IJAE
Vol. 122, n. 1 (Supplement): 32, 2017
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Effects of the endoplasmic reticulum signaling pathway on cadmium-induced impairment of the blood brain barrier

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Due to its high permeability to blood-brain barrier (BBB), cadmium (Cd) has been regarded as a possible etiological factor for human neurodegenerative diseases, such as Parkinson's disease, Alzheimer's disease, and Huntington's disease [1]. However, the mechanism underlying cadmium-induced BBB permeability remains unclear. In this study, we investigated the effect of Cd in RBE4 cells (rat brain endothelial cells) and delineated the signaling pathway that, triggering endoplasmic reticulum (ER) stress and caspase 3 activation, leads to cytoskeleton disorganization and tight junctions disassembly.

Our results demonstrate a possible downstream pathway mediated through the Cd-dependent ER stress, assessed by the cytoplasmic expression of an ER protein GRP78, and the consequent caspase-3 activation that results in an extracellular ATP increase, which in turns induces a dislocation, evaluated by immunofluorescent staining, of Zonula Occludens-1 (ZO-1), a tight junction protein, and F-actin.

These findings, whereby Cd-induced permeabilization of BBB through a ER stress-dependent pathway on endothelial cells represent a possible novel mechanism of action for Cd that could explain, at least in part, the Cd-related central effects.

References

[1] Monroe et al. (2006) Cadmium blocks receptor-mediated Jak/STAT signaling in neurons by oxidative stress. Free Radic Biol Med 41: 493-502.

Keywords

Cadmium neurotoxicity, blood brain barrier, ER stress, caspase-3 activation, tight junctions dislocation