

Changes in Human Microbiome Precede Alzheimer's Cognitive Declines

People with preclinical Alzheimer's disease had markedly different assemblages of gut bacteria.

July 3, 2023 By Lawrence Tabak and National Institutes of Health

In people with Alzheimer's disease, the underlying changes in the brain associated with dementia typically begin many years—or even decades—before a diagnosis. While pinpointing [the exact causes](#) of Alzheimer's remains a major research challenge, they likely involve a combination of genetic, environmental, and lifestyle factors. Now [an NIH-funded study](#) elucidates the role of another likely culprit that you may not have considered: the human gut [microbiome](#), the trillions of diverse bacteria and other microbes that live primarily in our intestines.

[Earlier studies](#) had showed that the gut microbiomes of people with symptomatic Alzheimer's disease differ from those of healthy people with normal cognition. What this new work advances is that these differences arise early on in people who will develop Alzheimer's, even before any obvious symptoms appear.

The science still has a ways to go before we'll know if specific dietary changes can alter the gut microbiome and modify its influence on the brain in the right ways. But what's exciting about this finding is it raises the possibility that doctors one day could test a patient's stool sample to determine if what's present from their gut microbiome correlates with greater early risk for Alzheimer's dementia. Such a test would help doctors detect Alzheimer's earlier and intervene sooner to slow or ideally even halt its advance.

The new findings, reported in the journal [Science Translational Medicine](#), come from a research team led by Gautam Dantas and Beau Ances, Washington University School of Medicine, St. Louis. Ances is a clinician who treats and studies people with Alzheimer's; Dantas is a basic researcher and expert on the gut microbiome.

The pair struck up a conversation one day about the possible connection between the gut microbiome and Alzheimer's. While they knew about the earlier studies suggesting a link, they were surprised that nobody had looked at the gut microbiomes of people in the earliest, so-called preclinical, stages of the disease. That's when dementia isn't detectable, but the brain has formed amyloid-beta plaques, which are associated with Alzheimer's.

To take a look, they enrolled 164 healthy volunteers, age 68 to 94, who performed normally on

standard tests of cognition. They also collected stool samples from each volunteer and thoroughly analyzed them all the microbes from their gut microbiome. Study participants also kept food diaries and underwent extensive testing, including two types of brain scans, to look for signs of amyloid-beta plaques and [tau protein accumulation](#) that precede the onset of Alzheimer's symptoms.

Among the volunteers, about a third (49 individuals) unfortunately had signs of early Alzheimer's disease. And, as it turned out, their microbiomes showed differences, too.

The researchers found that those with preclinical Alzheimer's disease had markedly different assemblages of gut bacteria. Their microbiomes differed in many of the bacterial species present. Those species-level differences also point to differences in the way their microbiomes would be expected to function at a metabolic level. These microbiome changes were observed even though the individuals didn't seem to have any apparent differences in their diets.

The team also found that the microbiome changes correlated with amyloid-beta and tau levels in the brain. But they did not find any relationship to degenerative changes in the brain, which tend to happen later in people with Alzheimer's.

The team is now conducting a five-year study that will follow volunteers to get a better handle on whether the differences observed in the gut microbiome are a cause or a consequence of the brain changes seen in Alzheimer's. If it's a cause, this discovery would raise the tantalizing possibility that specially formulated probiotics or [fecal transplants](#) that promote the growth of "good" bacteria over "bad" bacteria in the gut might slow the development of Alzheimer's and its most devastating symptoms. It's an exciting area of research and definitely one worth following in the years ahead.

This [blog post](#) was published by the National Institutes of Health on June 27, 2023.