The Effect of Lifetime Stress on Accelerated Epigenetic Aging
Amy Yu1, Chantel Martin1, Jane Monaco1, Allison Aiello1
1University of North Carolina at Chapel Hill, Gillings School of Global Public Health

Background

Allostatic load & Allostasis
- Allostatic load is a measure of the biological aging process and the cumulative effect of chronic exposure to stress
- Allostasis is the process by which the body alters physiological parameters in response to stress
- The cumulative burden of repeated adaptation to stressful events can exacerbate the ongoing progression of biological aging AND increase susceptibility to aging-related disease onset.

Epigenetic biomarkers for aging
- DNA methylation (DNAm) characteristically accumulate over time to represent biological progression
- Several studies on accelerated DNAm aging:
  - Associated with aging-related problems, morbidity, and mortality
  - Accelerated aging can provide insight on the relationship between allostatic load and biological aging

Lifetraime and DNAm Aging
- Lifetime PTSD severity and childhood maltreatment associated with accelerated DNAm age but current PTSD diagnosis and traumatic exposure are not.
- The cumulative effect of stress on biological aging throughout one’s lifetime remains to be elucidated.
- Significant stressors may further exacerbate accelerated biological aging and racial disparities in health among Black individuals in the U.S.
- We aim to measure the cumulative effect of a series of life stressors suspected to negatively impact health on accelerated DNAm aging in the Detroit Neighborhood Health Study (DNHS).

Project Aims

1. To develop a lifetime stress measure to assess stress burden among DNHS participants.
2. To evaluate the association between a measure of cumulative lifetime stress and accelerated DNAm aging while taking into account gender-related differences in aging biomarkers using two measures of DNAm aging - Horvath’s epigenetic clock and Hannum’s epigenetic clock.
3. To examine variables that might modify the potential association between lifetime stress burden and accelerated DNAm age.

Methods

DNA Methylation Assessment
- Genome-wide DNA methylation was measured in whole blood-derived DNA

DNA Methylation Age Acceleration
- Defined as the difference between Horvath/Hannum DNAm age and chronological age
- Positive and negative residuals represent accelerated and decelerated DNAm age, respectively.

Statistical Analysis
- Multiple linear regression models of accelerated DNAm age on lifetime stress using Horvath and Hannum epigenetic clocks.
- Models adjusted for smoking status, education, and race.

Figure 1. Scatter plot comparing DNAm age and chronological age in a random subset of DNHS participants.

Figure 2. Relationship between lifetime stress and DNAm age.

Figure 3. Comparison of DNAm age across different levels of social support.

Study Participant Characteristics

- Majority of study participants were women (61.0%) and identified as Black (82.5%)
- On average, women were 6.6 years older than men
- Completed high school education (55.8%)
- Smoked at least once in their lifetime (74.7%)

Figure 4. Distribution of DNAm age across different levels of social support.

Results & Discussion

- Observed associations between lifetime stress and accelerated DNAm age are consistent across analyses using both the full and reduced versions of the Holmes-Rahe life stress score.
- Association appears to be negative, and primarily driven by women using the Horvath clock.
- However, for the reduced version of the stress score, including the estimated proportion of immune cells in the blood also increases the negative association among the total sample to the null.
- No evidence of effect measure modification by social support.

Secondary Analyses
- Examined association between lifetime stress and accelerated DNAm aging unique to participants in DNHS or whether biases within the study remain to be uncovered.
- 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.

Figure 5. Association between DNAm age and lifetime stress.

Figure 6. Association between DNAm age and lifetime stress by gender.

Figure 7. Association between DNAm age and lifetime stress by race.

References