Flame-retardant exposure increases anxiety, affects social behaviors in prairie vole

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New research led by North Carolina State University has shown that early life exposure to a commonly used flame-retardant mixture increases anxiety and affects socioemotional behaviors in prairie voles, particularly in females. The work supports the hypothesis that chemical flame retardants can adversely affect neurological development and social behavior.

FireMaster 550 (FM550) is a flame-retardant mixture used in foam-based baby products and furniture. First identified nearly a decade ago, it was developed to replace PBDEs, a class of fire retardants being phased out because of safety concern

"There is concern that early life exposure to flame retardants is contributing to neurodevelopmental disorders," says Heather Patisaul, professor of biology at NC State and corresponding author of a paper describing the work. "We decided to look at the effects of exposure on social and emotional behavior using a prairie vole model. Prairie voles are socially monogamous animals that partner for life and co-parent offspring. They are commonly used in neuroscience studies that address social behavior, and so were a good choice for this study."

In collaboration with NC State graduate student Sagi Enicole Gillera and colleagues from NC State and Duke University, Patisaul exposed pregnant prairie voles to 0, 500, 1000, or 2000 micrograms of FM 550 via subcutaneous injections throughout gestation. Their offspring were directly exposed to FM 550 beginning the day after birth until weaning. The adult male and female offspring were then subjected to multiple behavior tests that assess anxiety, memory and sociability, including partner preference.

"Normally, voles are highly social and prefer to spend time with other animals, particularly their partners," Patisaul says.

But voles exposed to FM 550, particularly the females, were less social. For example, when given an opportunity to spend time with a female stranger or spend time alone, females exposed to FM 550 avoided the stranger. The effects were evident at the lowest dose and more pronounced at higher doses. Exposed males also had social deficits, with males in all three dose groups failing to show a partner preference, and the males in the two lower dose groups showing social avoidance.

Additionally, females exposed to FM 550 at even the lowest dose were also much more anxious and less likely to explore new spaces. "Normally, female prairie voles are very exploratory and less anxious than males," Patisaul says. "In tests like the open field test, where they are introduced to an empty, open box, females are more likely than males to explore the middle area, which is considered 'risky,' but exposed females remained in safe areas instead."

The researchers tested blood from a separate subset of similarly exposed voles to measure the levels of FM 550 chemicals in the body four hours

after the final exposure. This information is important for determining whether effects on the human brain are possible below the range currently considered safe for humans.

"FM 550 contains two different types of flame-retardant chemicals, brominated and organophosphates," Patisaul says. "We detected the primary brominated flame retardant in both male and female voles, but did not detect many organophosphates, possibly due to their being metabolized more quickly.

"This is the first study in mammals to show that developmental exposure to these flame retardants affects social behavior, and it supports the hypothesis that developmental exposure to flame retardants can impact the social brain. Future studies will probe the possible mechanisms by which these effects arise."

The research appears in *Neurotoxicology and Teratology*, and was funded by the Department of Defense (grant AR 160055) and the National Institute of Environmental Health Sciences. NC State graduate student Sagi Enicole Gillera is first author. NC State associate professor of biological sciences David Reif, graduate student William Marinello, lab manager Brian Horman, and Duke University Nicholas School of the Environment professor Heather Stapleton and graduate students Allison Phillips and Matthew Ruis also contributed to the work.

More information: Sagi Enicole A. Gillera et al, Sex-specific effects of perinatal FireMaster® 550 (FM 550) exposure on socioemotional behavior in prairie voles, *Neurotoxicology and Teratology* (2019). DOI: 10.1016/j.ntt.2019.106840