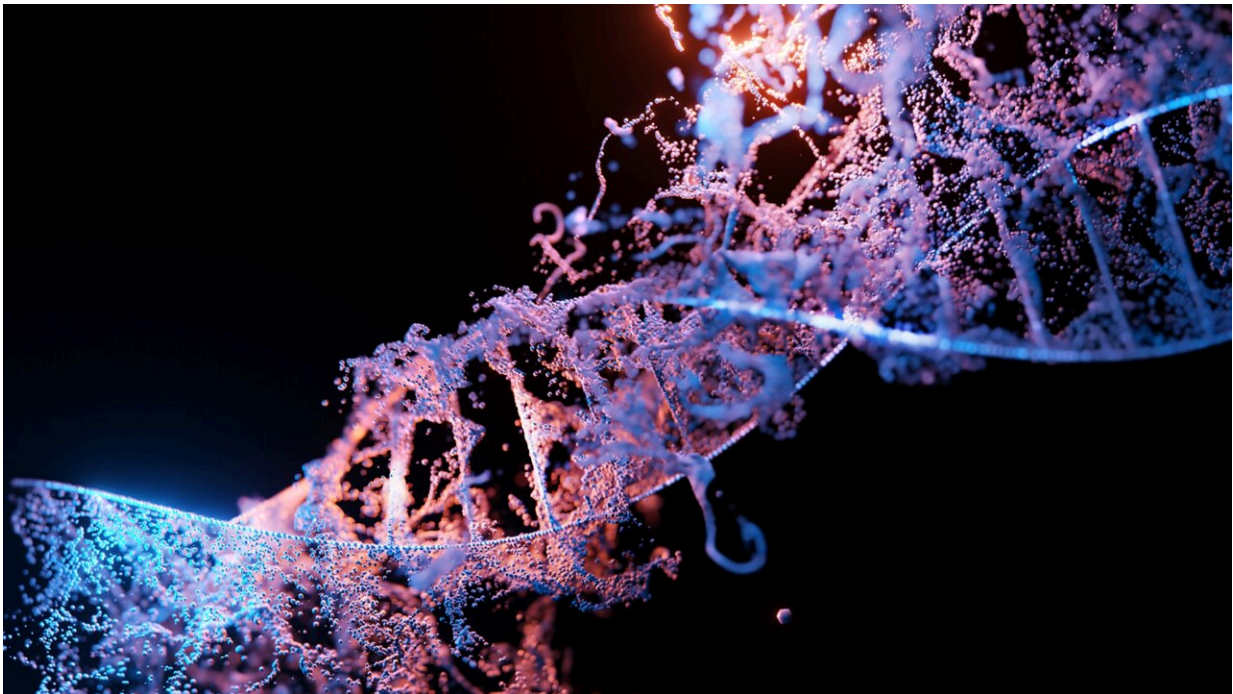


Scientists tie obesity to Alzheimer's-related genes

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In a new study, researchers from The University of Texas Health Science Center at San Antonio (UT Health San Antonio) link obesity with 21 Alzheimer's disease-related genes, providing a potential mechanistic explanation for why Alzheimer's is sometimes more frequent among adults who experienced obesity in midlife.

The findings from 5,619 participants of the Framingham Heart Study were published Feb. 22 in *Alzheimer's & Dementia*. The research team analyzed 74 Alzheimer's-related genes from Framingham data. Of those genes, 21 were either under-expressed or over-expressed in [obesity](#). Gene expression is activation of a gene in a cell to accomplish functions such as making a protein.

Thirteen Alzheimer's-related genes were associated with [body mass index](#) (BMI), the study found. Eight genes were associated with a second metric of obesity called waist-to-hip ratio.

"Several of the genes were more strongly related to obesity in midlife versus in late life, and also to obesity in women versus men," said Claudia Satizabal, Ph.D., of the Glenn Biggs Institute for Alzheimer's and Neurodegenerative Diseases at UT Health San Antonio. Satizabal, assistant professor of population health sciences in UT Health's Joe R. and Teresa Lozano Long School of Medicine, is the study's corresponding author.

Those observations are in line with prior epidemiological studies that suggested midlife obesity may be a factor in Alzheimer's disease risk in women, Satizabal said.

Interestingly, people who develop dementia tend to lose weight about five to 10 years before the onset of the disease. This may be unhealthy weight loss driven by the disease. "We think it is more important to address obesity and begin healthy weight loss in midlife, in one's 40s and 50s, when obesity may be impacting expression of the genes we studied," Satizabal said.

BMI is the classical marker for obesity, but some studies suggest that waist-to-hip ratio, which measures abdominal obesity (belly fat), is a more sensitive marker of metabolic dysregulation in individuals. Obesity

is a component of metabolic syndrome and among the chief risk factors for cardiovascular disease and stroke.

The 21 dementia-related genes associated with obesity in the new analysis are implicated in several Alzheimer's disease processes, including neuro-inflammation, programmed [cell death](#) and deposition of amyloid-beta protein in neurons, said study first author Sokratis Charisis, MD, [resident physician](#) in the Department of Neurology and Biggs Institute at the Long School of Medicine.

Obesity has been linked to Alzheimer's disease in late life. With 85% of U.S. adults projected to be overweight or obese by 2030, and with dementia estimated to impact 131 million people by 2050, understanding the connection between brain health and body weight is crucial.

The Framingham Heart Study is conducted in a mostly white population. "We think the associations between Alzheimer's-related [genes](#) and obesity might be even more relevant in Hispanics, who have a higher prevalence of obesity, but that is yet to be tested," Satizabal said. "We need to increase the sampling of diverse populations to find more [genetic markers](#) related to dementia."

A genetic studies team at the Biggs Institute is working to expand the institute's biobank. "Members of the public can volunteer to provide a [blood sample](#), and we biobank that and of course keep it private," Satizabal said. "We recommend also participating in cognitive testing, having an MRI and completing other questionnaires. This is a study conducted by our South Texas Alzheimer's Disease Research Center (ADRC). We are collecting information and following people over time."

No medication or device interventions are offered; the study is observational only. To inquire about participation, contact Monica Goss,

Ph.D., coordinator of the South Texas ADRC observational study, at 210-450-8073 or gossm@uthscsa.edu, or visit <https://biggsinstitute.org/clinical-trials/volunteer-sign-up/>.

"A team led by Dr. Satizabal, and including others such as Helen Hazuda, Ph.D., professor in the Long School of Medicine, will soon lead a study similar to the Framingham Heart Study," said Sudha Seshadri, MD, professor of neurology and director of the Glenn Biggs Institute at UT Health San Antonio. "This research project will be called the San Antonio Heart Mind Study and will explore brain and heart functions in persons who were previously enrolled in UT Health San Antonio studies of diabetes, including persons who are normal weight as well as persons who are obese."

Seshadri, a co-author of the newly published *Alzheimer's & Dementia* paper, stated, "I am so grateful for the altruism, the time and the trouble taken by our volunteer research participants in Framingham and in San Antonio. They are truly selfless champions helping us uncover the dark secrets of dementia, understand how lifestyle factors change dementia risk, and find new ways to prevent and treat it."

More information: Sokratis Charisis et al, Obesity impacts the expression of Alzheimer's disease–related genes: The Framingham Heart Study, *Alzheimer's & Dementia* (2023). [DOI: 10.1002/alz.12954](https://doi.org/10.1002/alz.12954)

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