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PC12 and Cortical Neuron cell Death by Bisphenol A Through ERK Signal Pathway : Role of Estrogen-Receptor β

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Bisphenol A (BPA) mimics estrogen and its activity is one third to one quarter that of estradiol. BPA, an ubiquitous environmental contaminent has been shown to cause development reproductive toxicity and carcinogenic effect. BPA may do physiological action through ERα and ERβ which are expressed in central nerve system. We previously found that expose of BPA to immature mice resulted in behavial alternation, suggesting that overexposure of BPA could be neurotoxic. In this study, to further investigate molecular mechanisms by which BPA induced behaviral alternation, we examined whether BPA may interfere differentiation of undifferentiated neuronal cells, thereby modify the behaviral development. BPA concentration dependently increased vulnerability (increased cell viability and decreased differentiation) of undifferentiated PC12 cells and undifferentiated neurocortical cells isolated postnatal (Day 1) rat brain. These effects were prevented in the presence of estrogen receptor-beta antagonists, ICI 182, 780 and Tamoxifen. The greater increase of cell vulnerability was also found in the PC12 cells overexpressing ER-β. The increased vulnerabilty by BPA were mediated by phosphorylation of ERK. Activation of ERK signaling was further augumented in the PC12 cells overexpressing ER-β. The present data show that BPA dose dependently increased neuronal cell vulnerability through activation of ERK signals, and this effect was associated with ER-β receptor. This study demonstrated that exposure of certain level of BPA may interfere normal neuronal cell differentiation, and thereby alter behavial development.

Keyword : Cytotoxicity; estrogen-receptor β; bisphenol A;