Exploring the molecular overlap in the brain and plasma of TBI and AD mouse models using proteomic and lipidomic technology.

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Abstract

Traumatic brain injury (TBI) is a major cause of disability in the military and civilian population, and for many years has been known to be a major risk factor for Alzheimer's disease (AD). Although the existence of this relationship is well recognized, and the overlap and distinction between pathological features of AD and TBI, have long been the subject of reporting and discussion, the precise nature of how TBI leads to or precipitates AD pathogenesis is currently not understood. To address this problem we are generating time-dependent molecular profiles of response to TBI and AD pathogenesis in mouse models, using proteomic and lipidomic analyses. We are using the well-validated hTau mouse models that develops age-related tau pathological features, and our well-established model of mTBI in C57BL/6 mice. Brain and plasma from these animals have been collected at different ages (for hTau mice), or at different timepoints after repetitive mTBI (C57BL/6). Liquid chromatography/mass spectrometry (LC-MS) and in source collision induced dissociation (SCID) approaches are being applied to develop molecular profiles of proteins and lipid species that are significantly differentially expressed as a consequence of AD or mTBI. We show an age-related upregulation in phosphotidylcholine (PC/ePC) and lysophosphotidylcholine (LPC) species in the plasma of both TBI and hTau mouse models. We anticipate that the exploration of molecular profiles from these animal models will enable us to identify cellular pathways that have pathogenic significance in human conditions. Moreover, we further aim to explore these identified pathways as potential targets for therapeutic intervention. Generation of Omic analyses are ongoing for comparisons of TBI profiles at 24hrs, 3, 6, 9 and 12 months post-injury with profiles at 3, 9 and 15 months of age in the hTau models.

Key words: mild traumatic brain injury, Alzheimer's disease, animal models, lipidomics, proteomics.

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