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New trends in toxicological studies of metal exposure- Associated neurodegenerative diseases

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Abstract

Disordered homeostasis of various essential elements and exposure to toxic metals have been associated with the etiopathology of Parkinson's disease (PD), Alzheimer's disease (AD), essential tremor and other neurodegenerative disorders. Despite more than 50 year's research, the mechanisms of metal-caused neurotoxicities remain elusive. This presentation starts with a brief overview of the similarities and differences between metals and organic chemicals with regards to their physical, chemical and biological properties, which underlie metal's unique effect on the central nervous system (CNS). The research advances in manganese (Mn) exposure-induced Parkinsonian disorder and lead (Pb) exposure in Alzheimer's disease progression then be extensively discussed. Recent results from this group by using synchrotron X-ray fluorescent (XRF) imaging and quantitation reveal an abundant accumulation of Mn in substantia nigra of rat brain following chronic Mn exposure. Evidence also indicates that elevated Mn levels in brain barriers diminish iron (Fe) clearance from the CNS, leading to Fe dyshomeostasis in the CNS. These observations offer the clue to the current understanding of the overlapping pathogenesis between manganism and idiopathic PD. The speaker will also present the evidence that links Pb-induced vascular injuryto extravascular aggregation of amyloid polypeptides, which is the hallmark of AD pathogenesis. Recent data in transgenic mice that over-express amyloid plaques establish that Pb exposure directly participates in physiochemical reaction with Aβ molecules, hinders Aβ clearance from the CNS, and promotes the formation of amyloid plaques. Based on these and other observations in literature, the speaker will discuss the new trends in metal toxicological studies of neurodegenerative diseases by focusing on (1) metal accumulation in the bone as the possible internal source of neurotoxicity using Mn accumulation in bone as an example, (2) fast evolving trend in using newly developed/developing technologies such as XRF and neutron-activation based noninvasive analysis technology for precise location and quantitation of trace metals in tissues, and (3) newly revitalized research interest in chelating therapy of metal neurotoxicity. The presentation will be of interest to those who engage in metal neurotoxicity research and, more broadly, to those working in toxicological research of CNS disease and disorders. (Supported in part by NIEHS ES-008146, NIEHS ES-017055, NINDS NS-039422, and NIOSH OH010044-01).

Biography

Zheng is a Professor of Toxicology and the Head of School of Health Sciences at Purdue University. He is a recognized researcher in the fields of metal-induced neurodegenerative disorders such as Mn-caused Parkinsonism and Pb-associated cognitive deficiency. Zheng received his Ph.D. in Toxicology from University of Arizona. He was an Assistant/Associate Professor at Columbia University (1993-2003) and joined Purdue in 2003. Zheng has served in various NIH study sections and journal editorial board, and published one book, 137 research manuscripts. His research has been supported by NIH/NIEHS (since 1994), Dept of Defense and awards from pharmaceutical companies.