

Transmitting stress response patterns across generations

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Children of survivors of extremely stressful life events face adjustment challenges of their own, as has been most carefully studied among the children of Nazi Death Camp survivors. This "intergenerational" transmission of stress response has been studied predominately from the psychological perspective. However, recent research points to biological contributions as well.

Indeed, a new study just published in *Biological Psychiatry* demonstrates that offspring born to stressed mothers show stress-induced changes at birth, with altered behavior and gender-related differences that continue into adulthood.

"The notion that biological traits that are not coded by the sequence of DNA can be transmitted across generations is the focus of a field of research called epigenetics. This new paper implicates epigenetic regulation of a well-studied contributor to stress response, CRF1, in the intergenerational transmission of patterns of <u>stress response</u>," said Dr. John Krystal, Editor of *Biological Psychiatry*.

The researchers, led by Dr. Inna Gaisler-Salomon at University of Haifa in Israel, were interested in how stress modulates behavior and gene expression across generations. Previous studies in both humans and animals have shown that females exposed to stress even before they conceive can affect their children and even grandchildren.

In this study, they looked for a possible mechanism for these effects, focusing on the CRF1 gene. They studied adolescent <u>female rats</u> that went through a mild stress procedure before mating.

Stress led to an increase in CRF1 expression in the frontal cortex, a brain region involved in emotional regulation and decision making. Also, there was a dramatic increase in CRF1 expression in the egg cells of stressed females.

In the offspring of stressed female rats, brain CRF1 expression was increased as well, already at birth. "It seems that CRF1 is a marker molecule that tracks the stress experience across generations, perhaps via the germline, and maternal care is minimally involved in this particular effect," explained Gaisler-Salomon.

They also found behavioral differences between the offspring of stressed and non-stressed females, particularly in tests of emotional and exploratory behavior. Interestingly, CRF1 expression was increased in adult daughters of stressed females, but only if the offspring themselves were exposed to stress. This indicates that in adults, CRF1 expression depends on the mother's stress experiences in combination with the individual's stress experience and their sex.

"So why is this important?" asked Gaisler-Salomon. "Traditionally, it was believed that only genetic information is transferred from generation to generation via eggs and sperm cells. This study contributes to the notion that soft-wired information that is not written into the genetic code can also be transferred from one generation to the next via the germline."

Many psychiatric illnesses, such as schizophrenia and posttraumatic stress disorder, are related to stress. Better understanding of the related mechanisms can contribute to the development of better diagnostics and improved treatments.

More information: The article is "Prereproductive Stress to Female Rats Alters Corticotropin Releasing Factor Type 1 Expression in Ova and Behavior and Brain Corticotropin Releasing Factor Type 1 Expression in Offspring" by Hiba Zaidan, Micah Leshem, and Inna Gaisler-Salomon (DOI: 10.1016/j.biopsych.2013.04.014). The article appears in *Biological Psychiatry*, Volume 74, Issue 9 (November 1, 2013)



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