

# Gene protects adults abused as children from depression

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Some forms of a gene that controls the body's response to stress hormones appear to protect adults who were abused in childhood from depression, psychiatrists have found.

People who had been abused as children and who carried the most protective forms of the gene, called corticotropin-releasing hormone receptor one (CRHR1), had markedly lower measures of depression, compared with people with less protective forms, the researchers found in a recent study.

The findings could guide doctors in finding new ways to treat depression in people who were abused as children, says senior author Kerry Ressler, MD, PhD, assistant professor of psychiatry and behavioral sciences at Emory University School of Medicine.

"We know that childhood abuse and early life stress are among the strongest contributors to adult depression, and this study again brings to light the importance of preventing them," Dr. Ressler says. "But when these tragic events do occur, studies like this one ultimately can help us learn how we might be able to better intervene against the pathology that often follows."

The results of the study, performed on two separate racially and economically distinct groups from the Atlanta area, were published in the February 4 issue of the *Archives of General Psychiatry*.

The first and second authors of the study are Rebekah Bradley, PhD, at the Atlanta Veterans Affairs Medical Center and Elisabeth Binder, MD, PhD, at Emory University and the Max Planck Institute for Psychiatry in Munich, Germany. Dr. Ressler, who also is a scientist at Emory's Yerkes National Primate Research Center and a member of the Center for Behavioral Neuroscience, and Joseph Cubells, MD, PhD, associate professor of human genetics at Emory University School of Medicine, are co-senior authors.

The team's research illustrates how life events and genetic influences can combine in complex ways, leading to depression or protection from it. Almost 15 million U.S. adults have major depression, according to the National Institute of Mental Health.

The study also supports previous evidence that corticotropin-releasing hormone (CRH) and related hormones play a role in depression. Other studies have found increased levels of CRH and altered levels of its receptor in the brains of patients with depression.

Some pharmaceutical firms are testing compounds that block CRHR1 as potential medications for depression.

The receptor for a hormone acts like a receiver or radar dish for messages sent between cells. CRH stimulates the pituitary gland to release another hormone, adrenocorticotropin, which in turn induces the release of cortisol from the adrenal cortex.

Extreme stress in childhood can over-activate this cascade of hormones, increasing the risk of depression in adulthood, Dr. Ressler says.

"Our results suggest that genetic differences in signals mediated by CRH may amplify or soften the developmental effects that childhood abuse can have -- effects that can raise the risk of depression in adults," he

says.

In the study, scientists began by interviewing more than 470 adults and testing their DNA, looking for alternative spellings or SNPs (single nucleotide polymorphisms) in several parts of the CRHR1 gene.

This first group was mostly black and a majority had a monthly income less than \$1,000. The researchers measured their symptoms of depression and had them answer questionnaires about childhood trauma. Their responses were categorized as low, mild, moderate and severe.

Overall, people with a history of moderate or severe child abuse had depression symptoms that averaged about double the level of those with low or mild child abuse scores.

Roughly 30 percent of the group had variations in the CRHR1 gene that together appeared to be protective if moderate to severe abuse had occurred. People who had inherited two copies of the most protective forms of the gene, or "haplotypes," had average depression symptoms that were about half those of people who had not inherited those haplotypes. A haplotype comprises several SNPs that frequently appear together.

These differences in depression symptoms were only seen in people with histories of moderate to severe abuse; depression levels were not significantly different in people with low to mild abuse.

The most significant SNPs appear in the part of the gene preceding the region that encodes the receptor protein, suggesting that the variations may affect its regulation rather than the composition of the protein, the authors say.

The findings were strengthened when the researchers repeated the study

in 199 white, middle-income adults and came up with similar results, suggesting that the genetic variations act in a way that is independent of ethnic background or economic status.

Source: Emory University

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