

Reversing influences of intergenerational stress offers hope for addressing public health

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In an effort to help protect children from intergenerational vulnerabilities associated with parental trauma and stress, researchers at



the Yerkes National Primate Research Center, Emory University, have shown for the first time in an animal model it is possible to reverse influences of parental stress by exposing parents to behavioral interventions following their own exposure to stress. Yerkes researcher Brian Dias, Ph.D., led the research team in this discovery that has important implications for preventing future generations from bearing influences of stressors their parents faced before the children were conceived. The study results are published online in *Biological Psychiatry*.

In the study, Dias and his research team performed olfactory, cue-based fear conditioning experiments in adult male <u>mice</u> to identify optimal strategies to break the cycle of intergenerational <u>stress</u>. They began the study with each mouse participating in one of three protocols: 1) exposed the mice to an odor; 2) trained the mice to associate an odor with a mild stressor; or 3) trained the mice to associate the odor with a mild stressor and then extinguished the fear via extinction training during which the researchers presented the odor in the absence of any stress. The researchers used Acetophenone, known for its cherry blossom-like smell, and Lyral, which has a woody scent.

By extinguishing parental fear to the two specific odors, the researchers found three key results: 1) the offspring did not show any behavioral sensitivity to the same two odors; 2) the nervous systems of the offspring did not show any structural imprints of the parental olfactory stress; and 3) the sperm of the parental male mice did not bear chemical imprints of the olfactory stress.

"These results in our mouse model are an important public health contribution because they provide optimism for applying similar interventional approaches in humans and breaking intergenerational cycles of stress," says Dias, who is an assistant research professor at the Yerkes Research Center and the Emory University School of Medicine



Department of Psychiatry and Behavioral Sciences, and a CIFAR Azrieli Global Scholar.

The current study results build upon a 2013 study in which Dias and his post-doctoral mentor at the time, Kerry Ressler MD, Ph.D., published in *Nature Neuroscience* demonstrating mice can inherit learned sensitivity to a smell. In that study, Dias trained mice to associate the <u>odor</u> of Acetophenone with a mild stressor. He determined the sperm of those mice bore chemical imprints of the olfactory stress and the offspring of those mice were more sensitive to Acetophenone as well as had more cells in their noses that processed Acetophenone.

"Our previous study was key in setting the stage for our current research to determine how we can reverse intergenerational influences of stress," says Dias. "These latest data provide our research team a platform from which we can address larger public health concerns, including the intergenerational influences of parental neglect and maltreatment during childhood. We want to know whether reversals such as what we showed in our current study can be observed after we apply interventions to populations exposed to these negative environmental influences."

More information: Hadj S. Aoued et al. Reversing behavioral, neuroanatomical, and germline influences of intergenerational stress, *Biological Psychiatry* (2018). DOI: 10.1016/j.biopsych.2018.07.028

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