Bcl-2 gene family expression in the brain of rat offspring after gestational and lactational dioxin exposure

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Abstract

Recent epidemiological studies have shown that dioxin, a persistent organic pollutant, is related to cognitive and behavioral abnormalities in the offspring of exposed cohort. In order to investigate the possible impact of dioxin in survival gene expression during brain development, we established an animal model of gestational and lactational dioxin-exposed rat offspring. The expressions of dioxin-responsive gene cytochrome P450 1A1 (CYP1A1), apoptotic gene Bax, and anti-apoptotic genes Bcl-2 and Bcl-xL were examined in rat liver and brains using Western blot analysis and RT-PCR. The results showed that treatment of pregnant rats with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) (2 μg/kg body weight through oral delivery) at gestation day 15 resulted in an increase of Bcl-xL in offspring male liver and cerebral cortex, but a decrease in female offspring. In contrast, the expression of Bcl-xL in the cerebellum was decreased in male, but increased in female. Bcl-2, another anti-apoptotic gene, was also downregulated in PO female liver, cerebral cortex, but was not observed in male. In the 4-month-old offspring, however, the Bcl-2 protein levels in the liver and cerebellum of both male and female pups were higher in the TCDD group as compared with the control group. However, the Bcl-2 level in the cerebral cortex of TCDD-treated groups was higher than the control group only in female but not male offspring at 4 months old. The expression of Bax showed no significant changes upon TCDD exposure at PO stage, but was significantly reduced in the 4-month-old male cortex. These results indicate that early exposure of dioxin could affect the development of certain brain regions with gender difference, in terms of its differential effect on expressions of Bcl-xL, Bcl-2, and Bax.