BPA may affect the developing brain by disrupting gene regulation

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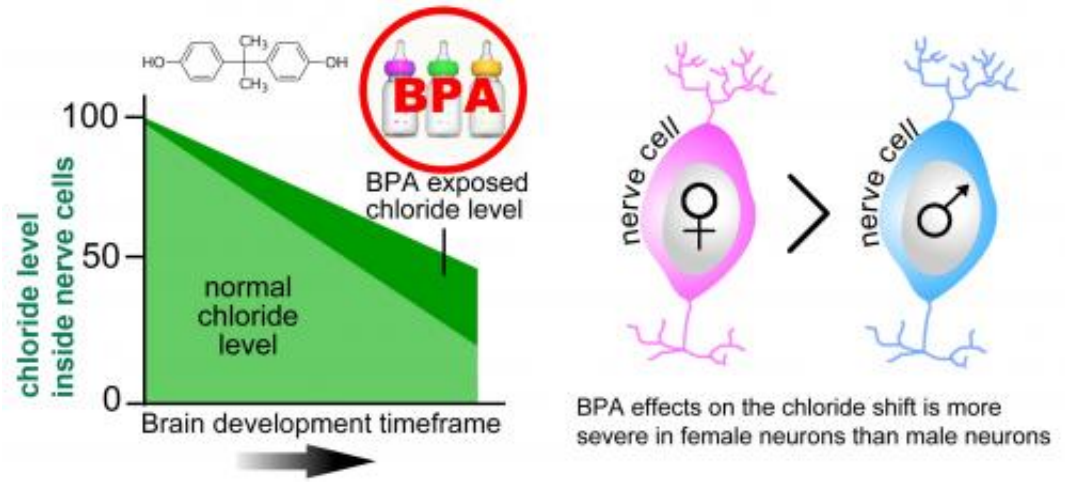

Exposure to BPA may disrupt development of the central nervous system by slowing down the removal of chloride from neurons. As an organism matures and the brain develops, chloride levels inside nerve cells drop. However, when exposed to BPA, the chloride is removed more slowly from neurons. Researchers also found female neurons to be more susceptible to the effects of BPA. Credit: Michele Yeo, Duke Medicine

Environmental exposure to bisphenol A (BPA), a widespread chemical found in plastics and resins, may suppress a gene vital to nerve cell function and to the development of the central nervous system, according to a study led by researchers at Duke Medicine.

The researchers published their findings - which were observed in

cortical neurons of mice, rats and humans - in the journal Proceedings of the National Academy of Sciences on Feb. 25, 2013.

"Our study found that BPA may impair the development of the central nervous system, and raises the question as to whether exposure could predispose animals and humans to neurodevelopmental disorders," said lead author Wolfgang Liedtke, M.D., PhD, associate professor of medicine/neurology and neurobiology at Duke.

BPA, a molecule that mimics estrogen and interferes with the body's endocrine system, can be found in a wide variety of manufactured products, including thermal printer paper, some plastic water bottles and the lining of metal cans. The chemical can be ingested if it seeps into the contents of food and beverage containers.

Research in animals has raised concerns that exposure to BPA may cause health problems such as behavioral issues, endocrine and reproductive disorders, obesity, cancer and immune system disorders. Some studies suggest that infants and young children may be the most vulnerable to the effects of BPA, which led the U.S. Food and Drug Administration to ban the use of the chemical in baby bottles and cups in July 2012.

While BPA has been shown to affect the developing nervous system, little is understood as to how this occurs. The research team developed a series of experiments in rodent and human nerve cells to learn how BPA induces changes that disrupt gene regulation.

During early development of neurons, high levels of chloride are present in the cells. These levels drop as neurons mature, thanks to a chloride transporter protein called KCC2, which churns chloride ions out of the cells. If the level of chloride within neurons remains elevated, it can damage neural circuits and compromise a developing nerve cell's ability to migrate to its proper position in the brain.

Exposing neurons to minute amounts of BPA alters the chloride levels inside the cells by somehow shutting down the Kcc2 gene, which makes the KCC2 protein, thereby delaying the removal of chloride from neurons.

MECP2, another protein important for normal brain function, was found to be a possible culprit behind this change. When exposed to BPA, MECP2 is more abundant and binds to the Kcc2 gene at a higher rate, which might help to shut it down. This could contribute to problems in the developing brain due to a delay in chloride being removed.

These findings raise the question of whether BPA could contribute to neurodevelopmental disorders such as Rett syndrome, a severe autism spectrum disorder that is only found in girls and is characterized by mutations in the gene that produces MECP2.

While both male and female neurons were affected by BPA in the studies, female neurons were more susceptible to the chemical's toxicity. Further research will dig deeper into the sex-specific effects of BPA exposure and whether certain sex hormone receptors are involved in BPA's effect on KCC2.

"Our findings improve our understanding of how environmental exposure to BPA can affect the regulation of the Kcc2 gene. However, we expect future studies to focus on what targets aside from Kcc2 are affected by BPA," Liedtke said. "This is a chapter in an ongoing story."

Provided by Duke University Medical Center