

Study shows how food preservatives may disrupt human hormones and promote obesity

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Can chemicals that are added to breakfast cereals and other everyday products make you obese? Growing evidence from animal experiments

suggests the answer may be "yes." But confirming these findings in humans has faced formidable obstacles - until now.

A new study published today in *Nature Communications* details how Cedars-Sinai investigators developed a novel platform and protocol for testing the effects of chemicals known as [endocrine disruptors](#) on humans.

The three chemicals tested in this study are abundant in modern life. Butylhydroxytoluene (BHT) is an antioxidant commonly added to breakfast cereals and other foods to protect nutrients and keep fats from turning rancid; perfluorooctanoic acid (PFOA) is a polymer found in some cookware, carpeting and other products; and tributyltin (TBT) is a compound in paints that can make its way into water and accumulate in seafood.

The investigators used hormone-producing tissues grown from human stem cells to demonstrate how chronic exposure to these chemicals can interfere with signals sent from the digestive system to the brain that let people know when they are "full" during meals. When this signaling system breaks down, people often may continue eating, causing them to gain weight.

"We discovered that each of these chemicals damaged hormones that communicate between the gut and the brain," said Dhruv Sareen, PhD, assistant professor of Biomedical Sciences and director of the Induced Pluripotent Stem Cell Core Facility at the Cedars-Sinai Board of Governors Regenerative Medicine Institute. "When we tested the three together, the combined stress was more robust."

Of the three chemicals tested, BHT produced some of the strongest detrimental effects, Sareen said.

While other scientists have shown these compounds can disrupt hormone systems in laboratory animals, the new study is the first to use human pluripotent stem cells and tissues to document how the compounds may disrupt hormones that are critical to gut-to-brain signaling and preventing obesity in people, Sareen said.

"This is a landmark study that substantially improves our understanding of how endocrine disruptors may damage human hormonal systems and contribute to the obesity epidemic in the U.S.," said Clive Svendsen, PhD, director of the institute and the Kerry and Simone Vickar Family Foundation Distinguished Chair in Regenerative Medicine. More than one-third of U.S. adults are considered to be obese, according to federal statistics.

The new testing system developed for the study has the potential to provide a much-needed, safe and cost-effective method that can be used to evaluate the health effects of thousands of existing and new chemicals in the environment, the investigators say.

For their experiments, Sareen and his team first obtained blood samples from adults, and then, by introducing reprogramming genes, converted the cells into induced [pluripotent stem cells](#). Then, using these [stem cells](#), the investigators grew human epithelium tissue, which lines the gut, and neuronal tissues of the brain's hypothalamus region, which regulates appetite and metabolism.

The investigators then exposed the tissues to BHT, PFOA and TBT, one by one and also in combination, and observed what happened inside the cells. They found that the chemicals disrupted networks that prepare signaling hormones to maintain their structure and be transported out of the cells, thus making them ineffective. The chemicals also damaged mitochondria - cellular structures that convert food and oxygen into energy and drive the body's metabolism.

Because the [chemical](#) damage occurred in early-stage "young" [cells](#), the findings suggest that a defective hormone system potentially could impact a pregnant mother as well as her fetus in the womb, Sareen said. While other scientists have found, in animal studies, that effects of endocrine disruptors can be passed down to future generations, this process has not been proved to occur in humans, he explained.

More than 80,000 chemicals are registered for use in the U.S. in everyday items such as foods, personal care products, household cleaners and lawn-care products, according to the National Toxicology Program of the U.S. Department of Health and Human Services. While the program states on its website that relatively few chemicals are thought to pose a significant risk to human health, it also states: "We do not know the effects of many of these chemicals on our health."

Cost and ethical issues, including the health risk of exposing human subjects to possibly harmful substances, are among the barriers to testing the safety of many chemicals. As a result, numerous widely used compounds remain unevaluated in humans for their health effects, especially to the hormone system.

"By testing these chemicals on actual human tissues in the lab, we potentially could make these evaluations easier to conduct and more cost-effective," Sareen said.

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