

Higher levels of protein hormone associated with lower risk of dementia, Alzheimer's disease

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Persons with higher levels of leptin, a protein hormone produced by fat cells and involved in the regulation of appetite, may have an associated reduced incidence of Alzheimer disease and dementia, according to a study in the December 16 issue of *JAMA*.

Previous studies have shown that overweight and [obesity](#) in mid-life are associated with poorer cognitive function in the general population and an increased risk of [dementia](#). There has been evidence that leptin exerts additional functions on the brain outside the hypothalamus (a region of the brain that controls body temperature, hunger, and thirst), according to background information in the article.

Wolfgang Lieb, M.D., of the Framingham Heart Study, Framingham, Mass., and colleagues examined the relationship between measurements of plasma leptin concentrations and incidence of dementia and Alzheimer disease (AD). For this study, plasma leptin concentrations were measured in 785 persons without dementia (average age, 79 years; 62 percent female), who were in the original Framingham study group at the 22nd examination cycle (1990-1994). A subsample of 198 dementia-free survivors underwent volumetric brain magnetic resonance imaging (MRI) between 1999 and 2005, approximately 7.7 years after leptin was measured. Two measures of [brain aging](#) were assessed: total cerebral brain volume and temporal horn (a region of the brain) volume, both of which are markers of early AD pathology and subsequent dementia risk.

The researchers conducted follow-up for new cases of dementia and AD until Dec. 2007. During a median (midpoint) follow-up of 8.3 years, 111 participants developed dementia; 89 of them were diagnosed with AD.

The researchers found that higher leptin levels were associated with a lower incidence of all-cause dementia and AD. The incidence of [dementia](#) decreased gradually across increasing levels of leptin: a person with a baseline leptin level in the lowest quartile group had a 25 percent risk of developing AD after 12 years of follow-up, whereas the corresponding risk for a person in the top quartile group was only 6 percent.

Higher leptin levels were also associated with higher total cerebral brain volume. Lower temporal horn volume was not significantly related to leptin levels.

"These findings are consistent with recent experimental data indicating that leptin improves memory function in animals through direct effects on the hippocampus and strengthens the evidence that leptin is a hormone with a broad set of actions in the central nervous system. Due to the exploratory character of the present analyses, we did not adjust for multiple comparisons and acknowledge that our findings require confirmation in independent samples," the authors write.

"If our findings are confirmed by others, leptin levels in older adults may serve as one of several possible biomarkers for healthy brain aging and, more importantly, may open new pathways for possible preventive and therapeutic intervention. Further exploration of the molecular and cellular basis for the observed association may expand our understanding of the pathophysiology underlying [brain](#) aging and the development of AD."

More information: JAMA. 2009;302[23]:2565-2572.

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