C/EBPβ induces motor impairment in the early stage of Alzheimer's Disease

Dae Ki Hong[1], and Seong Su Kang[1,*]

[1] Department of Pathology and Laboratory Medicine, Emory University School of Medicine, Atlanta GA, 30322, USA

Alzheimer's disease (AD) is increasingly recognized to affect motor function even in early disease stages, challenging the traditional view that motor impairment occurs only in advanced AD. The locus coeruleus (LC), the brain's primary source of norepinephrine (NE), projects to motor cortex as well as various brain regions and shows vulnerability in AD pathogenesis. However, mechanism underlying early motor dysfunction in AD progression remains unclear. Here we demonstrate that a CCAAT-enhancer-binding protein (C/EBPβ), an inflammation-regulated transcription factor, accelerates the activation of inflammatory cytokines and promotes motor impairment in a transgenic mouse model with neuronal overexpression of C/EBPβ at a young age. This study aims to examine how neuronal C/EBPβ and subsequent activation of IL-18 induce LC neurodegeneration, leading to motor impairment in the early stage of AD progression. Employing postmortem brain tissues of AD patients and C/EBPβ transgenic mice, we confirmed that LC-to-motor cortex noradrenergic pathway integrity is destroyed in both AD patients and C/EBPβ transgenic mice. Mechanistically, we found that C/EBPβ-induced IL-18 activation promotes noradrenergic neuronal death, while NE modulates IL-18-induced neuroinflammation through adrenergic receptor signaling. These findings suggest that C/EBPβ and IL-18 represent promising diagnostic and therapeutic targets for early stage of AD, particularly for identifying and addressing motor dysfunction before widespread cognitive decline.

Sponsored By: grant from NIH R01-AG08719001A1 and Emory URC 00126307

Presenter Name and contact information:
Dae Ki Hong, postdoc
Department of Pathology and Laboratory Medicine
Emory University School of Medicine
Atlanta, Georgia, USA
Email: dae.ki.hong@emory.edu