

New research shows childhood adversity causes changes in genetics

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In a look at how major stressors during childhood can change a person's biological risk for psychiatric disorders, researchers at Butler Hospital have discovered a genetic alteration at the root of the association. The research, published online in *PLoS ONE* on January 25, 2012, suggests that childhood adversity may lead to epigenetic changes in the human glucocorticoid receptor gene, an important regulator of the biological stress response that may increase risk for psychiatric disorders.

The association between childhood adversity, including parental loss and childhood maltreatment, and risk for psychiatric disorders such as depression and anxiety has been established in multiple studies. However, researchers have yet to define how and why this association exists in humans. "We need to understand the biology of this effect in order to develop better treatment and [prevention programs](#)," said Audrey Tyrka, MD, PhD, director of the Laboratory for Clinical and Translational Neuroscience at Butler Hospital and associate professor of Psychiatry and Human Behavior at Brown University. "Our research group turned to the field of epigenetics to determine how environmental conditions in childhood can influence the biological stress response."

Epigenetics is the study of changes to the genome that do not alter the DNA sequence, but influence whether genes will be expressed, or "turned on," versus whether they will be silenced. Knowing that the connection between childhood maltreatment and psychiatric disorders has been linked to the hormone system that coordinates biological stress responses, the researchers sought to identify the root cause at a [genetic](#)

[level](#).

The glucocorticoid receptor is an important regulator of the [stress response](#), and methylation is a particularly stable type of epigenetic modification. "We knew that [epigenetic changes](#) to this gene could be affected by childhood parenting experiences because previous animal research showed that rodents with low levels of [maternal care](#) had increased methylation of this gene, and consequently, as adults these animals had greater stress sensitivity and fear in stressful situations," said Tyrka.

The researchers looked at 99 healthy adults, some of whom had a history of parental loss or [childhood maltreatment](#). DNA was extracted from each of the participants using a blood sample, then analyzed to identify epigenetic changes to the glucocorticoid receptor. The researchers then performed a standardized hormone provocation test to measure the stress hormone, cortisol.

The researchers found that adults with a history of childhood adversity—maltreatment or parental loss—had increased methylation of the glucocorticoid receptor (GR) gene, which is thought to change the way this gene is expressed on a long-term basis. They also found that greater methylation was linked to blunted cortisol responses to the hormone provocation test. "Our results suggest that exposure to stressful experiences during childhood may actually alter the programming of an individual's genome. This concept may have broad public health implications, as it could be a mechanism for the association of childhood trauma with poor health outcomes, including psychiatric disorders as well as medical conditions such as cardiovascular disease," said Tyrka.

In early studies of animals, researchers have identified drugs that can reverse methylation effects. "More research is needed to better understand the epigenetic mechanism behind this association," said

Tyrka, noting a larger scale study currently underway at Butler and a study of this association in children. "This line of research may allow us to better understand who is most at risk and why, and may allow for the development of treatments that could reverse epigenetic effects of childhood adversity."

Provided by Brown University

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