Evaluation of the Effects of Trolox on MAPKs Activation in Striatal Slices Exposed to Manganese

Pedro, D.Z., Peres, T.V., Gonçalves, F.M., Lopes, M.W., Cordova, F.M., Leal, R.B.

Departamento de Bioquímica, Centro de Ciências Biológicas, Universidade Federal de Santa Catarina, Florianópolis, SC, Brazil

Manganese (Mn) is an essential metal for several physiological reactions. However, overexposure to the metal may result in loss of dopaminergic neurons and cause a Parkinson-like syndrome called manganism. In the early stages of central nervous system (CNS) development, exposure to the metal can change the process of neurogenesis and predispose to neurodegenerative diseases. The mechanism of manganese toxicity is not well understood, but oxidative stress has been suggested as an important feature. In order to analyze the signaling pathways involved in Mn neurotoxicity in immature rats, our group demonstrated that in vivo treatment with Mn induces the activation of AKT/PKB and mitogen-activated protein kinases (MAPKs) ERK1/2. Trolox, a vitamin E derivative with antioxidant properties, reversed ERK1/2 activation. In present study we evaluate the effects of Mn using an in vitro model of immature striatal slices exposed to the metal. Striatal slices from 14 days old rats (PN14) were incubated with 1mM MnCl$_2$, or Trolox (500µM or 1mM) or MnCl$_2$ plus Trolox for 6 hours, controls received only incubation medium. Phosphorylation of proteins ERK1/2 and JNK1/2 were analyzed by western blotting. Results showed that Mn activates the MAPKs JNK1/2 and ERK1/2 which may be involved in the mechanism of Mn neurotoxicity. Moreover, we investigated a possible reversal in the activation of these proteins by Trolox. Our results showed no significant reversal in the phosphorylation of these proteins, suggesting that the mechanisms of Mn neurotoxicity on striatal slices may be more complex than a directly induction of oxidative stress.

Key words: manganese, MAPK, oxidative stress, Trolox

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