RSNA Press Release

Metabolic Health and Body Composition Linked to Alzheimer's Disease

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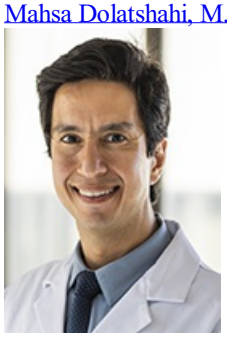
At A Glance

- Higher abdominal fat and less favorable metabolic features (lower good cholesterol and higher insulin resistance) in midlife are associated with higher levels of Alzheimer's-related proteins in the brain.
- Two leaner groups of patients showed different patterns: one had lower amyloid accumulation, while the other had lower tau accumulation.
- Leaner groups also had less brain inflammation.

CHICAGO – Midlife body composition and metabolic health, not simply body mass index (BMI) or weight alone, are associated with differences in Alzheimer's disease (AD)-related brain biomarkers, according to a large new study being presented next week at the annual meeting of the Radiological Society of North America (RSNA). The findings may eventually help doctors identify people who are at risk for AD and could benefit from earlier prevention.

Mahsa Dolatshahi, M.D., M.P.H.



Cyrus A. Raji, M.D., Ph.D.

"Metabolic health and body composition may contain information that BMI alone misses," said study lead author Mahsa Dolatshahi, M.D., M.P.H., research track radiology resident at Mallinckrodt Institute of Radiology (MIR) at Washington University School of Medicine in St. Louis. "Our study results support looking beyond BMI when studying midlife risk of Alzheimer's disease."

The researchers studied 92 cognitively normal adults, ages 40 to 60. MRI measures of abdominal fat, thigh muscle and thigh fat were combined with BMI, insulin resistance and cholesterol measures to identify specific patterns.

Based on the profiles that emerged, study participants were divided into four distinct groups. Group 1 had more fat both around the abdominal organs (visceral fat) and under the skin (subcutaneous fat), along with a less favorable metabolic profile, meaning lower levels of high-density lipoprotein (HDL), or "good" cholesterol, and higher insulin resistance, which increases the risk for diabetes. Group 4 had more thigh muscle, moderately high visceral fat, less subcutaneous fat and a more favorable metabolic profile, meaning higher HDL and lower insulin resistance compared to group 1.

Groups 2 and 3 were both leaner, with less measured fat and muscle and lower BMI. Group 3 had a more favorable metabolic profile, with higher HDL.

PET scans of the brain were used to measure the accumulation of amyloid and tau, two hallmarks of AD. While amyloid plaques can build up outside brain cells many years before symptoms appear, tau tangles form inside brain cells. Tau levels and their distribution in the brain are closely associated with cognitive decline.

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Amyloid levels were lowest, or most favorable, in group 2, one of the lean groups. After accounting for vascular risk factors like small blood vessel disease in the brain, diabetes or hypertension, group 1 had an average amyloid level 6.7 points higher than group 2 on a standard measurement scale. This was the only statistically significant difference in amyloid levels between groups after full adjustment.

Tau levels were lowest in group 3, the lean group with the more favorable metabolic profile. The other groups had average tau levels approximately 5% to 12% higher, with the largest difference observed between groups 3 and 4.

“Lean individuals generally had less buildup of the brain proteins linked to Alzheimer’s compared to those with metabolic issues or higher body fat,” said senior author Cyrus A. Raji, M.D., Ph.D., associate professor of radiology and neurology at MIR and incoming neuroradiology division chief and professor of radiology at Indiana University Health. “However, even among lean people, having a healthy metabolic profile—normal blood sugar and lipid levels—offered a distinct advantage, showing lower levels of tau protein regardless of any underlying blood vessel disease.”

The leaner groups also showed lower levels of brain inflammation, as measured by MRI.

The results do not show that body composition or metabolic health causes AD or that these factors can predict whether individuals will develop it.

“Our findings are an early signal, not proof, that changing one’s metabolic profile may alter the trajectory of amyloid and tau in the brain,” Dr. Dolatshahi said. “Understanding why the two leaner groups differed in their amyloid and tau findings may be more informative than treating weight alone as a complete measure of risk.”

Next steps include confirmation of the findings in larger, diverse study groups and research over time to determine whether these patterns predict subsequent cognitive change. Looking ahead, the researchers emphasized that these insights could help reshape how clinicians and patients approach prevention and early detection.

“Risk stratification of the general population for Alzheimer’s disease as early as midlife can inform potential lifestyle modifications, treatment with weight loss medications or other preventive measures,” Dr. Raji added.

Co-authors are Paul K. Commean, B.A., Mahshid Naghashzadeh, Ph.D., M.Sc., Mobina Amanollahi, M.D., Soheil Mohammadi, M.D., M.P.H., Mona Mirbeyk and Tammie S. Benzinger, M.D., Ph.D.

Note: Copies of RSNA 2026 news releases and electronic images will be available online at *RSNA.org/press26*.

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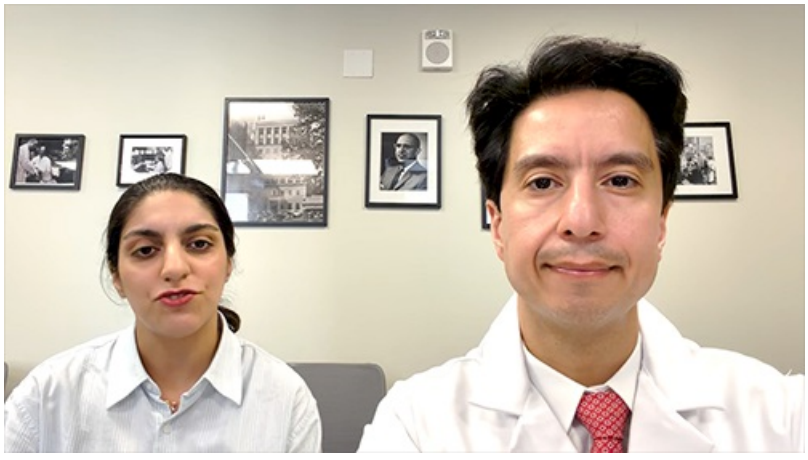
Editor’s note: The data in these releases may differ from those in the published abstract and those actually presented at the meeting, as researchers continue to update their data right up until the meeting. To ensure you are using the most up-to-date information, please call the RSNA Newsroom at 1-312-791-6610.

For patient-friendly information on brain MRI, visit *RadiologyInfo.org*.

Video (MP4):



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Video 1. Mahsa Dolatshahi, M.D., M.P.H., and Cyrus Raji, M.D., Ph.D., discuss their research, which showed that higher abdominal fat and less favorable metabolic features (lower good cholesterol and higher insulin resistance) in midlife are associated with higher levels of Alzheimer's-related proteins in the brain.

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Video 2. Dr. Cyrus Raji reviewing brain MRI images.
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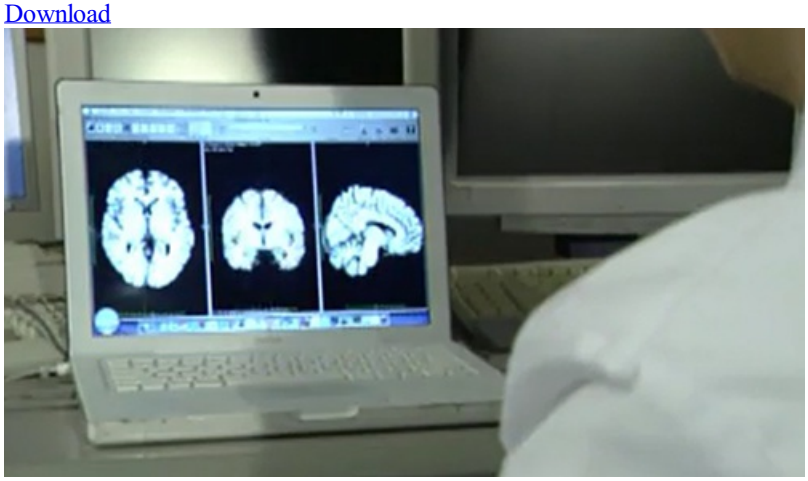

Video 3. Brain MRI

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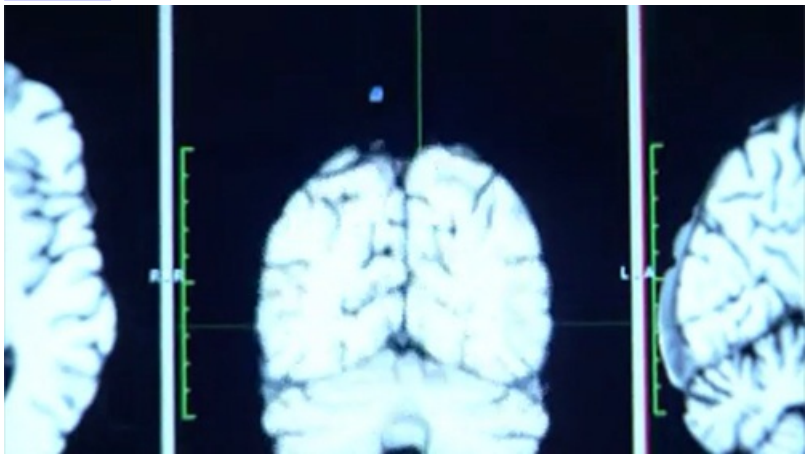

Video 4. Brain MRI

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Images (JPG, TIF):



Infographic

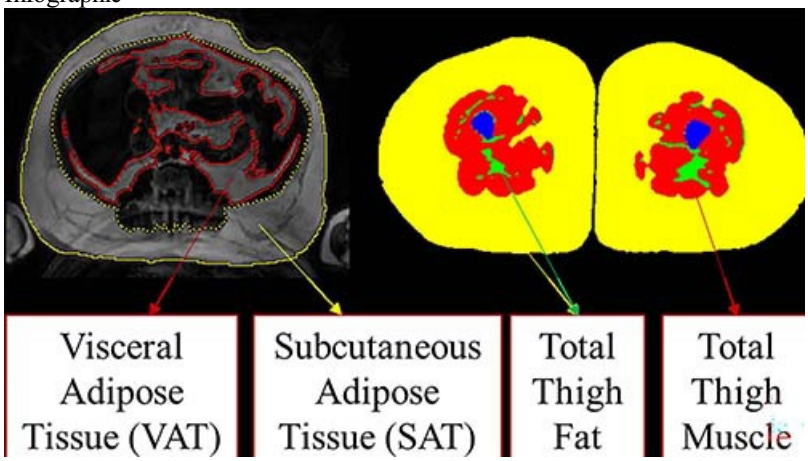

Figure 1. Segmented abdominal and thigh MRI showing visceral adipose tissue, subcutaneous adipose tissue, total thigh fat and total thigh muscle.

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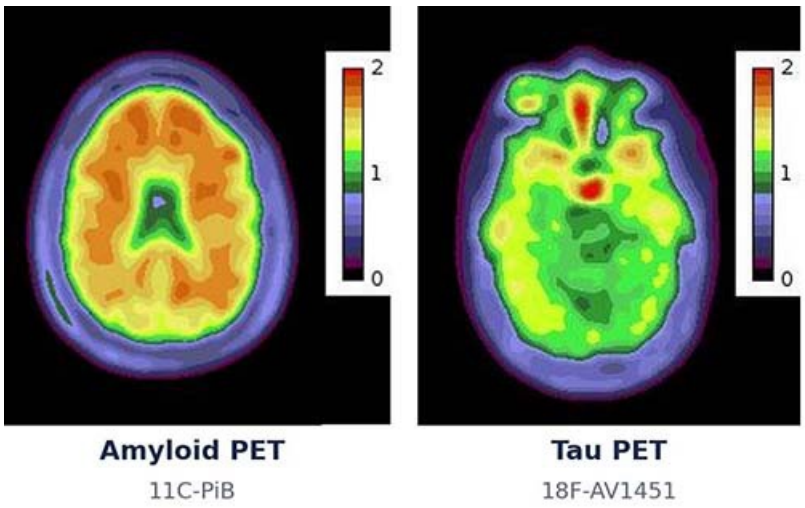

Figure 2. PET measures amyloid and tau. Example PET scans. Warmer colors = more tracer uptake (more proteins).

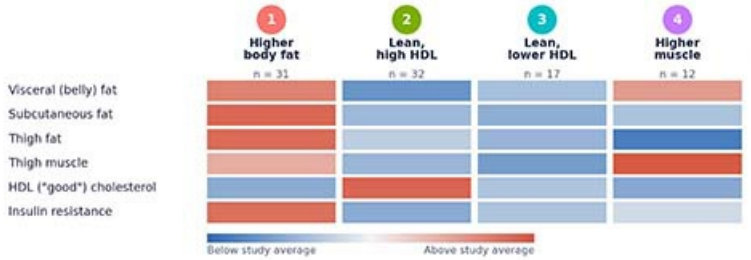

Figure 3. Four phenotypes identified by unsupervised clustering (Gaussian mixture model) of MRI-derived fat and muscle measures, BMI, cholesterol and insulin resistance; colors show each group's average compared with the study average.

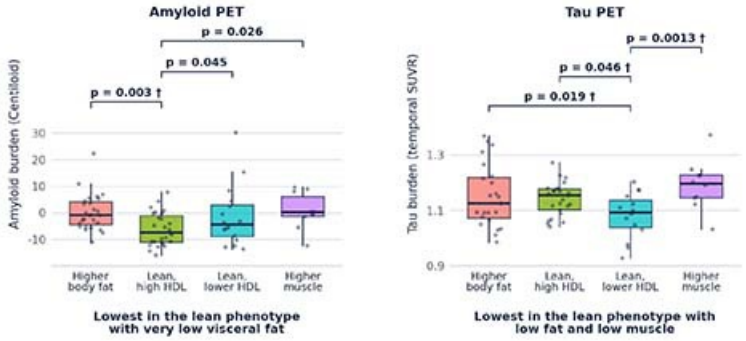

Figure 4. Amyloid (Centiloids) and tau (temporal meta-ROI SUVR) by phenotype. Boxes show the median and interquartile range, and dots are individual participants.

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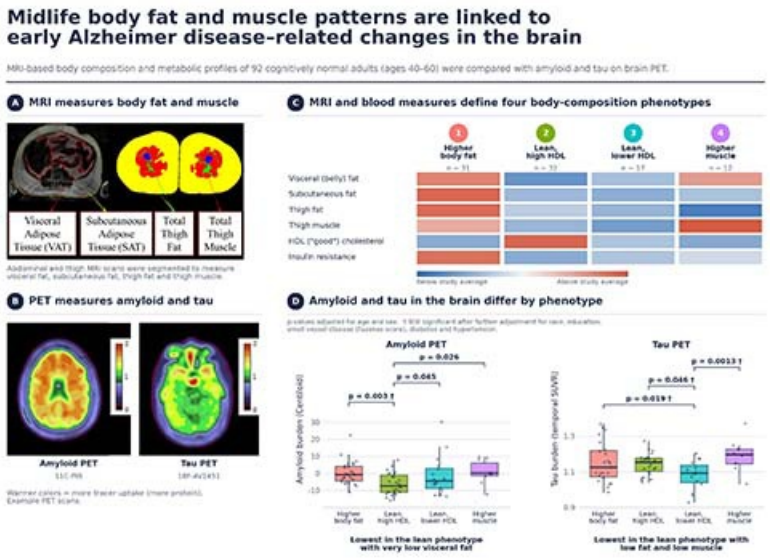

Figure 5. MRI-derived body composition phenotypes and brain amyloid and tau in cognitively normal midlife adults. For amyloid, only the difference between phenotypes 1 and 2 (high body fat with adverse metabolic profile vs. lean with favorable metabolic profile) remained significant.

Resources:

Abstract

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