Brain Trauma as a Risk Factor for Alzheimer’s Disease: Is There a Role for Beta-Amyloid?

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Research Abstract

Traumatic brain injury (TBI) is a major environmental risk factor for developing Alzheimer’s disease (AD), a chronic neurodegenerative disorder. Neuropathological evidence from multiple laboratories demonstrates that TBI is associated with increased brain accumulation of the amyloid precursor protein (APP) and its metabolite the β-amyloid (Aβ) peptide, a major pathological culprit in AD. Initial autopsy studies demonstrated accumulation of aggregated Aβ in neuropil plaques in 30% of victims of severe TBI. By examining biopsy tissue samples obtained within hours after injury from survivors of severe TBI, we demonstrated that neuropil plaques composed of Aβ peptides and other AD-related proteins, including apolipoprotein E, can form rapidly after head trauma in humans. Our studies using a transgenic mouse model of AD also show that TBI results in rapid and sustained increases in Aβ concentration. Our laboratory conducted several experimental TBI studies with the goal of developing novel therapeutic strategies designed to lower brain Aβ concentration while at the same time targeting additional pathological pathways initiated after TBI. One group of drugs capable of such pleiotropic effects are the HMG-coenzyme A reductase inhibitors, statins. This presentation will review evidence from human TBI and experimental TBI models demonstrating that both acute and chronic sequelae of TBI involve AD-like pathology, and how these changes are amenable to therapy interventions in preclinical studies. New treatment strategies designed to attenuate injury-induced increases in Aβ peptides, brain inflammation, oxidative stress, and detrimental changes in cerebral blood flow, with a goal of reducing the risk of developing AD later in life, will be discussed.

References