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N-acetyl-L-cysteine and Mn^{2+} attenuate Cd^{2+}-induced disturbance of the intracellular free calcium homeostasis in cultured cerebellar granule neurons

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H I G H L I G H T S

Viability of cultured cerebellar neurons decreases as a result of cadmium toxicity.

Mn^{2+} and NAC diminish toxic effects of cadmium.

Mn^{2+} and NAC attenuate intracellular calcium increase in cultured neurons.

Cadmium induces ultrastructural alterations in cultured cerebellar neurons.

NAC attenuates cadmium-induced ultrastructural alterations.

Abstract

Cadmium is a highly toxic heavy metal that is capable of accumulating in the body via direct exposure or through the alimentary and respiratory tract, leading to neurodegeneration. In this article, we show that the application of $CdCl_2$ (0.001–0.005 mM) for 48 h induced high dose-dependent death rate of cultured cerebellar granule neurons (CGNs). Unlike Trolox or vitamin E, antioxidant N-acetyl-L-cysteine (NAC, 1 mM) and Mn^{2+} (0.0025-0.005mM) significantly protected CGNs from this toxic effect. Using Fluo-4 AM, measurements of intracellular calcium ions demonstrated that 24 h-exposure to Cd^{2+} induced intensive increase of Fluo-4 fluorescence in neurons accompanied by mitochondria swelling. These data imply that the cadmium-induced Ca^{2+} increase is an important element in the death of neurons due to toxic effect of cadmium and the mechanism of protective action of manganese and NAC is mediated by the prevention of increase in calcium levels.