Postmenopausal estrogen decline largely unrelated to changes in cognition, mood

November 25 2013

A new study led by a Stanford University School of Medicine researcher shows that decreased estrogen levels after menopause are largely unrelated to changes in cognitive ability and mood. It did find, however, a possible link between levels of another hormone—progesterone—and cognition among younger postmenopausal women.

The research is the first to investigate associations between sex hormones and cognition in both younger and older postmenopausal women, and to determine whether the hormones affect women differently based on their age and how much time has elapsed since they reached menopause.

The work helps clarify the role of hormones in age-related brain disturbances, lead author Victor Henderson, MD, professor of health research and policy and of neurology and neurological sciences, and his colleagues note in the study, which will be published online Nov. 25 in the *Proceedings of the National Academy of Sciences*.

Estrogen, the main sex hormone for women, plays a crucial role in a woman's reproductive cycle and overall health. After menopause, the depletion of ovarian follicles leads to a permanent reduction in a woman's levels of estradiol (the predominant estrogen before menopause), estrone (the predominant estrogen after) and progesterone, another hormone involved in the menstrual cycle. Several studies have examined the association between hormone concentrations and cognition, but results have been inconsistent.

Some researchers have speculated that the effect of estrogen on cognitive aging might differ depending on when exposure occurs. "Some effects might be more beneficial for younger postmenopausal women closer to the time of menopause than for older postmenopausal women," Henderson said of the so-called "critical-window" hypothesis.

For their study, Henderson and his colleagues analyzed data on 643 healthy postmenopausal women who were part of the ongoing Early Versus Late Intervention Trial With Estradiol. The women, none of whom were on hormone therapy, ranged in age from 41 to 84.

They were sorted into two categories: those who had gone into menopause less than six years previously, and those who had gone into menopause more than 10 years previously. The researchers gave the women a series of neuropsychological tests to gauge their memory and overall cognition. Then, the researchers assessed them for depression and measured their levels of estradiol, estrone, progesterone and testosterone.

"We viewed the availability of hormone levels as an opportunity to test one aspect of the critical-window hypothesis—especially since we had two fairly large samples of women," Henderson said.

Based on the critical-window theory, along with results of past animal studies showing that the timing of estradiol replacement affects memory, Henderson said he and his colleagues had hypothesized that higher levels of estradiol would be positively associated with memory performance in women who had experienced menopause more recently but not those who had experienced it longer ago. "Instead, we found no significant link—positive or negative—in either group," he said.

Henderson added that the findings don't "necessarily mean that estrogens are irrelevant to cognition, since we have no way of measuring estrogen

directly at the brain level. But they imply that boosting blood levels of estradiol or estrone—even in younger postmenopausal women—may not have a substantial effect on cognitive skills one way or the other."

Other hormone levels were unrelated to verbal memory, executive function or overall cognition, or to mood, the researchers found, with one exception: Higher progesterone levels in younger postmenopausal women were positively associated with better memory and global cognition.

"This finding has not been previously reported and needs to be confirmed," Henderson added.

The study's strengths, the authors wrote, include "the large sample size for both early and late postmenopausal women, the examination of multiple sex hormones in the same population, and the use of a comprehensive neuropsychological battery that allowed for the assessment of different cognitive domains."

More information: Transcriptomic and biochemical analyses identify a family of chlorhexidine efflux proteins, www.pnas.org/cgi/doi/10.1073/pnas.1317052110

Provided by Stanford University Medical Center

provided for information purposes only.