Learning to Care for Those in Harm's Way

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Early Childhood Trauma Re-Wires the Brain, Increasing Risk for Depression

Bethesda, Md. – Federal researchers have discovered that severe stress or trauma early in life could actually change how the brain responds to stress hormones, essentially "re-wiring" the brain for later neuropathological disorders, according to a study, "A role for corticotrophin releasing factor signaling in the lateral habenula and its modulation by early life stress," published in Science Signaling, March 6.

"We know that early childhood abuse and trauma can increase the risk of developing depression and anxiety-related disorders later in life - an estimated 80 percent of those children will experience one of these episodes in their adulthood, but until now, no one has known why," said Dr. Fereshteh Nugent, the study's corresponding author and associate professor of Pharmacology and Neuroscience at the Uniformed Services University of the Health Sceinces (USU).

The lateral habenula (LHb) region of the brain is associated with stress and depression. Scientists know that activity of LHb neurons is increased when an individual experiences unpleasantness. In this study, the USU research team sought to understand the correlation between the corticotropin-releasing factor (CRF) hormone (a hormone involved in stress response) and the LHb neurons. The researchers demonstrated for the first time that dopamine signaling in the brain is shut down as a result of the CRF stress hormone signaling through LHb by increasing LHb activity. Dopamine is the neurotransmitter of the brain that signals feelings of reward or pleasure.

The team used animal models of child abuse (maternal deprivation in rats) to monitor LHb activity in the brain, since this model has been associated with an increased activity of CRF signaling in the brain. They compared the LHb activity to rats that did not experience maternal deprivation and found that those exposed to the severe trauma early in life did, in fact, have a heightened activity of LHb neurons. The scientists also found that the response of LHb neurons was blunted by the CRF signaling. Therefore, they suggest that these changes in LHb neuronal responses to the CRF stress hormone could potentially change the "wiring" in the brain, setting it up for an increased susceptibility to stress- and anxiety-related disorders.

"For the first time, we're showing this stress hormone has an effect on LHb neurons," Nugent said. "By understanding the effects of early life stress on this part of the brain, we can expand our knowledge of an important part of the cellular basis of child abuse."

"This is an important discovery because it will allow for development of early interventions, which could potentially prevent later development of depression and other stress-related disorders," she said.

Nugent explained that her team is now studying the use of various types of early interventions, including fast-acting ketamine, which they hope can help reverse this "re-wiring" by targeting the dopamine signaling itself, thus regulating the firing of these neurons.

The work was supported by the National Institutes of Health - National Institute of Drugs of Abuse Grant #R01 DA039533, Brain & Behavior Research Foundation (formerly known as NARSAD) grant and Department of Defense intramural grant from the Uniformed Services University to Fereshteh S. Nugent.

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