TRANSPORT OF ε-AMYLOIDS BY BRAIN BARRIER SYSTEMS: RELATIONSHIP TO LEAD-INDUCED BRAIN AMYLOID AGGREGATION

WEI ZHENG, PH.D., ATS
Professor of Health Sciences and Toxicology
Fellow, Academy of Toxicological Sciences

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Seminar Synopsis:
Aggregation of β-amyloid proteins (Aβ) in brain extracellular fluid is the hallmark of pathoetiolog of Alzheimer’s disease. While Aβ in brain extracellular fluid, i.e., interstitial fluid (ISF) and cerebrospinal fluid (CSF), is about 6 fold higher than that in plasma, the absolute amount of free Aβ in blood is nearly 10 times greater than that in ISF/CSF. Both blood-brain barrier and blood-CSF barrier play critical roles in regulating brain homeostasis of Aβ peptides so as to prevent them from aggregation. Cumulative data in literature and from this lab have shown that chronic exposure to toxic metal lead (Pb) can result in increased amyloid plaques in the brain. This presentation will introduce an ongoing research project in Dr. Zheng’s Trace Elements Neurotoxicology Laboratory with a particular focus on the mechanism whereby Aβ is transported by brain barriers and how Pb exposure may alter the dynamics of Aβ transport across brain barriers. After a brief discussion of historical human subject and wet-lab studies on Pb exposure, hypocampal volume, and Aβ conducted in this lab, the attention will be directed to the new discoveries from recent studies using in-situ single-pass brain infusion, ventriculo-cisternal perfusion, and in-vitro tissue incubation techniques. Evidence to support a far more abundant Aβ in normal cerebral capillaries than brain parenchyma and a Pb-associated increase of Aβ in cerebral capillary, as well as the ensuing Pb-induced cerebral amyloidal angiopathy (CAA), will be extensively discussed. Finally, the perspectives in this research area will be briefly introduced. (Funded in part by NIH R01 ES027078 and R01-NS039422)