Long-term hormone treatment increases synapses in rat prefrontal cortex

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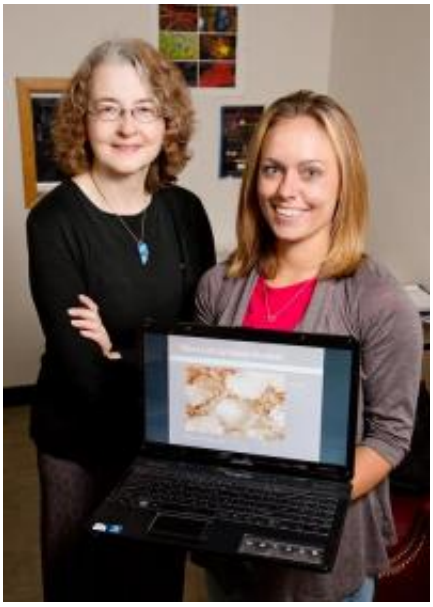

University of Illinois psychology professor and Beckman Institute affiliate Janice Juraska (left) and doctoral student Nioka Chisholm found that long-term exposure to estrogen and a synthetic progesterone increased synapse number in the prefrontal cortex of aged rats. Credit: L. Brian Stauffer

A new study of aged female rats found that long-term treatment with estrogen and a synthetic progesterone known as MPA increased levels of a protein marker of synapses in the prefrontal cortex, a brain region known to suffer significant losses in aging.

The new findings appear to contradict the results of the Women's Health

Initiative, a long-term study begun in 1991 to analyze the effects of hormone therapy on a large sample of healthy postmenopausal women aged 50 to 79. Among other negative findings, the WHI found that long-term exposure to estrogen alone or to estrogen and MPA resulted in an increased risk of stroke and dementia. More recent research, however, suggests that starting hormone replacement therapy at the onset of menopause, rather than years or decades afterward, yields different results.

The new study, from researchers at the University of Illinois, is the first to look at the effects of long-term treatment with estrogen and MPA on the number of synapses in the prefrontal cortex of aged animals. The researchers describe their findings in a paper in the journal *Menopause*.

The prefrontal cortex, just behind the forehead in humans, governs what researchers call "executive function" – planning, strategic thinking, working memory (the ability to hold information in mind just long enough to use it), self-control and other functions that tend to decline with age.

"The prefrontal cortex is the area of the human brain that loses the most volume with age," said U. of I. psychology professor and Beckman Institute affiliate Janice Juraska, who led the study with doctoral student Nioka Chisholm. "So understanding how anything affects the prefrontal cortex is important."

Most studies of the effects of hormone treatments on the brain have focused on the hippocampus, a structure important to spatial navigation and memory consolidation. The studies tend to use young animals exposed to hormones for very brief periods of time (one or two days to a few weeks at the most). They have yielded mixed results, with most research in young female animals indicating an increase in hippocampal synapses and hippocampal function after exposure to estrogen and MPA.

"For some reason, a lot of researchers still look at the effects of hormones in young animals," Chisholm said. "And there's a lot of evidence now saying that the aged brain is different; the effect of these hormones is not going to be the same."

The new study followed middle-aged rats exposed to estrogen alone, to no additional hormones, or to estrogen in combination with MPA for seven months, a time period that more closely corresponds to the experience of women who start hormone therapy at the onset of menopause and continue into old age. The researchers removed the rats' ovaries just prior to the hormone treatment (or lack of treatment) to mimic the changes that occur in humans during menopause.

"Our most important finding is that estrogen in combination with MPA can result in a greater number of synapses in the prefrontal cortex than (that seen) in animals that are not receiving hormone replacement," Chisholm said. "Estrogen alone marginally increased the synapses, but it took the combination with MPA to actually see the significant effect."

"Our data indicate that re-examining the effects of estrogen and MPA, when first given to women around the time of menopause, is merited," Juraska said.

More information: The paper, "Effects of Long-Term Treatment with Estrogen and Medroxyprogesterone Acetate on Synapse Number in the Medial Prefrontal Cortex of Aged Female Rats," is available online.

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