Female rats struggle to find their way in BPA study

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Information from Cheryl Rosenfeld's study will allow researchers to better

compare the effects of fixed doses of BPA on the brain, various cognitive behaviors, reproduction and fertility, accumulation of fat tissue, heart disease, the immune system, and several types of cancers. Credit: Roger Meissen, Bond Life Sciences Center

Despite concerns about bisphenol A (BPA), academic and regulatory scientists have yet to reach a consensus on BPA's safety.

The National Institute of Environmental Health Sciences (NIEHS), the National Toxicology Program (NTP), the Food and Drug Administration and independent university researchers are working together to change that.

Five years after the Consortium Linking Academic and Regulatory Insights on BPA Toxicity, or CLARITY-BPA for short—launched, results are beginning to come in. This new information will allow researchers to better compare the effects of fixed doses of BPA on the brain, various cognitive behaviors, reproduction and fertility, accumulation of fat tissue, heart disease, the immune system, and several types of cancers.

"The idea of this Consortium is to examine the potential systems that have been previously suggested to be affected by BPA," said Cheryl Rosenfeld, an associate professor of biomedical sciences at the University of Missouri and one of twelve researchers involved in the project.

Rosenfeld's group looked at spatial navigation learning and memory. They found that prenatal exposure to BPA could potentially hinder the ability of female rats to learn to find their way through a maze. This effect was not seen in male rats.

Approved by the FDA in the early 1960s, BPA can be found in a wide variety of products, including plastic food and drink containers with recycle codes 3 or 7, water and baby bottles, toys, the linings of metal cans and water pipes, even patient blood and urine samples.

BPA has structural similarities to estrogen and can potentially act as a weak estrogen in the body.

In Rosenfeld's experiment, researchers at the National Center for Toxicology Research gave pregnant rats a fixed dose of BPA every day: a low, medium, or high dose.

After the baby rats were born, researchers continued to dose the babies, both male and female, according to what their mothers had received.

When these rats reached three months old, they were tested in a circular maze with twenty possible exit holes, one of which was designated as the correct escape hole. Every day for seven days, researchers tested the rats' abilities to solve the maze in five minutes and timed them as they ran.

Rats solve mazes in three ways, Rosenfeld said.

They can run through the labyrinth in a spiral pattern, hugging the outer walls, and work their way in until they find the correct exit hole in what is called a serial search strategy.

Or they might move aimlessly in the maze using an indirect search strategy, Rosenfeld said. "In this case, the rats seemingly find the correct escape hole by random chance."

Lastly, they can travel directly from the center of the maze to the correct escape hole. The third strategy is considered the most efficient method because the rats find their way swiftly, Rosenfeld said.

Sarah Johnson, a graduate student and first author on the paper, assessed each rat's performance in the maze using a three-point tracking program that recognizes the rat's nose, body, and tail.

Using the program, Johnson measured their performances in terms of the total distance traveled, the speed at which the rat ran the maze, how long it took the rats to solve the maze (latency), and how often the rat sniffed at an incorrect hole.

The last two parameters are considered the best gauges of spatial navigation learning and memory.

"What you expect to see is that they should start learning where that correct escape hole is," Rosenfeld said. "Thus, their latency and sniffing incorrect holes should decrease over time."

Rosenfeld's group found that female rats that had been exposed to the highest dose of BPA since fetal development were less likely to find the escape hole than rats that hadn't been exposed to BPA.

As for how this study may translate to people, Rosenfeld said, "the same brain regions control identical behaviors in rodents and humans."

She considers it a starting point for setting up future experiments that take into consideration sex differences in cognitive behaviors and neurological responses to BPA.

Immediate next steps for the Rosenfeld group include analyzing tissue collected from the brains of rats that had undergone maze testing. Rosenfeld's team of researchers will measure DNA methylation and RNA expression in the brain to determine which genes might be involved in navigational learning memory. Their overarching goal is to determine the molecular basis underlying the changes in observed sex-

and dose-dependent behaviors.

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