# A complex link between body mass index and Alzheimer's

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Though obesity in midlife is linked to an increased risk for Alzheimer's disease, new research suggests that a high body mass index later in life doesn't necessarily translate to greater chances of developing the brain

disease.

In the study, researchers compared data from two groups of people who had been diagnosed with mild cognitive impairment—half whose disease progressed to Alzheimer's in 24 months and half whose condition did not worsen.

The researchers zeroed in on two [risk factors](link): body mass index (BMI) and a cluster of genetic variants associated with higher risk for Alzheimer's disease.

Their analysis showed that a higher genetic risk combined with a lower BMI was associated with a higher likelihood for progression to Alzheimer's, and that the association was strongest in men.

The finding does not suggest people should consider gaining weight in their later years as a preventive effort—instead, researchers speculate that lower BMI in these patients was likely a consequence of neurodegeneration, the progressive damage to the brain that is a hallmark of Alzheimer's. Brain regions affected by Alzheimer's are also involved in controlling eating behaviors and weight regulation.

"We don't want people to think they can eat everything they want because of this lower BMI association," said senior study author Jasmeet Hayes, assistant professor of psychology at The Ohio State University.

"We know that maintaining a healthy weight and having a healthy diet are extremely important to keeping inflammation and oxidative stress down—that's a risk factor that is modifiable, and it's something you can do to help improve your life and prevent neurodegenerative processes as much as possible," she said. "If you start to notice rapid weight loss in an older individual, that could actually be a reflection of a potential neurodegenerative disease process."

The study was published online recently in the *Journals of Gerontology: Series A*.

Previous research has found a link between obesity and negative cognitive outcomes, but in older adults closer to the age at which Alzheimer's disease is diagnosed, the results have been mixed, Hayes said. And though a variant to the gene known as APOE4 is the strongest single genetic risk factor for Alzheimer's, it explains only about 10 to 15% of overall risk, she said.

Hayes has focused her research program on looking at multiple risk factors at the same time to see how they might interact to influence risk—and to identify health behaviors that may help reduce the risk.

"We're trying to add more and more factors. That is my goal, to one day build a more precise and better model of the different combinations of risk factors," said Hayes, also an investigator in Ohio State's Chronic Brain Injury Initiative. "Genetic risk is important, but it really explains only a small part of Alzheimer's disease, so we're really interested in looking at other factors that we can control."

For this study, the research team obtained data from the Alzheimer's Disease Neuroimaging Initiative, compiling a sample of 104 people for whom BMI and polygenic risk scores were available. Fifty-two individuals whose mild cognitive impairment (MCI) had progressed to Alzheimer's in 24 months were matched against demographically similar people whose MCI diagnosis did not change over two years. Their average age was 73.

Statistical analysis showed that individuals with mild cognitive impairment who had both a lower BMI and higher genetic risk for Alzheimer's were more likely to progress to Alzheimer's disease within 24 months compared to people with a higher BMI.

"We think there's interaction between the genetics and lower BMI, and having both of these risk factors causes more degeneration in certain brain regions to increase the likelihood of developing Alzheimer's disease," said Jena Moody, a graduate student in psychology at Ohio State and first author of the paper.

The effect of the BMI-genetic risk interaction was significant even after taking into account the presence of beta-amyloid and tau proteins in the patients' cerebrospinal fluid—the core biomarkers of Alzheimer's [disease](#).

The relationship between low BMI and high genetic risk and progression to Alzheimer's was stronger in males than in females, but a larger sample size and additional biological data would be needed to expand on that finding, the researchers said.

Because brain changes can begin long before cognitive symptoms surface, a better understanding of the multiple risk factors for Alzheimer's could open the door to better prevention options, Moody said.

"If you can identify people at higher risk before symptoms manifest, you could implement interventions and prevention techniques to either slow or prevent that progression from happening altogether," she said.

To date, scientists have suggested preventive steps include maintaining a healthy weight and diet and participating in activities that reduce inflammation and promote neurofunctioning, such as exercise and mentally stimulating activities.

"We're finding again and again how important inflammation is in the process," Hayes said. "Especially in midlife, trying to keep that inflammation down is such an important aspect of maintaining a healthy

lifestyle and preventing accelerated aging."

  **More information:** Jena N Moody et al, Body Mass Index and Polygenic Risk for Alzheimer's Disease Predict Conversion to Alzheimer's Disease, *The Journals of Gerontology: Series A* (2021). DOI: 10.1093/gerona/glab117