

## **Effects of Volatile Organic Compound on Sexual Differentiation of the Brain**

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Mammalian brain is sexually differentiated under the influence of sex steroid on developing periods. In perinatal rats, a large amount of testosterone is produced by testes, and estradiol, which is locally synthesized from testosterone by aromatase in the brain, is implicated in the sexual differentiation of the brain. In this study, we attempted to determine whether developmental exposure to toluene, a volatile organic compound widely used as a solvent, affects the levels of sex steroids involved in the sexual differentiation of the brain. Plasma testosterone concentrations in male but not female fetuses were significantly decreased by maternal toluene exposure during late pregnancy, although there was significant sex difference in the testosterone levels with or without the toluene exposure. Estradiol content of the brain was also significantly decreased in male but not female fetuses by the toluene exposure. Accordingly, sex difference in the estradiol level was eliminated in fetal offspring of toluene-exposed pregnant rats. Maternal toluene exposure significantly reduced the protein level of aromatase in the brain of male fetuses, suggesting that decrease in the brain estradiol level is due to the negative effects of toluene on aromatase. In addition, we recently showed that estradiol modulates the expression of apoptosis-related molecules (Bcl-2 and Bax), which are involved in the formation of the sexually dimorphic nucleus. These findings suggest that maternal toluene exposure adversely affects the levels of sex steroids of male offspring. Alteration of sex steroid levels with toluene exposure may have an influence on the processes of the sexual differentiation of the brain.