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The Co-Occurrence of Internalizing Disorders and Alcohol Use Disorder: An Examination of Childhood Trauma and Epigenetic Cellular Aging

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Childhood trauma (CT) is linked to accelerated cellular aging, with higher DNA methylation age associated with negative health outcomes. While research has shown links between CT, PTSD, MDD, and AUD with advanced cellular aging, few studies have explored additive effects of comorbid psychopathology. This project examines these relationships using five epigenetic clocks: Horvath, Altumage, GrimAge Version2, and DunedinPACE, using data from the Grady Trauma Project. We hypothesized that individuals with comorbid conditions would have more advanced cellular aging compared to those with one diagnosis.

Stepwise regressions modeled CT and individual or comorbid diagnoses of AUD, PTSD, and MDD as predictors of epigenetic aging, controlling for sex, race, BMI, smoking, GWAS derived polygenic risk scores (PRS), ancestral principal components, and white blood cell count.

Findings suggest that CT uniquely accelerates cellular aging over and above PTSD (Horvath clock: $\beta=0.12$, $SE=0.04$; Altumage clock: $\beta=0.11$, $SE=0.04$). In general, individuals with PTSD also showed advanced cellular aging (Altumage clock: $\beta=0.08$, $SE=0.04$; DunedinPACE clock: $\beta=0.07$, $SE=0.03$). Further, PTSD was consistently associated with advanced aging over and above the effects of AUD ($\beta=0.08$, $SE=0.03$), CT trauma ($\beta=0.07$, $SE=0.03$), and both AUD and CT ($\beta=0.07$, $SE=0.03$), supporting PTSD as a robust indicator of cellular aging.

Whereas accelerated aging was less consistently found for AUD (Altumage clock: $\beta=0.08$, $SE=0.04$) and MDD (DunedinPACE clock: $\beta=0.09$, $SE=0.04$). Notably, the DunedinPACE clock showed a positive association with comorbid psychopathology ($\beta=0.09$, $SE=0.04$), supporting our hypothesis. This study strengthens established findings and expands the field by examining comorbid effects on cellular aging.