

Manganese-induced Parkinsonism and Alzheimer's-like pathology in Non-Human Primates: Implications to Human Neurological Disease.



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Dean

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Biography

Tomás R. Guilarte is the dean of the FIU Robert Stempel College of Public Health & Social Work. He took the helm of FIU Stempel College in January 2016. As the head of FIU Stempel College—which consists of the Departments of Biostatistics, Dietetics & Nutrition, Environmental & Occupational Health, Epidemiology, Health Policy & Management, Health Promotion & Disease Prevention, and the School of Social Work—Guilarte is focusing on initiatives to engage faculty and expand research opportunities. But perhaps most importantly, Dean Guilarte is leading improvements in student success as FIU Stempel College works toward its goal of enrolling 200 doctoral students by 2020. Guilarte's research has focused on mechanism-based neurotoxicology and neuroscience using behavioral, cellular and molecular approaches, ranging from studies using primary culture of neural cells to the application of brain imaging technologies. He is recognized worldwide for revealing the effects of low-level lead exposure on the central nervous system during development, and subsequently developing therapies to reverse these neurodegenerative effects. Dean Guilarte comes to FIU after success as the inaugural Leon Hess Professor and Chairman of the Department of Environmental Health Sciences at Columbia University's Mailman School of Public Health.

Abstract

Chronic manganese (Mn) exposure has been associated with a neurological syndrome comprising cognitive deficits, neuropsychological abnormalities and Parkinsonism. Historically, studies on the effects of Mn in humans and experimental animals have focused on the effects on the basal ganglia and the dopaminergic system as it relates to movement abnormalities. However, emerging studies are beginning to provide significant evidence of Mn effects on cortical structures and cognitive function at levels lower than those needed to induce Parkinsonism. Our laboratory has been examining the effect of chronic exposure to moderate levels of Mn in a non-human primate model system using behavioral endpoints, multiple neuroimaging techniques such as Positron Emission Tomography (PET), Magnetic Resonance Imaging (MRI), and Magnetic Resonance Spectroscopy (MRS), as well as many neuropathological endpoints. PET studies have revealed a highly significant impairment of in vivo dopamine release in the

caudate/putamen with no changes in dopamine transporter levels, indicating that chronic exposure to Mn does not result in dopamine neuron degeneration but results in a dysfunctional dopaminergic system. Recent neuroimaging studies in human populations have revealed similar findings in a particular group of young drug users intravenously injecting the Mn-containing psychostimulant ephedron and in individuals with inherited mutations of the Mn transporter gene SLC30A10. In addition, neuropathological studies in our lab have led to the novel finding of diffuse α -amyloid plaques and neurodegeneration in the frontal cortex that resemble those found in the early stages of Alzheimer's disease. These findings strongly support the need for more studies to determine the role of chronic Mn exposure on neurological disease relevant to those encountered in human populations occupationally or environmentally exposed to Mn.