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Exposure to environmental chemicals in the womb reprograms the rodent brain to disrupt reproduction

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Prenatal exposure to the environmental contaminants polychlorinated biphenyls, or PCBs, causes long-term changes to the developing brain that have adverse effects on reproductive function later in life, a new study finds. Results will be presented Saturday at The Endocrine Society's 94th Annual Meeting in Houston.

The study used rats, whose genes and molecules in the hypothalamus—the region of the brain important for reproductive function—are virtually identical to those in humans, according to co-author Andrea Gore, PhD, professor of pharmacology and toxicology at the University of Texas at Austin. These PCB-induced brain changes delayed puberty in male offspring and disrupted reproductive cycles in adult female offspring, she reported.

In addition, the researchers identified five genes that PCB disrupted. Gore said that all five are critical to the normal hypothalamic control of reproduction.

"By identifying five genes that are most perturbed by PCBs in the developing rat brain, we may one day be able to develop targeted interventions or therapeutics for reproductive problems, focusing on these molecular endpoints," Gore said.

PCBs are industrial chemicals used in many plastics, insulation

materials, floor finishes and electrical equipment before their ban in 1979, according to the U.S. Environmental Protection Agency. Still present in air, water and soil, PCBs are known endocrine disruptors, compounds in the environment that interfere with hormones and their actions in the body.

In this study, funded by the National Institutes of Health, the investigators exposed rats late in pregnancy to low levels of a mixture of PCBs, as one might encounter in the environment, Gore said. Control rats received an inactive substance. After birth, the offspring had monitoring throughout their life to determine if their reproductive development was disrupted. The research team also examined the brains of some of the animals at different ages to determine whether and how prenatal exposure affected gene expression in the hypothalamus.

Effects on gene expression depended on age, the scientists found. Effects were most profound on day 15 in the life of males and day 45 in females, corresponding roughly to childhood and after puberty, respectively.

In females, PCB exposure also resulted in altered reproductive cycles in adulthood, and in males, puberty was delayed, compared with the offspring of nonexposed control rats.

Depending on age and sex, five genes in the hypothalamus were affected by PCB treatment: Kiss1 (which stands for kisspeptin 1), Kiss1r (kisspeptin 1 receptor), Gper (G-protein-coupled estrogen receptor), Tac2 (neurokinin B) and Pdyn (prodynorphin). These genes are known to be very important for the control of reproduction. However, because the effects of PCBs on the brain were specific to age, sex and developmental stage, Gore suggested that PCBs might alter development of the hypothalamus, rather than just altering individual genes.

"We can look gene by gene, but it's the big picture of how these genes are affected in concert that's important to development," she said.

Provided by The Endocrine Society