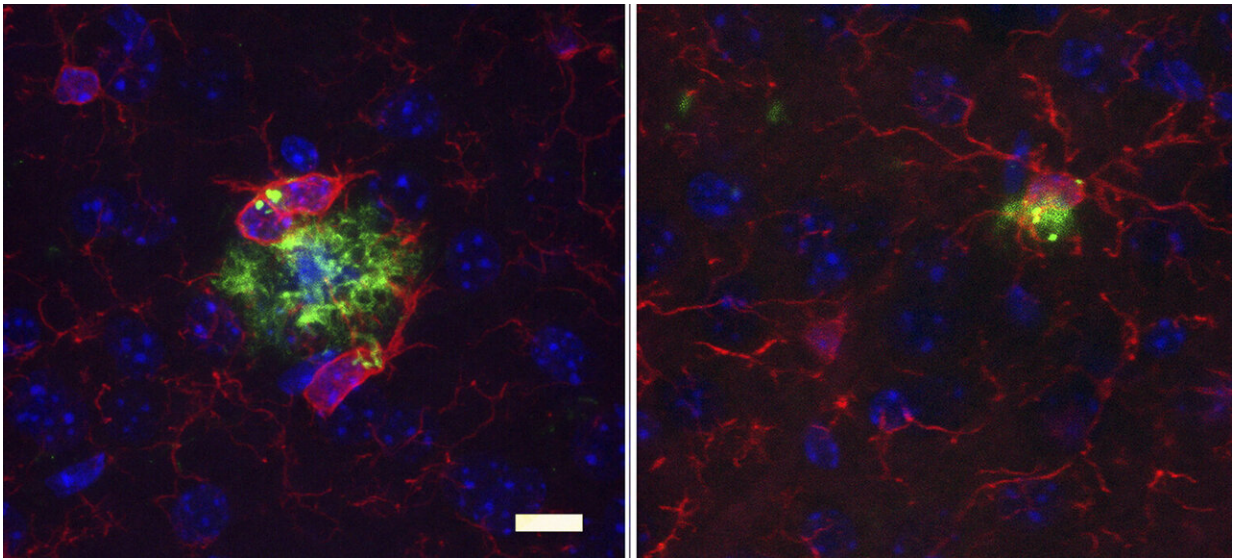


Antibiotic treatment alleviates Alzheimer's disease symptoms in male mice, study reveals

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Compared with a control (left), long-term antibiotic treatment (right) reduces the size of amyloid plaques (green) and alters the appearance of microglia (red) in the brains of male APPS1-21 mice. Credit: Dodiya *et al.*, 2019

Researchers at The University of Chicago have demonstrated that the type of bacteria living in the gut can influence the development of Alzheimer's disease symptoms in mice. The study, which will be published May 16 in the *Journal of Experimental Medicine*, shows that, by altering the gut microbiome, long-term antibiotic treatment reduces inflammation and slows the growth of amyloid plaques in the brains of

male mice, though the same treatment has no effect on female animals.

The community of bacteria that live in the gastrointestinal tract—the [gut microbiome](#)—is generally harmless, but, because they affect the activity of the body's [immune system](#), these bacteria can influence a wide range of diseases, even in distant tissues such as the brain.

"Recent evidence suggests that intestinal bacteria could play a major role in various neurological conditions including [autism spectrum disorders](#), multiple sclerosis, Parkinson's disease, and Alzheimer's disease," explains Professor Sangram S. Sisodia, director of the Center for Molecular Neurobiology at The University of Chicago.

Alzheimer's disease is characterized by the formation of amyloid plaques and the activation of immune cells present in the brain known as microglia. These cells can help remove amyloid plaques, but their activation may also exacerbate the disease by causing neuroinflammation.

Alzheimer's patients exhibit changes in their gut [microbiome](#), and Sisodia and colleagues have previously reported that gut bacteria may influence the development of these symptoms in rodents. Long-term antibiotic treatment limited the formation of amyloid plaques and reduced microglia activation in male, but not female, mice expressing mutant proteins associated with familial Alzheimer's disease. "While compelling, our published studies on the role of the gut microbiome on amyloid [plaque](#) formation were limited to a single strain of mice," Sisodia says.

In the new study, Sisodia and colleagues therefore examined the effects of antibiotics on a different mouse model of Alzheimer's disease known as APPS1-21. Long-term treatment with a cocktail of antibiotics again reduced the formation of [amyloid plaques](#) in male mice but had no

effect on females. Antibiotic treatment also appeared to alter the activation of microglia in male mice, changing them from a form that is thought to promote neurodegeneration to a form that helps to maintain a healthy brain.

To prove that these improvements in Alzheimer's symptoms were caused by alterations in the gut microbiome, the researchers transplanted fecal matter from untreated mice into antibiotic-treated animals. This procedure restored the gut microbiome and caused an increase in amyloid plaque formation and microglial activation.

But why do alterations in the gut microbiome only affect male mice? Sisodia and colleagues discovered that long-term antibiotic treatment changed the gut bacteria of male and female mice in different ways. The changes in the microbiome of female [mice](#) caused their immune systems to increase production of several proinflammatory factors that could influence the activation of microglia.

"Our study shows that antibiotic-mediated perturbations of the gut microbiome have selective, sex-specific influences on amyloid plaque formation and microglial activity in the brain," Sisodia says. "We now want to investigate whether these outcomes can be attributed to changes in any particular type of bacteria."

More information: Dodiya et al., 2019. *J. Exp. Med.* [DOI: 10.1084/jem.20182386](https://doi.org/10.1084/jem.20182386)

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