Exposure to toxins makes great granddaughters more susceptible to stress

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A pyramid of sleeping rat pups. Credit: Photo: Andrea Gore.

Scientists have known that toxic effects of substances known as endocrine disrupting chemicals (EDCs), found in both natural and human-made materials, can pass from one generation to the next, but new research shows that females with ancestral exposure to EDC may show especially adverse reactions to stress.

According to a new study by researchers from The University of Texas at Austin and Washington State University, male and female rats are affected differently by ancestral exposure to a common fungicide, vinclozolin. Female rats whose great grandparents were exposed to vinclozolin become much more vulnerable to stress, becoming more anxious and preferring the company of novel females to familiar females. Males who have the same combination of ancestral exposure and stress do not have the same adverse effects.

"These results should concern us all because we have been exposed to endocrine disrupting chemicals for decades and we all go through natural challenges in life," said David Crews, the Ashbel Smith Professor of Zoology and Psychology at The University of Texas at Austin and lead author of the study. "Those challenges are now being perceived differently because of this ancestral exposure to environmental contamination."

The study was published July 22 online in the journal *Endocrinology*.

Vinclozolin is a fungicide commonly used by farmers to treat fruits and vegetables.

To test the effects of stress on rats, the researchers confined some of them to soft, warm cylinders for six hours a day for three weeks. This was done during adolescence, a developmentally sensitive time of life for rats, just as for humans. Months later, the researchers tested the brain chemistry, brain function, gene expression and behavior of the rats as adults.

They discovered that for female rats, ancestral exposure to vinclozolin alone or stress during the animal's adolescence alone had negligible effects on the rats' hormonal balance and behavior. However, the combination of ancestral exposure and stress caused the female rats to have dramatically higher levels of corticosterone (a stress hormone similar to cortisol in humans), higher expression of genes associated with anxiety and more anxious behaviors. Other research has shown that stress hormones cause degeneration of a region of the brain associated with memory and learning.

Crews said that following exposure to EDCs, what is being passed down from generation to generation is not a change in the genetic code of the animals, but rather a change in the way specific genes are expressed. Gene expression is the process by which a cell uses the genetic code to make useful products such as proteins. If a section

of a person's genetic code were a cookie recipe, gene expression would refer to how many cookies, if any, a cook makes with the recipe. The observation that changes in gene expression can be passed on to future generations has led to a new field of research known as epigenetics.

Crews and others have shown that EDCs can increase the risk in future generations for human illnesses such as autism, obesity and cardiovascular disease. Crews noted that environmental levels of EDCs are continuing to rise, as well as the rates of these diseases, particularly mental disorders.

More information: "Sexually dimorphic effects of ancestral exposure to vinclozolin on stress reactivity in rats": press.endocrine.org/doi/abs/10.1210/en.2014-1253

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