

# New biological pathway identified for post-traumatic stress disorder

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High blood levels of a hormone produced in response to stress are linked to post-traumatic stress disorder in women but not men, a study from researchers at Emory University and the University of Vermont has found.

The results are scheduled for publication in the Feb. 24 issue of *Nature*.

The hormone, called PACAP (pituitary adenylate cyclase-activating polypeptide), is known to act throughout the body and the brain, modulating central nervous system activity, metabolism, blood pressure, [pain sensitivity](#) and immune function. The identification of PACAP as an indicator of PTSD may lead to new diagnostic tools and eventually, to new treatments for [anxiety disorders](#).

"Few biological markers have been available for PTSD or for psychiatric diseases in general," says first author Kerry Ressler, MD, PhD, associate professor of psychiatry and behavioral sciences at Emory University School of Medicine and a researcher at Yerkes National Primate Research Center. "These results give us a new window into the biology of PTSD."

Women, but not men, with high blood levels of PACAP display more of the symptoms of PTSD, such as difficulty discriminating between fear and safety signals and being easier to startle. In a group of 64 people, most of whom had experienced significant trauma, women with above-average PACAP levels had PTSD symptom scores five times those of

women with less-than-average PACAP levels.

In addition, a variation in the gene for PACAP's receptor, which may change how that gene responds to estrogen, was also linked to PTSD risk in women only.

Ressler notes that despite comparable levels of trauma, women in the study with the more protective PACAP receptor [gene variation](#) have lower rates of PTSD than men, whereas those with the risk gene variation had higher rates of PTSD.

"What this says is that men and women who have been traumatized may arrive at PTSD by different biological pathways," Ressler says. "In this case, we have a clue how that works, in that the [genetic data](#) point to changes in the ability to respond to estrogen."

The findings emerged from the Grady Trauma Project, a study of more than 1200 low-income Atlanta residents with high levels of exposure to violence and physical and sexual abuse, resulting in high rates of civilian PTSD. Beginning in 2005, interviewers asked patients in primary care, ob-gyn, and other clinic waiting areas of Grady Memorial Hospital in Atlanta to complete questionnaires on their life histories and to provide saliva and blood samples for DNA and other analyses.

Ressler, a Howard Hughes Medical Institute Investigator, is co-director of the Grady Trauma Project, along with co-author Bekh Bradley, PhD, assistant professor of psychiatry and behavioral sciences at Emory and director of the Trauma Recovery Program at the Atlanta Veterans Affairs Medical Center.

To explore how the PACAP pathway responds to stress and hormones, Ressler and his team teamed up with colleagues at the University of Vermont who had been studying PACAP in animals. The Vermont

researchers were led by Victor May, PhD, professor of anatomy and neurobiology. Co-authors Jom Hammack, PhD, and Donna Toufexis, PhD, both assistant professor of psychology at the University of Vermont, were previously postdoctoral fellows at Yerkes National Primate Research Center.

The Vermont team's previous experiments showed that in rats experiencing stress, PACAP is increased ten-fold in a part of the brain called the BNST (bed nucleus of the stria terminalis), which scientists have shown is critical for anxiety behavior. In the *Nature* paper, they demonstrate that the gene for the PACAP receptor is also activated by stress and the hormone estrogen.

"In the brain, PACAP can activate brain cells, and it is also neurotrophic, helping brain cells survive, grow and form connections," Hammack says. "In many brain areas, this is great, but in others, such as those involved in sustained anxiety behavior, this might not be so good."

"These studies may offer opportunities to distinguish people with PTSD and related anxiety disorders from other behavioral disorders, and identify people in high stress occupations or environments who may be prone to PTSD," says May.

Ressler says that it will be important to replicate the finding in separate population groups including in veterans with PTSD. In addition, identifying when PACAP levels rise in the brain and blood during the development of PTSD will help determine whether drugs that act against PACAP could aid in treatment.

Provided by Emory University

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