Brain's 'wakeful rest' network may be key to Alzheimer's risk

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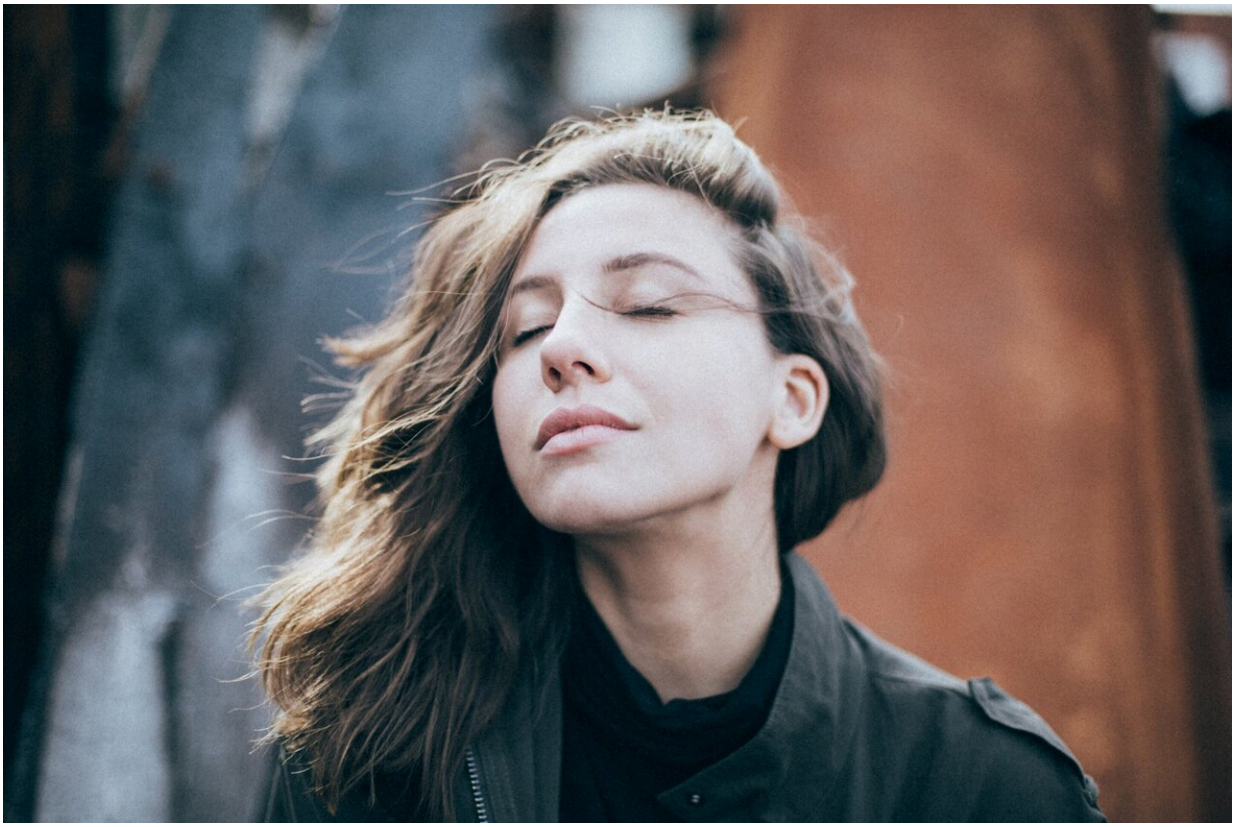

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If you have ever let your mind wander, you have relied on the brain's default mode network (DMN). Scientifically, the DMN is a connection of brain regions that interact when a person is in a state of wakeful rest.

This network is important for using our short-term memory, posing the question: Do changes in the DMN play a key role in the short-term memory loss seen in the progression of Alzheimer's disease (AD)? And is the DMN affected differently in women and men?

Women's Health Research at Yale (WHRY) collaborator Carolyn Fredericks, MD, assistant professor of neurology, has been working to understand AD and why it affects women disproportionately. Robust research shows that women clearly have an increased risk for AD compared to men. While there has been much research on AD, there are far fewer studies that take sex differences into account.

Fredericks' newest study, published in *Cerebral Cortex*, specifically examines sex differences in DMN connectivity in healthy aging adults. Fredericks and her team, including University of Washington second-year medical student Bronte Ficek-Tani, set out to identify the differences in these connections for both women and men, which may provide clues to why the risk for AD is greater in women.

Previous studies have shown that brain connectivity within the DMN change in association with symptomatic and preclinical AD, but investigation of sex differences in such changes have been limited. Fredericks' study also examined how connectivity changes in women and men as they age.

Using data from the Human Connectome Project-Aging, the team analyzed brain scans from patients who were in a state of wakeful rest. They found differences in how central communication points in the brain work for women and men. For example, in women compared to men, the parts of the DMN responsible for memory recollection and retrieval, and spatial cognition were more likely to be connected to the overall DMN brain network. These patterns of connectivity, correlated with brain structures responsible for short-term memory performance,

resembled changes seen in preclinical AD.

In addition, greater sex differences were observed during aging. In their 30s and 40s, women relied more on connection to the part of the brain responsible for spatial and verbal memory. In the decades surrounding menopause (40s and 50s), areas critical for memory retrieval showed higher connectivity to the overall DMN. Men, on the other hand, showed a different pattern and their highest connectivity was not observed until their later years (60s–80s). For men, the highest connection to the DMN was in a part of the brain responsible for habit forming and long-term memory.

The researchers believe their findings show that women rely on DMN connections more than men for memory and for a longer period of time. A high level of connectivity may result in a network under stress and more vulnerability to disorders like AD. This "wear and tear" on the portions of the brain critical for memory could explain, in part, why women are at a higher risk for AD.

Fredericks suggested that these findings can help doctors as well as scientists better understand memory performance and how it is related to brain networks, even in people without AD, and in turn, inform the type of memory loss in AD. By identifying patterns in the brains of healthy, aging people, scientists may not only have a future target for intervention but have a larger window of time in which to treat before symptoms are seen.

More information: Bronte Ficek-Tani et al, Sex differences in default mode network connectivity in healthy aging adults, *Cerebral Cortex* (2022). DOI: 10.1093/cercor/bhac491

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