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Allostatic load and neuropsychiatric outcomes following TBI in the AoU Database

Chronic stress causes autonomic and hypothalamic-pituitary-adrenal axis dysregulation which has profound impacts on the brain. There is an inherent bidirectional relationship between chronic stress and traumatic brain injury (TBI), with TBI causing increased physiological stress and chronic stress impacting TBI recovery. Allostatic load (AL) is a conceptual framework developed to capture the burden of chronic stress using an aggregate of blood-based and anthropomorphic biomarkers. Utilizing the All of Us (AoU) Database, we have developed a comprehensive AL index (ALI) to investigate the relationship between AL and incident neuropsychiatric outcomes following TBI. ALI was estimated with a single-factor confirmatory factor analysis model using seven previously established markers: systolic BP, diastolic BP, HDL, triglycerides, BMI, HbA1c, and c-reactive protein. Neuropsychiatric outcomes were assessed in individuals with an established diagnosis of TBI and estimated ALI. The final ALI model achieved appropriate fit (CFI=.988; RMSEA=.035) with partial scalar invariance observed across race/ethnicity groups, gender, and medication status (ΔCFI<-.01; ΔRMSEA<.015); subsequent comparisons used the model that was invariant across race/ethnicity. We observed disparities in ALI, with the non-Hispanic (NH) White group having the lowest ALI while the NH-Black group had the highest ($p<.001$). Consistent with prior research, ALI was positively correlated with area-level social deprivation ($R=.17$; $p<.001$). Amongst the TBI cohort, higher ALI was observed in those diagnosed with schizophrenia or psychosis; mood disorders; PTSD; sleep disorders; substance use disorders; suicidal ideation or attempt, and headache disorders ($p<.01$). ALI may serve as an important measure to investigate the role of pre-existing chronic stress on outcomes following TBI, and further work aims to understand the underlying genetic architecture of stress resilience in the context of TBI.