MANGANESE-INDUCED NEUROTOXICITY: LESSONS FROM WORMS TO HUMAN NEONATES

Michael Aschner

Department of Molecular Pharmacology, Albert Einstein College of Medicine, 1300 Morris Park Blvd., Bronx, NY 10461, USA.

Abstract: Manganese (Mn), is a trace metal required for normal physiological processes in humans. Mn levels are tightly regulated, as high levels of Mn result in accumulation in the brain and cause a neurological disease known as manganism. Manganism shares many similarities with Parkinson’s disease (PD), both at the physiological level and the cellular level. Exposure to high Mn-containing environments increases the risk of developing manganism. Combining genetics and biochemical assays, we established in the nematode (C. elegans) and other experimental models that dopamine (DA) is responsible for Mn-induced DAergic neurodegeneration, and that this process (1) requires functional DA-reuptake transporter (DAT-1), (2) is associated with oxidative stress and lifespan reduction, (3) and is enhanced by iron deficiency. The presentation will focus on the mechanisms of Mn uptake and efflux into the brain, genetic susceptibility to Mn-induced damage, and molecular mechanisms of neurotoxicity. Additional studies will address the role of parenteral nutrition (PN) as a risk factor for increased Mn brain deposition, and demonstrate that hepatic cholestasis is a risk factor for increased brain Mn deposition in neonates receiving PN.

Key words: Manganese (Mn), Parkinson’s disease (PD), molecular neurotoxicity, genetic susceptibility, parenteral nutrition (PN)

Acknowledgements: This research was supported by a grant from the National Institutes of Health, National Institute of Environmental Health Sciences (NIEHS) R01 ES10563.