Cadmium-induced oxidative stress damage causes neuron cells apoptosis through JNK/mitochondria-dependent/endoplasmic reticulum stress pathways

Ling-Mei Tsai[1], To-Jung Tseng [2], Tien-Hui Lu[1], Dong-Zong Hung[3], Chin-Chuan Su[4], Cheng-Chieh Yen[5], Yi-Chang Su[6], Chun-Fa Huang[6], Shing-Hwa Liu[7], Ya-Wen Chen[8]

[1]Graduate Institute of Basic Medical Science, China Medical University, Taichung, Taiwan
[2]Department of Anatomy, China Medical University, Taichung, Taiwan
[3]Toxicology Center, China Medical University Hospital, Taichung, Taiwan
[4]Department of Otorhinolaryngology, Head and Neck Surgery, Changhua Christian Hospital, Changhua, Taiwan
[5]Department of Occupational Safety and Health, Chung Shan Medical University, Taichung, Taiwan
[6]School of Chinese Medicine, China Medical University, Taichung, Taiwan
[7]Institute of Toxicology, National Taiwan University, Taipei, Taiwan
[8]Department of Physiology, China Medical University, Taichung, Taiwan

Abstract

Cadmium (Cd), a well-known toxic metal, is an important pollutant throughout the world. In mammalian, exposure to Cd causing injuries of kidney, liver and osseous system has been demonstrated. Although some studies have shown the possible connections between neurodegenerative disorders and Cd exposure, the toxic effects of Cd on neuron cell are still unclear. In this study, we designed to investigate the effects and possible mechanisms of Cd-induced neuron cell death. Our results found that after exposed to Cd in cultured Neuro-2a cells for 24 h obviously decreasing the viable cells ,mitochondrial membrane potential, and led to glutathione depletion in a dose-dependent manner with a range from 1 to 20 M, which accompanied by a marked Cd accumulation in cytosol. Cd also induced the protein phosphorylation of

JNK, the disruption of mitochondrial function, Bcl-2 down-regulation, Bax up-regulation, the activation of PARP and caspase cascades, displaying features of mitochondria-dependent apoptotic signaling pathways. Furthermore, exposed Neuro-2a cells to Cd could trigger endoplasmic reticulum (ER) stress as indicated by the alterations of glucose-regulated protein (GRP) 78, CHOP, caspase-12, and calpain expression. *N*-acetylcysteine could effectively reverse these Cd-induced cellular responses. Altogether, our data suggest that Cd-induced oxidative stress causes neuron cell apoptosis via JNK/mitochondria-dependent and ER stress-triggered signal pathways.

Keywords: Cadmium; Neurotoxicity; Apoptosis; Oxidative stress; JNK; ER stress