Surgical menopause may prime brain for stroke, Alzheimer's

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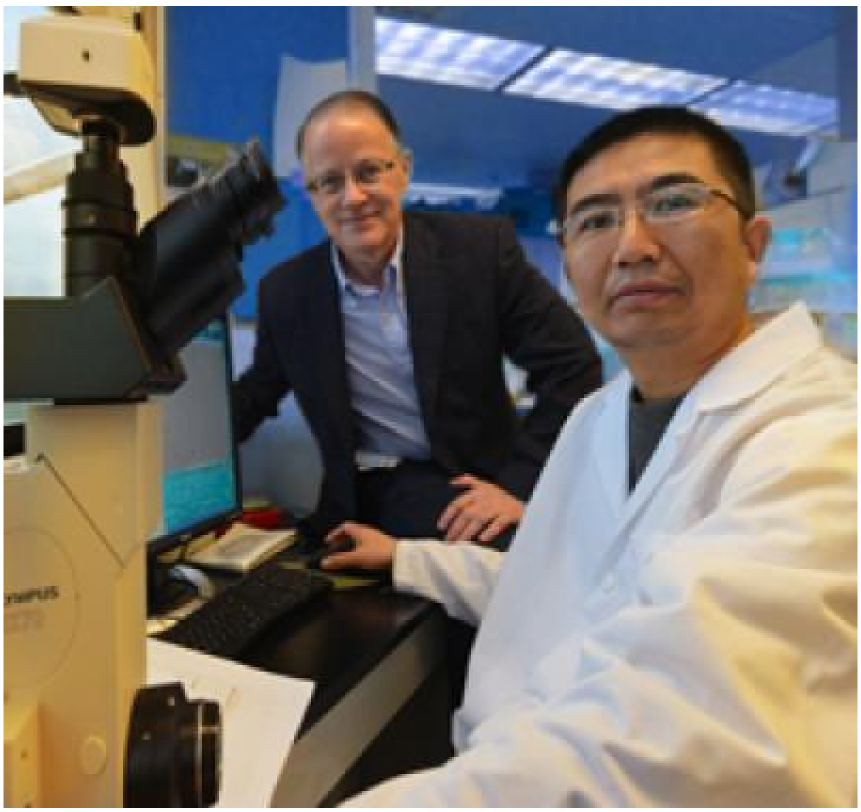

This is Dr. Brann and Dr. Zhang. Credit: GRU Photographer

Women who abruptly and prematurely lose estrogen from surgical menopause have a two-fold increase in cognitive decline and dementia.

"This is what the clinical studies indicate and our animal studies looking at the underlying mechanisms back this up," said Brann, corresponding author of the study in the journal *Brain*. "We wanted to find out why that is occurring. We suspect it's due to the premature loss of estrogen."

In an effort to mimic what occurs in women, Brann and his colleagues looked at rats 10 weeks after removal of their estrogen-producing ovaries that were either immediately started on low-dose estrogen therapy, started therapy 10 weeks later or never given estrogen.

When the researchers caused a stroke-like event in the brain's hippocampus, a center of learning and memory, they found the rodents treated late or not at all experienced more brain damage, specifically to a region of the hippocampus called CA3 that is normally stroke-resistant.

To make matters worse, untreated or late-treated rats also began an abnormal, robust production of Alzheimer's disease-related proteins in the CA3 region, even becoming hypersensitive to one of the most toxic of the beta amyloid proteins that are a hallmark of Alzheimer's.

Both problems appear associated with the increased production of free radicals in the brain. In fact, when the researchers blocked the excessive production, heightened stroke sensitivity and brain cell death in the CA3 region were reduced.

Interestingly the brain's increased sensitivity to stressors such as inadequate oxygen was gender specific, Brann said. Removing testes in male rats, didn't affect stroke size or damage.

Although exactly how it works is unknown, estrogen appears to help protect younger females from problems such as stroke and heart attack. Their risks of the maladies increase after menopause to about the same as males. Follow up studies are needed to see if estrogen therapy also reduces sensitivity to the beta amyloid protein in the CA3 region, as they expect, Brann noted.

Brann earlier showed that prolonged estrogen deprivation in aging rats dramatically reduces the number of brain receptors for the hormone as well as its ability to prevent strokes. Damage was forestalled if estrogen replacement was started shortly after hormone levels drop, according to the 2011 study in the journal Proceedings of the National Academy of Sciences.

The surprising results of the much-publicized Women's Health Initiative – a 12-year study of 161,808 women ages 50-79 – found hormone therapy generally increased rather than decreased stroke risk as well as other health problems. Critics said one problem with the study was that many of the women, like Brann's aged rats, had gone years without hormone replacement, bolstering the case that timing is everything.

Provided by Medical College of Georgia

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