# PTSD linked to low levels of fat hormone

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Credit: University of Texas Health Science Center at San Antonio

Individuals with post-traumatic stress disorder (PTSD) relive past traumas again and again, bound in a virtual prison of their memories.

Researchers in the School of Medicine at The University of Texas

Health Science Center at San Antonio now report a biological mechanism that might explain why these individuals are less able to extinguish the fear of past dangers.

The Health Science Center has filed for patent protection on the finding because it may eventually lead to a drug to treat PTSD, which affects an estimated 8 percent of the civilian population and up to 15 percent of U.S. active-duty and retired service personnel.

The new research centers on the hormone adiponectin, which is secreted by fat cells called adipocytes. The scientists studied a mouse model of PTSD.

## Ability to unlearn fear

These mice were trained to associate a setting, such as a box, with a mild unpleasant stimulus. As expected, they showed a fear response when re-exposed to the setting.

Mice deficient for adiponectin and its receptor formed fearful memories just like healthy mice, but when placed again in the same setting minus the unpleasant stimulus, were slower to let go of the fear.

Injecting adiponectin prior to this training prompted faster learning to overcome fear, the measurements showed.

## Low level in PTSD model

"Once the threat is no longer there, the fear should go away, but in PTSD it keeps flashing back," said study senior author Xin-Yun Lu, M.D., Ph.D., professor of pharmacology and a member of the Barshop Institute for Aging and Longevity Studies at the UT Health Science Center. "In the PTSD animal model, the circulating adiponectin is low, data suggest.

If the genes encoding adiponectin and its receptor are disrupted, the mice extinguish fear responses much slower. If adiponectin levels are elevated in the brain, the mice get extinction faster."

Adiponectin impairment is implicated in metabolic diseases such as obesity and type 2 diabetes. The new research, published May 3 in the journal *Molecular Psychiatry*, shows the hormone has a role beyond its metabolic control, Dr. Lu said.

"It is interesting that this hormone promotes fear extinction," she said. "Increasing adiponectin levels or activating its specific receptors might facilitate extinction-based exposure treatments for PTSD and other trauma- and stress-related disorders."

## Promising, but still years to go

Dr. Lu said people who have low adiponectin levels might be more prone to developing PTSD symptoms if they are exposed to a traumatic event. She noted that it will take years of work to learn if adiponectin can be translated into a therapy for human PTSD.

"To date, medication treatments for PTSD have been of limited benefit," said Alan L. Peterson, Ph.D., ABPP, professor of psychiatry at the UT Health Science Center and director of the STRONG STAR Consortium and the Consortium to Alleviate PTSD. "Dr. Xin-Yun Lu's work holds significant promise for the development of new, more effective medication treatments for PTSD."

STRONG STAR and CAP, both based at the Health Science Center, involve collaborators nationwide to study PTSD.

## Defining an entire field

Alan Frazer, Ph.D., professor and chairman of the Department of Pharmacology at the Health Science Center, said: "Dr. Lu has been the investigator who has defined the field whereby hormones coming from fat, which had been thought only to be involved in energy balance, are now known to be capable of regulating mood and anxiety. She is the world leader in this area, which has great potential for furthering our understanding of illnesses such as PTSD and major depressive disorder as well as developing novel treatments for them."

**More information:** D Zhang et al, Adiponectin regulates contextual fear extinction and intrinsic excitability of dentate gyrus granule neurons through AdipoR2 receptors, *Molecular Psychiatry* (2016). DOI: 10.1038/mp.2016.58

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