

Sex hormone-related protein levels may impact stroke risk in women

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Low levels of a protein that binds to and transports sex hormones in the blood may indicate women who have a higher risk of ischemic stroke, according to preliminary research to be presented at the American

Stroke Association's International Stroke Conference 2020—Feb. 19-21 in Los Angeles, a world premier meeting for researchers and clinicians dedicated to the science of stroke and brain health.

Sex hormone binding globulin (SHBG) is a protein produced by the liver that binds to estradiol (a form of estrogen) and testosterone and transports these hormones in the bloodstream. When there are high levels of SHBG, there are lower active levels of estrogen and testosterone circulating in the body, and the balance between testosterone and estrogen changes. Conversely, low levels of SHBG mean that more of the hormones are active in [body tissues](#). In addition to affecting estrogen and testosterone levels, SHBG also affects the body's tissues by binding directly to cells.

In the past, low levels of SHBG have been linked to diabetes and heart disease and is a risk factor for both, according to study authors.

"In recent years, we have started to learn more about how well-established [stroke risk factors](#) like [high blood pressure](#) and diabetes differ between [women](#) and men. Unfortunately, we still lack an understanding of how female hormones affect stroke risk across the lifespan for women," said Tracy E. Madsen, M.D., Sc.M., lead author of the study and assistant professor of emergency medicine at the Warren Alpert Medical School of Brown University in Providence, Rhode Island.

The researchers examined the occurrence of ischemic (blockage) strokes in more than 13,000 postmenopausal women (average age 62.5 years; 67% white, 18.5% black, 5% Asian and 8% Hispanic). Study participants had SHBG levels measured between 1993 and 1998, at the time of their enrollment in the Women's Health Initiative, a large, national study of more than 160,000 postmenopausal women. Using patient health information collected through 2017, researchers compared

the occurrence of strokes between women with SHBG in the highest 25% and those with SHBG in the lowest 25%. They found:

- After adjusting for age, race, body mass index, high blood pressure, [alcohol use](#) and smoking, women with the lowest SHBG levels were 51% more likely to have had a stroke; and
- Even after accounting for diabetes, a possible link between low SHBG and stroke, women with the lowest SHBG were still 46% more likely to have a stroke during the follow-up period.

"More research is needed before measurements of SHBG are incorporated into clinical care and used to evaluate stroke risk," Madsen said. "However, we know that there are factors that tend to increase SHBG and are also linked to an overall healthy lifestyle. These include getting regular exercise, losing weight if your body mass index is higher than recommended and limiting your sugar intake. Drinking coffee in moderation may also be linked to improved SHBG levels."

The researchers plan further studies to demonstrate if there is a cause-and-effect relationship between low SHBG and stroke, and to evaluate whether adding hormonal biomarker screening (such as SHBG) to existing stroke risk scores might improve the prediction of stroke in women.

There are several possible mechanisms by which low SHBG levels might be associated with increased stroke risk. The researchers suggest: changes in the body's responsiveness to sex hormones; changes in how the body handles insulin (which can lead to dysfunction of blood vessels in the brain); or alterations in inflammation, immune function or the blood-clotting process. "Our group is currently working on some of these hypotheses," Madsen said.

Results from this study of postmenopausal women may not be

generalizable to men or to women prior to menopause. Because the Women's Health Initiative was not originally designed to address questions about SHBG and stroke, researchers were limited in only being able to use data from a fraction of the overall study participants.

Provided by American Heart Association

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