

Weight loss may be early predictor of Alzheimer's disease in those with Down syndrome

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Unintentional weight loss in people with Down syndrome may predict the onset of Alzheimer's disease long before typical cognitive symptoms

like memory loss and dementia are apparent.

As many as [90% of people with Down syndrome experience Alzheimer's symptoms](#) by the time they are 65, but [brain changes](#) associated with the disease appear decades earlier. A study published by University of Wisconsin-Madison researchers recently in the *Journal of Alzheimer's Disease* shows that unintentional [weight](#) loss starting in the mid-to-late 30s coincides with hallmark features of early Alzheimer's disease in people with Down syndrome. The findings indicate that weight loss may be a useful predictor of the disease prior to the onset of the cognitive problems that often trigger diagnosis.

"It could be possible to track weight loss as a way to make an earlier diagnosis of Alzheimer's disease," says Victoria Fleming, doctoral student of human development and family studies and first author of the study. "Measuring weight change is convenient and low-cost to track, in contrast to screening for early disease pathology through blood tests, imaging scans, or cerebrospinal fluid tests."

The high incidence of Alzheimer's disease in Down syndrome is rooted in Down's characteristic triplication of chromosome 21. This chromosome carries one of the genes responsible for regulating the production of amyloid beta, a short chain of amino acids that can accumulate in the brain and interfere with [brain function](#), leading to the cognitive impairments seen in Alzheimer's disease.

For people without Down syndrome, being overweight or obese in midlife adds to the risk of developing Alzheimer's disease. Fleming's original interest was looking at this link in people with Down syndrome. However, the results were surprising.

"We were really intrigued, because when we looked at the data and the time course of when weight was changing, we actually saw a stronger

story of unintentional weight loss being linked to early Alzheimer's disease pathology in the brain," says Sigan Hartley, a UW-Madison professor of human development and [family studies](#) and senior author of the new study.

The study looked at data from 261 adults with Down syndrome, aged 25-65, who were weighed at the outset and again about 18 months later. At both points, they also completed a battery of cognitive tests and underwent a brain scan to measure levels of amyloid beta and tau, proteins associated with Alzheimer's disease.

People with Down syndrome in the study started showing unintentional weight loss in their mid-30s, at the same time that amyloid buildup was forming. Moreover, the people with Down syndrome who lost the most weight were the ones who had the highest buildup of these proteins.

"The finding that unintentional weight loss appears to coincide in time with the accumulation of these proteins could signal that these processes are related or share causal pathways. This is something that we will be exploring next," Hartley says.

The results lead to what Hartley calls the weight paradox.

"In midlife, having a higher BMI may put you at risk for Alzheimer's disease. But Alzheimer's disease pathology may actually be connected to weight loss. So, both, in fact, could be true," Hartley says.

The scientists can only speculate the biological reasons for this relationship between unintentional weight loss and Alzheimer's disease pathology. One hypothesis is that amyloid accumulation causes a shift in brain metabolism and hormone balance that triggers loss of fat and muscle.

Fleming's next studies will focus on how unintentional weight loss happens, and on teasing apart the weight paradox by looking at midlife BMI and the trajectory of unintentional weight loss across multiple timepoints in Down [syndrome](#).

"We don't have many good clinical signs that somebody could be nearing that cusp of cognitive decline in Alzheimer's disease," Hartley says. "Our results are exciting, because they suggest that there may be some non-cognitive signs—including unintentional [weight loss](#)—that could help us predict who might be about to develop dementia earlier or later."

More information: Victoria Fleming et al, Weight Loss and Alzheimer's Disease in Down Syndrome, *Journal of Alzheimer's Disease* (2022). [DOI: 10.3233/JAD-220865](https://doi.org/10.3233/JAD-220865)

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