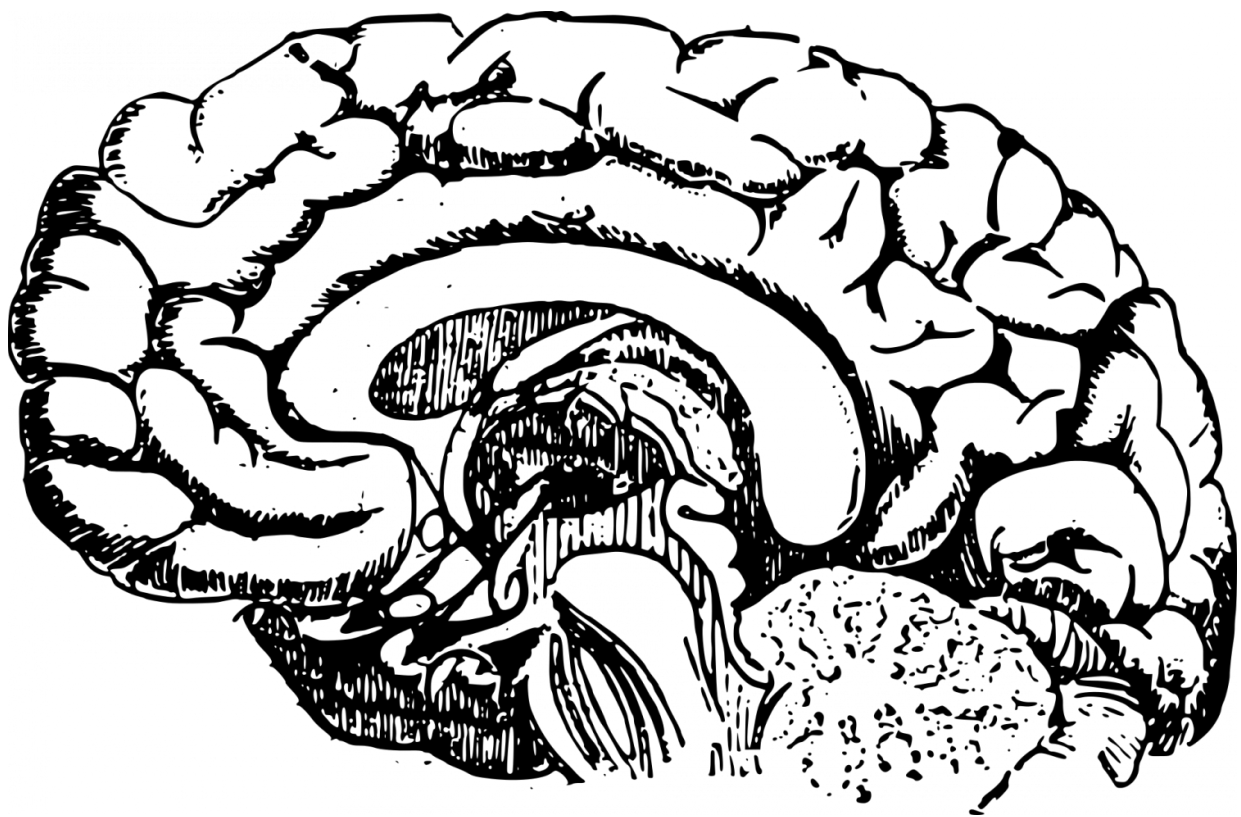


Research finds sex differences in immune response and metabolism drive Alzheimer's disease

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Cleveland Clinic researchers analyzed genes and brain tissue of patients with Alzheimer's and found that differences in brain

immunometabolism—the interactions between the immune system and the ways cells create energy—may contribute to women's increased risk for the disease and its severity.

The findings, published in *Alzheimer's and Dementia*, offer important insight into developing sex-specific treatment and prevention options for Alzheimer's disease, the sixth-leading cause of death in the United States.

"Our immune systems depend on communication between different cell types in our bodies, which are fueled by energy created from unique metabolic processes," said Justin Lathia, Ph.D., vice chair of the Department of Cardiovascular and Metabolic Sciences and co-author on the paper. "As sex influences both the [immune system](#) and metabolic process, our study aimed to identify how all of these individual factors influence one another to contribute to Alzheimer's disease."

A collaboration between researchers at the Lerner Research Institute and physicians at the Lou Ruvo Center for Brain Health in Ohio and Nevada, the team analyzed brain samples and publicly available sequencing data obtained from 469 Alzheimer's patients.

They looked for changes in gene expression between males and females in immune function, cellular metabolism, and communication between brain cells. They found sex-specific differences in all three areas, with the notable difference in microglia—immune cells in the brain. Changes in microglia were greater in the brains of female patients compared to males.

"Women are more likely to develop Alzheimer's disease and experience faster cognitive decline compared to their male counterparts. These sex differences should be accounted for when designing medications and conducting [clinical trials](#)," said Feixiong Cheng, Ph.D., Associate Staff,

Genomic Medicine Institute and lead author of the paper. "These findings build on our knowledge of each part of the systems that play into Alzheimer's and are critical to determining appropriate treatments."

This study is part of an ongoing effort between Cleveland Clinic and the Women's Alzheimer's Movement (WAM) to further understand the link between sex and all neurodegenerative conditions.

"At its core, Alzheimer's disease is a woman's health issue. To address it, we must understand how biological sex contributes to the underpinnings of this disease," said Jessica Caldwell, Ph.D., director of the WAM Prevention Center at Cleveland Clinic and another co-author of the paper. "These findings confirm that we need to look at sex differences in the way the body and brain systems communicate to be able to truly offer women personalized care, and we look forward to continuing this research."

More information: Jessica Caldwell et al, Microglial immunometabolism endophenotypes contribute to sex difference in Alzheimer's disease, *Alzheimer's & Dementia* (2023). [DOI: 10.1002/alz.13546](https://doi.org/10.1002/alz.13546)

Provided by Cleveland Clinic

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