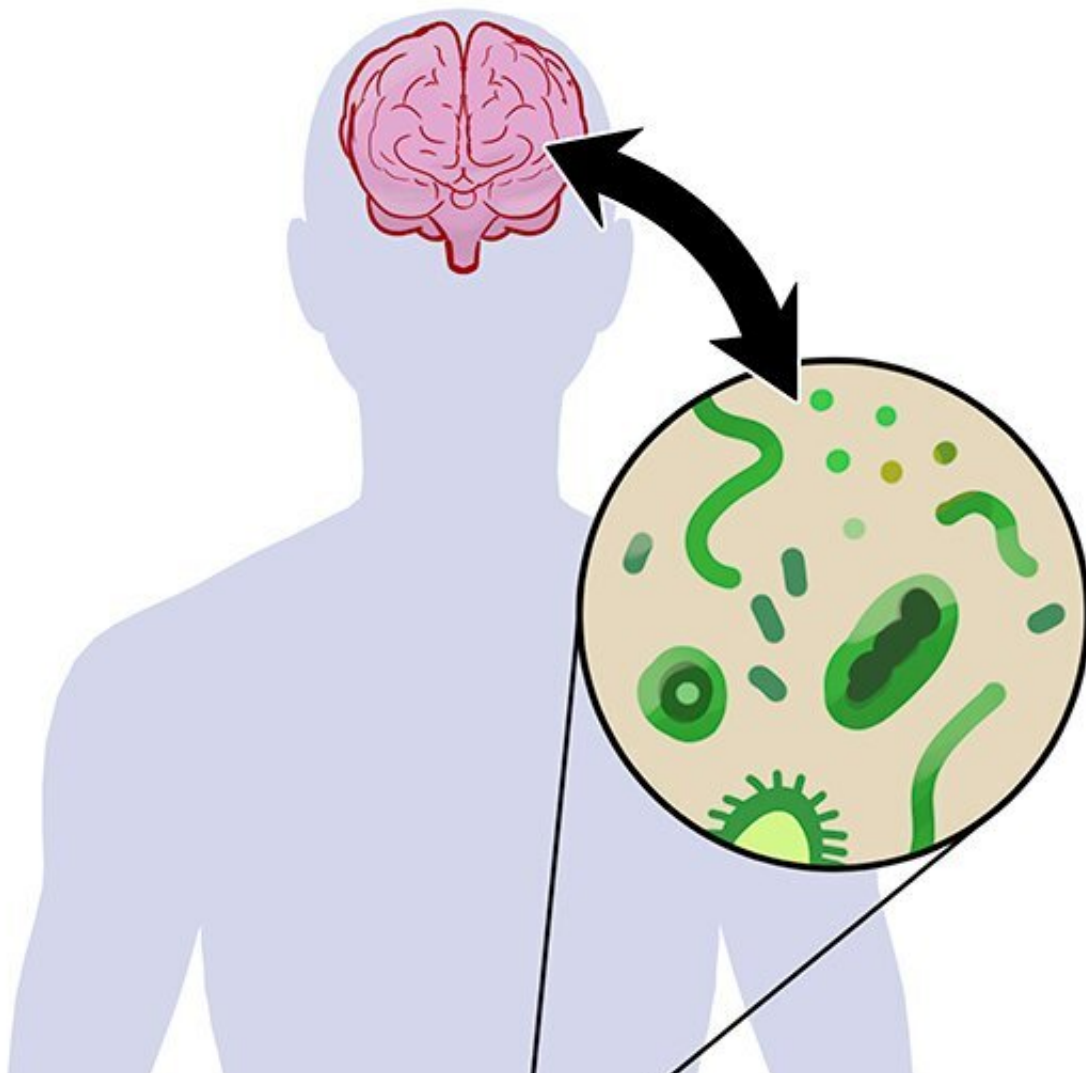


New study puts gut microbiome at the center of Parkinson's disease pathogenesis

December 1 2022, by Bob Shepard



The study, utilizing the relatively new field of metagenomics, demonstrated an imbalance in the gut microbiome of patients with Parkinson's disease. Credit: University of Alabama at Birmingham

New research from the University of Alabama at Birmingham says the gut microbiome is involved in multiple pathways in the pathogenesis of Parkinson's disease. The findings, published in *Nature Communications*, show a wide imbalance in microbiome composition in persons with Parkinson's disease. The study is the largest microbiome study conducted at the highest resolution.

The investigators employed metagenomics, the study of genetic material recovered directly from the stool microbiome of persons with PD and neurologically healthy control subjects.

"The primary aim of this study was to generate a full, unaltered view of the imbalance in PD [gut microbiome](#)," said Haydeh Payami, Ph.D., professor in the Marnix E. Heersink School of Medicine Department of Neurology and senior author on the study.

The study reports Parkinson's disease metagenome is indicative of a disease-promoting microbiome.

"We found evidence for multiple mechanisms that we know are linked to PD, but we didn't know they were happening in the gut also and are orchestrated by the microbiome," Payami said.

Investigators found an overabundance of opportunistic pathogens and immunogenic components, which suggest infection and inflammation at play, overproduction of toxic molecules, and overabundance of the bacterial product curli. This induces PD pathology and dysregulation of neurotransmitters, including L-dopa. At the same time, there was a shortage of neuroprotective molecules and anti-inflammatory components, which makes recovery difficult.

Payami, who is the John T. and Juanelle D. Strain Endowed Chair in Neurology, and her team enrolled 490 persons with Parkinson's disease and 234 healthy controls. Just over half of the subjects were male and were predominately older than 50. All were from the Deep South region of the United States, which helped to eliminate confounding by geographic and cultural influence on composition of microbiome.

The researchers studied 257 species of organisms in the microbiome, and of these, analysis indicated 84, more than 30%, were associated with Parkinson's disease.

"Of the 84 PD-associated species, 55 had abnormally high abundance in persons with PD, and 29 were depleted," Payami said. "We found that over 30% of the micro-organisms and bacterial genes and pathways tested have altered abundances in Parkinson's disease, which indicates a widespread imbalance."

At one end of the spectrum, *Bifidobacterium dentium* was elevated by sevenfold, *Actinomyces oris* by 6.5-fold and *Streptococcus mutans* by sixfold. At the other end of the spectrum, *Roseburia intestinalis* was reduced by 7.5-fold and *Blautia wexlerae* by fivefold. Overall, 36% of PD-associated species had higher than twofold change in abundance, reflecting a 100% to 750% increase or decrease in PD versus the healthy control group.

"This study created a large dataset at the highest resolution currently feasible and made it public with no restriction to promote open science," Payami said. "It includes extensive metadata on 490 persons with PD, the largest PD cohort with microbiome data, and a unique cohort of 234 neurologically healthy elderly, which can be used in a wide range of studies. We have shown that there is a widespread imbalance in the Parkinson's metagenome, creating an environment that is permissive for neurodegenerative events and is prohibitive of recovery."

Parkinson's disease is a progressively debilitating disorder that affected 4 million individuals in the year 2005 and is projected to double to 8.7 million individuals by the year 2030. Although historically defined as a movement disorder, PD is a multi-systemic disease. It is speculated that PD is caused by various combinations of genetic susceptibility and environmental triggers, although no causative combination has yet been identified. The connection between PD and the gastrointestinal system has long been established.

"This is exciting research, as metagenomics is a new, albeit fast-evolving field, and the resources, methods and tools, while state-of-the-art, are still in development," Payami said.

"Undoubtedly more information will be revealed as we increase the sample size and others also conduct metagenomics studies and share the data. We anticipate that in the near future we will have the tools and the analytic power to use [metagenomics](#) as a new approach to study PD heterogeneity, search for biomarkers, delve deeper into the origin and progression of PD sub-phenotypes, and investigate the potential in manipulating the microbiome to prevent, treat and halt the progression of PD."

More information: Zachary D. Wallen et al, Metagenomics of Parkinson's disease implicates the gut microbiome in multiple disease mechanisms, *Nature Communications* (2022). [DOI: 10.1038/s41467-022-34667-x](https://doi.org/10.1038/s41467-022-34667-x)

Provided by University of Alabama at Birmingham

Citation: New study puts gut microbiome at the center of Parkinson's disease pathogenesis (2022, December 1) retrieved 26 April 2024 from <https://medicalxpress.com/news/2022-12-gut->

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