

Long-Term Impact of Childhood Trauma Explained

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May 02, 2023

Dysregulated stress systems may help explain why childhood trauma has such a dramatic and enduring psychiatric impact, new research suggests.

"We already knew childhood trauma is associated with the later development of depressive and [anxiety disorders](#), but it's been unclear what makes sufferers of early trauma more likely to develop these psychiatric conditions," study investigator Erika Kuzminskaite, PhD candidate, Department of Psychiatry, Amsterdam University Medical Center (UMC), the Netherlands, told *Medscape Medical News*.

"The evidence now points to unbalanced stress systems as a possible cause of this vulnerability, and now the most important question is, how we can develop preventive interventions," she added.

The findings were presented at the Anxiety and [Depression](#) Association of America (ADAA) 2023.

Elevated Cortisol, Inflammation

The study included 2,779 adults from the Netherlands Study of Depression and Anxiety (NESDA). Two thirds of participants were female.

Participants retrospectively reported childhood trauma, defined as emotional, physical, or sexual abuse or emotional or physical neglect, before the age of 18 years. Severe trauma was defined as multiple types or increased frequency of abuse.

Of the total cohort, 48% reported experiencing some childhood trauma — 21% reported severe trauma, 27% reported mild trauma, and 42% reported no childhood trauma.

Among those with trauma, 89% had a current or remitted anxiety or depressive disorder, and 11% had no psychiatric sequelae. Among participants who reported no trauma, 68% had a current or remitted disorder, and 32% had no psychiatric disorders.

At baseline, researchers assessed markers of major bodily stress systems, including the hypothalamic-pituitary-adrenal (HPA) axis, the immune-inflammatory system, and the autonomic nervous system (ANS). They examined these markers separately and cumulatively.

In one model, investigators found that levels of cortisol and inflammation were significantly elevated in those with severe childhood trauma compared to those with no childhood trauma. The effects were largest for the cumulative markers for HPA-axis, inflammation, and all stress system markers (Cohen's $d = 0.23, 0.12, \text{ and } 0.25$, respectively). There was no association with ANS markers.

The results were partially explained by lifestyle, said Kuzminskaite, who noted that people with severe childhood trauma tend to have a higher body mass index, smoke more, and to have other unhealthy habits that may represent a "coping" mechanism for trauma.

Those who experienced childhood trauma also have higher rates of other disorders, including [asthma](#), diabetes, and cardiovascular disease. Kuzminskaite also noted that people with childhood trauma have at least double the risk of cancer in later life.

When researchers adjusted for lifestyle factors and chronic conditions, the association for cortisol was reduced and that for inflammation disappeared. However, the cumulative inflammatory markers remained significant.

Another model examined lipopolysaccharide-stimulated (LPS) immune-inflammatory markers by childhood trauma severity. This provides a more "dynamic" measure of stress systems than looking only at static circulating levels in the blood, as was done in the first model, said Kuzminskaite.

"These levels should theoretically be more affected by experiences such as childhood trauma and they are also less sensitive to lifestyle."

Here, researchers found significant positive associations with childhood trauma, especially severe trauma, after adjusting for lifestyle and health-related covariates (cumulative index $d = 0.19$).

"Almost all people with childhood trauma, especially severe trauma, had LPS-stimulated cytokines upregulated," said Kuzminskaite. "So again, there is this dysregulation of immune system functioning in these subjects."

And again, the strongest effect was for the cumulative index of all cytokines, she said.

Personalized Interventions

Kuzminskaite noted the importance of learning the impact of early trauma on stress responses. "The goal is to eventually have personalized interventions for people with depression or anxiety related to childhood trauma, or even preventative interventions. If we know, for example, something is going wrong with a patient's stress systems, we can suggest some therapeutic targets."

Investigators in Amsterdam are examining the efficacy of [mifepristone](#), which blocks progesterone and is used along with [misoprostol](#) for medication abortions and to treat high blood sugar. "The drug is supposed to reset the stress system functioning," said Kuzminskaite.

It's still important to target unhealthy lifestyle habits "that are really impacting the functioning of the stress systems," she said. Lifestyle interventions could improve the efficacy of treatments for depression, for example, she added.

Commenting for *Medscape Medical News*, Luana Marques, PhD, associate professor, Department of Psychiatry, Harvard Medical School, said such research is important.

"It reveals the potentially extensive and long-lasting impact of childhood trauma on functioning. The findings underscore the importance of equipping at-risk and trauma-exposed youth with evidence-based skills for managing stress," she said.

No conflicts of interest were reported.

Anxiety and Depression Association of America (ADAA) Conference 2022: Abstract 78. Presented April 14, 2022.

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Cite this: Long-Term Impact of Childhood Trauma Explained - *Medscape* - May 02, 2023.