Short communication

Acta Psychopathologica

2021

Vol.7 No.7

Reduction in Biliverdin Reductase A favors Tau hyper-phosphorylation in Alzheimer disease: A complex interaction between Alzheimer associated proteins

Nidhi Sharma

Institute of Public Health, University of Lahore, Pakistan. E: smrmep@gmail.com

Abstract

Hyper-active GSK-3β favors Tau phosphorylation during the progression of Alzheimer disease (AD). Akt is one of the main kinases inhibiting GSK-3β and its activation occurs in response to neurotoxic stimuli including, i.e., oxidative stress. Biliverdin reductase-A (BVR-A) is a scaffold protein favoring the Akt-mediated inhibition of GSK-3β. Interestingly, reduced BVR-A levels along with increased oxidative stress were observed early in the hippocampus of 3xTg-AD mice (at 6 months), thus suggesting that loss of BVR-A could be a limiting factor in the oxidative stress-induced Akt-mediated inhibition of GSK-3β in AD. In this study we evaluated changes in the level of BVR-A, Akt, GSK-3β, oxidative stress and Tau phosphorylation (1) in young (6-months) and old (12-months) 3xTg-AD mice; and (2) in post-mortem IPL samples from MCI, AD and age-matched controls. Furthermore, similar analyses were performed in vitro in cells lacking BVR-A and treated with H2O2. In result we have found reduced BVR-A levels along with (1) increased oxidative stress; (2) reduced GSK-3β inhibition and (3) increased Tau Ser404 (target of GSK-3β activity) phosphorylation without changes of Akt activation both in young mice and in MCI, were observed. Interestingly, cells lacking BVR-A and treated with H2O2 showed reduced GSK-3β inhibition and increased Tau Ser404 phosphorylation, which resulted from a defect of Akt and GSK-3β physical interaction. Reduced levels of Akt/GSK-3β complex were confirmed in young 3xTg-AD and MCI. Conclusively here we demonstrate that loss of BVR-A levels but not in its activity impairs the neuroprotective Akt-mediated inhibition of GSK-3β in response to oxidative stress, thus contributing to Tau hyper-phosphorylation in early stage AD.