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The Role of Genetics in Modifying the Link Between Earlier Menopause and Memory Decline

New study suggests that for women with earlier menopause, the presence of the APOE e4 gene or age-related inflammation accelerates memory decline

CLEVELAND, Ohio (Oct 22, 2025)—Women are significantly more likely than men to develop Alzheimer's disease. Earlier age at menopause is associated with a greater risk for late-life cognitive decline and Alzheimer's disease. A new study suggests that this risk is even higher in women who carry the APOE e4 gene variant or who have systemic inflammation. Study results will be presented at the 2025 Annual Meeting of The Menopause Society in Orlando October 21-25.

There are a number of reasons why women are more likely than men to develop Alzheimer's disease, including women's longer life expectancy, hormonal changes and genetic predispositions like the APOE4 gene. In a new study involving nearly 2600 women, researchers investigated whether the association between age at menopause and memory decline was modified by the APOE e4 genotype and/or systemic inflammatory markers.

They found that APOE e4 carriers showed the strongest association between earlier menopause and faster memory decline. In more than 250 participants with available data for inflammatory markers, higher levels of inflammation exacerbated the effect of earlier menopause on memory decline. Post hoc analyses suggested that the effect of inflammation exacerbating menopause-related memory decline was stronger in APOE e4 carriers than in non-carriers.

As a result, the researchers concluded that the presence of APOE e4 and age-related inflammation strengthened the link between earlier age at menopause and faster memory decline, suggesting that these factors may be especially salient contributors to Alzheimer's disease dementia risk in women with earlier menopause.

More detailed results will be discussed at the 2025 Annual Meeting of The Menopause Society as part of the abstract presentation entitled "Inflammation and APOE e4 genotype modify the link between earlier menopause and memory decline."

"Approximately 20% of Alzheimer's therapeutics in development target genetic and inflammatory factors. Yet, sex differences and female-specific risk factors like menopause are often overlooked in clinical trials. Understanding how female biology influences Alzheimer's disease risk is key to ensure we develop effective treatments for all individuals at risk," says Madeline Wood Alexander, lead author from the University of Toronto and Sunnybrook Research Institute.

"Given that women are at greater risk for Alzheimer's disease than men, understanding the nuanced sex- and gender-specific mechanisms underlying these differences is essential for the development of targeted,

individualized preventive and treatment strategies," says Dr. Stephanie Faubion, medical director for The Menopause Society.

Both Madeline Wood Alexander and Dr. Faubion are available for interviews.

For more information about menopause and healthy aging, visit menopause.org.

The Menopause Society is dedicated to empowering healthcare professionals and providing them with the tools and resources to improve the health of women during the menopause transition and beyond. As the leading authority on menopause since 1989, the nonprofit, multidisciplinary organization serves as the independent, evidence-based resource for healthcare professionals, researchers, the media, and the public and leads the conversation about improving women's health and healthcare experiences. To learn more, visit menopause.org.