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Prenatal xenobiotic exposure and intrauterine hypothalamus-pituitary-adrenal axis programming alteration

Xu Dan¹ and **Wang Hui**¹ ¹Wuhan University, China

The hypothalamic-pituitary-adrenal (HPA) axis is one of the most important neuroendocrine axes and plays an important role in stress defense responses before and after birth. Prenatal exposure to xenobiotics, including environmental toxins (such as smoke, sulfur dioxide and carbon monoxide), drugs (such as synthetic glucocorticoids), and foods and beverage categories (such as ethanol and caffeine), affects fetal development indirectly by changing the maternal status or damaging the placenta. Certain xenobiotics (such as caffeine, ethanol and dexamethasone) may also affect the fetus directly by crossing the placenta into the fetus due to their lipophilic properties and lower molecular weights. All of these factors probably result in intrauterine programming alteration of the HPA axis, which showed a low basal activity but hypersensitivity to chronic stress. These alterations will, therefore, increase the susceptibility to adult neuropsychiatric (such as depression and schizophrenia) and metabolic diseases (such as hypertension, diabetes and non-alcoholic fatty liver disease). The "over-exposure of fetuses to maternal glucocorticoids" may be the main initiation factor by which the fetal HPA axis programming is altered. Meantime, xenobiotics can directly induce abnormal epigenetic modifications and expression on the important fetal genes (such as hippocampal glucocorticoid receptor, adrenal steroidogenic acute regulatory protein, et al) or damage by in situ oxidative metabolism of fetal adrenals, which may also be contributed to the programming alteration of fetal HPA axis.

Biography

Xu Dan has completed her PhD in 2010 from basic medical school of Wuhan University. Her research work focus on xenobiotics developmental toxicology. She has published 12 papers in journals related to the field of toxicology.

xuyidan70188@163.com

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