

Researchers Show Why Estrogen's Memory Benefits Have Age Limits

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(PhysOrg.com) -- Hormone therapy seems to preserve the memories of women just entering menopause but is of little benefit to older women and leaves them at increased risk of breast cancer, heart disease and stroke, according to a research team at Yale University.

A new paper from Yale researchers led by Karyn Frick, associate professor of psychology, pinpoints a biological reason why estrogen must be administered during this “critical window” to prevent [cognitive decline](#) in women. The paper was published March 24 in the *Journal of Neuroscience*.

“Giving hormones as treatment for cognitive decline is tricky because hormones can bind to receptors all over the body, which can lead to

harmful side effects,” Frick said. “My lab is trying to identify the specific molecules in the brain that are necessary for hormones to influence memory formation, which could lead to the development of novel drugs that provide the cognitive benefits of hormones without adverse effects.”

Frick and her team investigated a cell-signaling pathway in the [hippocampus](#) - an area of the brain critical to learning and memory - that her lab had previously identified as crucial to estrogen’s ability to enhance memory. In the new study, the team found that estrogen activated this signaling pathway in the hippocampus and improved the ability of middle-aged female mice to recall objects. However, estrogen had no effect on memory or cell signaling in older female mice. The inability of estrogen to activate certain cell signaling pathways in the hippocampus may underlie its failure to improve memory in older females, the findings suggest.

These data support the notion of a window of opportunity early in menopause in which [hormone treatment](#) can benefit cognition, and indicate that the failure of estrogen to improve memory in older females may result from dysfunction of specific molecular pathways in the brain.

Other authors of the paper included Lu Fan, Zaorui Zhao, Patrick Orr, Michael Lewis, and Cassie Chambers.

In a related study, Frick and her colleagues demonstrated that epigenetic processes—those in which access to DNA is altered rather than the genetic code itself—regulate the ability of estrogen to enhance memory in young female mice. This study, published March 8 in the Proceedings of the National Academy of Sciences, showed that estrogen altered two key epigenetic processes in the hippocampus, and that these alterations were necessary for estrogen to improve [memory formation](#). By targeting these epigenetic mechanisms, it may be possible to develop drugs that

mimic the beneficial effects of [estrogen](#) on memory, Frick said.

Provided by Yale University

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