Effect of Cadmium on Neuronal Differentiation

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Environmental risk factors can induce neurotoxicity, leading to disorders in both neuronal structure and function. Structural disorders encompass neurons or glia cell cytotoxicity, developmental inhibition, and eventual degeneration. Cadmium (Cd) is a well-documented environmental hazard causing global public concern due to its high environmental impact as it can contaminate soil, water, and air. Although heavy metal exposure has been linked to neurotoxicity, the underlying mechanisms remain to be better understood. This study focuses on examining whether exposure to low levels of Cd affects neuronal differentiation and identifying the underlying molecular mechanisms. Employing a commonly used mouse neuroblast cell line Neuro-2a (N2A) that is commonly used as a neurite outgrowth model, we were able to find the following data: (I) A low dose of cadmium at the μM level, which mimics environmental cadmium exposure, significantly inhibited N2A cell neurite outgrowth while showing little direct cytotoxicity. (II) Exposure to Cd increased the level of activated β-catenin (i.e. non-phosphorylated β-catenin). While exposure to an activator of Wnt/β-catenin showed a similar increase of activated β-catenin when compared to Cd. (III) An activator of the Wnt/β-catenin signaling pathway reduced the neurite outgrowth to a similar extent as the cadmium exposure. Moreover, the co-treatment of the Wnt/β-catenin activator and Cd further reduced the neurite outgrowth. The results collectively suggest that cadmium inhibits neuron differentiation by activating the Wnt/β-catenin signaling pathway.