

The Effect of Lifetime Stress on Accelerated Epigenetic Aging

Allostatic load, a measure of the biological aging process, describes the cumulative effect of chronic exposure to stress. The cumulative burden presented by repeated adaptation to stressful events in one's environment can alter and more importantly, exacerbate the ongoing progression of biological aging and increase susceptibility to aging-related disease onset. Epigenetic biomarkers, such as DNA methylation (DNAm), characteristically accumulate over time to represent biological progression. Current evidence from the literature reports that lifetime PTSD severity and childhood maltreatment are associated with accelerated DNAm age. Despite the robust evidence linking accelerated DNAm aging to these different types of stressors, much remains unknown about the cumulative effect of stress on biological aging throughout one's lifetime. In the Detroit Neighborhood Health Study (DNHS), we evaluated the effect of a series of life stressors suspected to negatively impact health on accelerated DNAm aging using Horvath and Hannum epigenetic clocks. Cumulative stress was measured and validated using the Holmes-Rahe Stress Scale (full and reduced versions); multiple linear regression models were stratified by gender and social support and adjusted for smoking status, education level, race, and immune cell proportion estimates. We found no evidence of an association between Holmes-Rahe lifetime stress and accelerated DNAm aging (total sample: $\beta = -0.09$, 95% CI: -0.94, 0.76); women: $\beta = -0.76$, 95% CI: -1.86, 0.33; and men: $\beta = 0.77$, 95% CI: -0.68, 2.21). Findings were consistent using the reduced version of the lifetime stress score and among secondary analyses that assessed the association between the count of Holmes-Rahe stressful life events and presence of survivorship bias. It is unclear whether these results between lifetime stress and accelerated DNAm aging are unique to participants in DNHS. Future studies should examine other measures of cumulative life stress in DNHS or other similar neighborhood studies to determine the validity of these observed associations.