Placental accumulation of flame retardant chemical alters serotonin production in rats

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A North Carolina State University-led research team has shown a connection between exposure to a widely used flame retardant chemical mixture and disruption of normal placental function in rats, leading to altered production of the neurotransmitter serotonin. Evidence of endocrine, inflammatory and neurotransmitter signaling pathway disruption was also identified in the placentas. These data show, for the first time, that flame retardants can have sex-specific effects on placental functions critical for brain development.

FireMaster 550 (FM550) is a flame-retardant mixture used in foam-based baby products and furniture. First identified by collaborating researchers at Duke University nearly a decade ago, it was developed to replace PBDEs, a class of fire retardants being phased out of use because of safety concerns. The interuniversity research team recently demonstrated that FM 550 is an endocrine disruptor, with developmental exposure affecting anxiety- and hyperactivity-related behaviors in rats in sex-specific ways. They also showed that three of the FM 550 components dose-dependently accumulate in placenta, with levels higher in male-associated placentas.

Heather Patisaul, professor of biology at NC State, and her graduate student, Kylie Rock, wanted to know if FM 550 could sex-specifically impact the developing brain by altering placental function. They exposed pregnant female rats to 0, 300, or 1,000 micrograms of the chemical mixture per day for 10 days during gestation. The team used a variety of tools, including metabolomics and high throughput RNA sequencing, to examine the placentas and the developing brains of the offspring to identify possible pathways impacted by the chemical mixture. The dose levels used were all below the 50 milligrams per day currently considered safe.

In rat offspring exposed to 300 or 1,000 micrograms of FM550, the researchers found dose-dependent upregulation of multiple genes related to inflammatory and endocrine processes. Some were sex-specific. For example, levels of estrogen and androgen receptors were upregulated in female-associated placentas while inflammatory markers associated with increased risk of behavioral disorders were upregulated in placentas from both sexes. Additionally, the ratio of the serotonin metabolite 5-HIAA to serotonin was reduced in female placentas and fetal forebrains compared to the control group, demonstrating disruption of neurotransmitter production in the placenta and developing brain.

"We found that exposure to FM 550 can impact multiple placental pathways critical for early brain development, which is particularly concerning given that it is commonly found in baby products and furniture," Patisaul says. "Most intriguingly, we found some evidence that placental serotonin production is altered. This is important because in early development the placenta is the sole source of serotonin for the developing forebrain."

More information: Kylie R Baldwin et al, EDC IMPACT: Molecular effects of developmental FM 550 exposure in Wistar rat placenta and fetal forebrain, *Endocrine Connections* (2018). DOI: 10.1530/EC-17-0373

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