Women have a higher genetic risk for PTSD, study finds

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Women are twice as likely as men to develop post-traumatic stress disorder, but the factors contributing to this disparity have largely remained unsettled. A research team led by Virginia Commonwealth University and Lund University in Sweden conducted the largest twin-sibling study of PTSD to date to shed light on how genetics may play a role.

Their results, published in the *American Journal of Psychiatry*, are the first to demonstrate that women have a higher genetic risk for the disorder compared with men.

By analyzing health data from over 16,000 twin pairs and 376,000 sibling pairs, the research team discovered that heritability for PTSD was 7 percentage points higher in women (35.4%) than in men (28.6%). They also found evidence that the genes that make up the heritable risk for PTSD vary between the two sexes.

The researchers say their findings could inform strategies for PTSD prevention and intervention following a traumatic event, as well as help address stigmas related to women's mental health.

"Women are at higher risk for developing PTSD than men, even when controlling for the type of trauma, income level, social support and other environmental factors. Some of the theories as to why that is have frankly been unkind to women, such as attributing the sex difference to a weakness or lack of ability to cope," said Ananda B. Amstadter, Ph.D., a professor in the VCU School of Medicine's departments of Psychiatry and Human and Molecular Genetics and lead author of the study.

"I think this study can help move the narrative that people can have an inherited biological risk for PTSD, and that this genetic risk is greater in women."

Nearly 70% of the global population is exposed to at least one traumatic event in their lifetime, such as physical or sexual assault, a motor vehicle accident, exposure to combat or a natural disaster. About 6% of those who are exposed to trauma develop PTSD. Amstadter's research focuses on understanding the conditions that might increase or decrease a person's risk of experiencing PTSD, particularly how a person's genes impact their risk.

"If you think of risk for PTSD like a pie chart, we're trying to better understand what factors make up the pieces of this pie," she said. "Some of the risk is influenced by a person's environment, such as the experiences they have while growing up. On the other hand, some of the risk will be influenced by the genes they inherit from their parents."

Previous research has looked into how genes influence the likelihood of developing PTSD, but the study conducted by Amstadter and her colleagues is the first of its kind to investigate how genetic risk varies by sex.

For this project, the research team examined anonymized clinical data from Swedish population-based registries. Their analysis consisted of more than 400,000 pairs of twins or siblings born up to two years apart in Sweden between 1955 and 1980. Studies on twins and siblings, because of their genetic similarities, can help researchers determine how a person's genes influence their risk for mental illnesses.

"Every time a person within this age group interacts with Sweden's health care system, whether that's visiting their primary care doctor, filling a prescription or going to the hospital, that information is recorded in their national registries. This kind of data is a really powerful tool for addressing questions related to genetic risk for medical conditions," Amstadter said.

"Prior PTSD studies involving twins and siblings have typically only included a few thousand individuals. Because our sample size was so large in comparison, we were able to make calculations with a higher degree of certainty."

Through statistical modeling, the researchers calculated how much a person's genetic makeup influenced their likelihood of developing PTSD following a traumatic event. In finding that PTSD was 35.4% heritable

in women but only 28.6% heritable in men, they demonstrated that women have a higher biological risk for PTSD.

Their models also revealed that the genes associated with PTSD were highly correlated (0.81) but not entirely the same between men and women. This suggests that the genetic underpinnings of sex hormones, like testosterone, estrogen and progesterone, may be involved in the development of PTSD.

The research team is collaborating with the Psychiatric Genomics Consortium to identify the molecular genetic variants that may contribute to sex-specific pathways of risk.

More information: Ananda B. Amstadter et al, Testing Quantitative and Qualitative Sex Effects in a National Swedish Twin-Sibling Study of Posttraumatic Stress Disorder, *American Journal of Psychiatry* (2024). DOI: 10.1176/appi.ajp.20230104

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