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[Background and Aim]
Phosphate esters are added to consumer and industrial products in order to reduce flammability. Very limited studies have been conducted to examine the toxicity of phosphate ester flame retardants in next generation. In this study, we aim to examine the effects of gestational and lactational exposure to a phosphate ester flame retardant having estrogenic activity on memory function and related gene expressions in adult mice.
[Methods]
C57BL/6J pregnant mice (gestational day 11) were purchased from CLEA, Japan (Tokyo, Japan). Offspring of male and female mice were given the phosphate ester flame retardant having estrogenic activity (XP) subcutaneously daily from embryonic day 14 to delivery to dam and from delivery to postnatal day 9 to pups. Dams were given XP at the dose of 500 µg/0.2 ml/day during gestational period and pups were given XP at the dose of 50 µg/20 µl/day during postnatal period. The control mice were given sesame oil on the same schedule. We performed the novel object recognition test composed of 2 habituation phases, one training phase and one test phase in 13 week-old male and female mice. After completion of behavioral test, the hippocampus from each mouse was removed and examined for the expression level of memory function-related genes using real-time RT-PCR.
[Results]
Body and brain weights were not different between groups. Regarding the novel object recognition test, the discrimination ability between novel and familiar objects was significantly impaired in both male and female mice exposed to XP. The mRNA expression levels of memory function-related genes such as the N-methyl-D aspartate (NMDA) receptor subunits NR1 and NR2B, and their signaling pathway genes Ca2+/calmodulin-dependent protein kinase (CaMK)-IV and cAMP response

element-binding (CREB)-1 were significantly increased in the hippocampus of the mice of both sexes exposed to XP.

[Discussion and Conclusion]

Our results indicate the possibility that the developmental exposure to a phosphate ester flame retardant impairs novel object recognition ability in mice by modulating the expression level of NMDA receptors and related signaling pathway genes in the hippocampus. Further studies are required to evaluate whether XP directly enters the developing brain and how XP impairs neuronal development.

に関する研究）