BPA and BPS affect embryonic brain development in zebrafish

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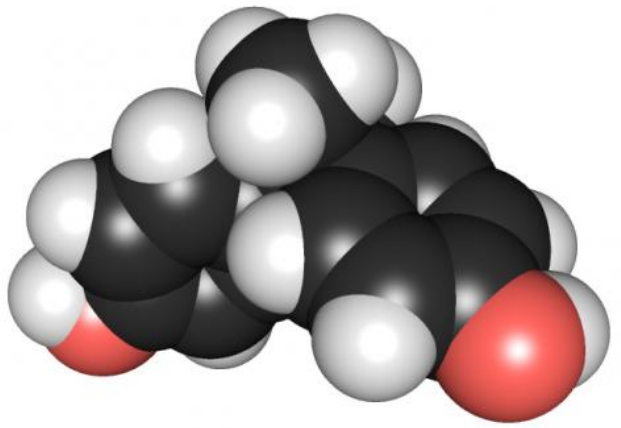

3D chemical structure of bisphenol A. Credit: Edgar181 via Wikimedia Commons

Bisphenol A, known as BPA, is produced in massive quantities around the world for use in consumer products, including household plastics. In response to public concerns, many manufacturers have replaced BPA with a chemical called bisphenol S (BPS), which is often labeled as "BPA-free" and presumed to be safer.

In a study published Monday, Jan. 12, in the *Proceedings of the National Academy of Sciences* (*PNAS*), researchers in Deborah Kurrasch's lab at the University of Calgary have provided evidence that BPA and BPS cause alterations in brain development leading to hyperactivity in zebrafish.

"I was actually very surprised at our results. This was a very, very, very low dose, so I didn't think using a dose this low could have any effect," says Kurrasch, PhD, a researcher in the University of Calgary's Cumming School of Medicine and corresponding author on the paper.

For the study, Kurrasch worked with University of Calgary researcher Hamid Habibi, PhD, and Cassandra Kinch, a PhD student, to expose zebrafish embryos to concentrations of the chemicals at levels found in the Bow and Old Man rivers of Alberta, Canada. By doing this, exposure to BPA and BPS changed the timing when neurons were formed in the brains of the zebrafish.

"These findings are important because they support that the prenatal period is a particularly sensitive stage, and reveals previously unexplored avenues of research into how early exposure to chemicals may alter brain development, " says Kinch.

"In the second trimester, brain cells become the specialized neurons that make up our brain. What we show is that the zebrafish exposed to BPA or BPS were getting twice as many neurons born too soon and about half as many neurons born later, so that will lead to problems in how the neurons connect and form circuits," says Kurrasch, a member of the Alberta Children's Hospital Research Institute and the department of medical genetics.

Researchers discovered the number of neurons generated in the developing zebrafish brains increased by 180 per cent compared with unexposed fish. They also learned that BPS increased the number of neurons by 240 per cent in similar experiments. The result was a change in behaviour, with the fish demonstrating greater hyperactivity later in life.

Another surprise finding was that zebrafish receptors targeted by BPA and BPS to mediate this early neuronal birth in zebrafish brains were androgen receptors. Assumptions based on numerous reports postulated that BPA and BPS modulate normal physiology by mimicking the endogenous sex steroid estrogen, and not testosterone.

"Finding the mechanism linking low doses of BPA to adverse brain development and hyperactivity is almost like finding a smoking gun," says Habibi, a professor of environmental toxicology and comparative endocrinology in the Faculty of Science.

Although further research is needed to explore that link and the potential effect on human brains developing in the womb, Kurrasch says the findings add weight to other studies suggesting pregnant women should try to limit their exposure to items containing bisphenols. The evidence also supports removing all bisphenols and structurally similar chemicals from consumer products, she says.

Zebrafish are a widely accepted biomedical model for understanding embryonic brain development. About 80 per cent of the genes found in people have a counterpart in zebrafish - and possess very similar developmental processes as humans.

More information: Low-dose exposure to bisphenol A and replacement bisphenol S induces precocious hypothalamic neurogenesis in embryonic zebrafish, *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1417731112

Provided by University of Calgary

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