Weathering and social epigenetics: racial disparities in biological aging

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Dr. Eddy Lee
BiND lab

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Racial disparities in age-related health are mediated by biological aging

Weathering: “Blacks experience early health deterioration as a consequence of the cumulative impact of repeated experience with social or economic adversity and political marginalization.”

Probability of having a high allostatic load score

DNA methylation aging
Racial disparities in age-related health are mediated by biological aging

GrimAge and Dunedin Pace of Aging Methylation (DunedinPoAm) are robust markers of biological aging

Associated with:
- Mortality
- Cognitive decline
- Functional decline
- Age-related disease (heart, lung, diabetes)

Biological aging mediates racial disparities in:
- Mortality
- Functional decline
- General health

Graf GH, et al. 2021
Individual SES and neighborhood social environment are associated with biological aging

Similar associations found in other studies (e.g. MESA and FACHS)

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** p<0.001; ** p<0.01; * p<0.05

Schmitz LL, et al. 2021

Liu Z, et al. 2019

Fig. 1. Levine DNAmAgeAccel by race/ethnicity and education.
Threefold decomposition: quantify contribution to disparities

Total difference

- Endowment
- Coefficient
- Interaction

Outcome

Exposure

Group 1

Group 2

Higher neighborhood deprivation for Black Americans contributes to disparity in GrimAge

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall, N = 2,960¹</th>
<th>White, N = 2,438¹</th>
<th>Black, N = 522¹</th>
<th>p-value²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>71.33 (9.53)</td>
<td>72.08 (9.54)</td>
<td>67.81 (8.69)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male</td>
<td>1,218 (41%)</td>
<td>1,051 (43%)</td>
<td>167 (32%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1,742 (59%)</td>
<td>1,387 (57%)</td>
<td>355 (68%)</td>
<td></td>
</tr>
<tr>
<td>GrimAge aging</td>
<td>0.03 (1.00)</td>
<td>-0.02 (0.99)</td>
<td>0.28 (1.03)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DunedinPoAm aging</td>
<td>0.03 (1.00)</td>
<td>-0.03 (0.98)</td>
<td>0.31 (1.04)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&lt; High School</td>
<td>374 (13%)</td>
<td>251 (10%)</td>
<td>123 (24%)</td>
<td></td>
</tr>
<tr>
<td>High School</td>
<td>974 (33%)</td>
<td>803 (33%)</td>
<td>171 (33%)</td>
<td></td>
</tr>
<tr>
<td>Some College</td>
<td>773 (26%)</td>
<td>644 (26%)</td>
<td>129 (25%)</td>
<td></td>
</tr>
<tr>
<td>College +</td>
<td>839 (28%)</td>
<td>740 (30%)</td>
<td>99 (19%)</td>
<td></td>
</tr>
<tr>
<td>Quartile</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Wealth/Income</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>704 (24%)</td>
<td>443 (18%)</td>
<td>261 (50%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>803 (27%)</td>
<td>644 (26%)</td>
<td>159 (30%)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>751 (25%)</td>
<td>671 (28%)</td>
<td>80 (15%)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>702 (24%)</td>
<td>680 (28%)</td>
<td>22 (4.2%)</td>
<td></td>
</tr>
<tr>
<td>Social Deprivation Index</td>
<td>-0.12 (0.98)</td>
<td>-0.32 (0.89)</td>
<td>0.79 (0.80)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

¹Mean (SD); n (%)  
²Wilcoxon rank sum test; Pearson's Chi-squared test

Data from Health and Retirement Study DNAm subsample  
Included non-Hispanic Black and White participants with complete data

Yannatos, I. In preparation
Vulnerability to PM2.5 exposure is higher for Black than White Americans

<table>
<thead>
<tr>
<th>N (cases)</th>
<th>HR_{PM2.5} (95% CI)</th>
<th>Lower risk of Alzheimer’s disease</th>
<th>Higher risk of Alzheimer’s disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Crude</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All participants</td>
<td>6485 (158)</td>
<td>1.24 (1.02, 1.51)</td>
<td></td>
</tr>
<tr>
<td>Black participants</td>
<td>481 (21)</td>
<td>2.14 (1.38, 3.31)</td>
<td></td>
</tr>
<tr>
<td>White participants</td>
<td>6004 (137)</td>
<td>1.15 (0.93, 1.42)</td>
<td></td>
</tr>
</tbody>
</table>

**Race**

- **White**
  - Hazard Ratio: 1.00
  - 95% CI: (-0.02, 0.01)

- **Black**
  - Hazard Ratio: 0.21**
  - 95% CI: (0.09, 0.33)

**PM2.5**

- Hazard Ratio: 0.00
  - 95% CI: (0.01, 0.06)

**Race * PM2.5**

- Hazard Ratio: 0.10*
  - 95% CI: (0.03, 0.17)

**Gender**

- **Male**
  - Hazard Ratio: 0.30
  - 95% CI: (-0.05, 0.65)

- **Female**
  - Hazard Ratio: 0.20***
  - 95% CI: (-0.27, -0.13)

**Gender * PM2.5**

- Hazard Ratio: -0.05*
  - 95% CI: (-0.09, -0.02)

*Beta (95% confidence intervals)*

- *p<0.05; **p<0.01; ***p<0.001

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Di Q, et al. 2017  
Younan D, et al. 2021  
Yannatos, I. In preparation
Individual- and neighborhood-level SES may play a role in PM2.5 vulnerability

<table>
<thead>
<tr>
<th>Race</th>
<th>Individual SES</th>
<th>SDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>—</td>
<td>0.19**</td>
</tr>
<tr>
<td>Second</td>
<td>—</td>
<td>0.16</td>
</tr>
<tr>
<td>Black</td>
<td>0.07, 0.32</td>
<td>0.03, 0.29</td>
</tr>
<tr>
<td>PM2.5</td>
<td>0.03</td>
<td>0.01</td>
</tr>
<tr>
<td>Wealth/Income</td>
<td>0.01</td>
<td>0.03, 0.29</td>
</tr>
<tr>
<td>PM2.5 Wealth/Income</td>
<td>0.03</td>
<td>0.01</td>
</tr>
<tr>
<td>Wealth/Income</td>
<td>0.01</td>
<td>0.03, 0.29</td>
</tr>
<tr>
<td>Social Deprivation</td>
<td>-0.14</td>
<td>0.02</td>
</tr>
<tr>
<td>Social Deprivation</td>
<td>-0.32, 0.05</td>
<td>0.00, 0.04</td>
</tr>
</tbody>
</table>

Beta (95% confidence intervals)
*p<0.05; **p<0.01; ***p<0.001

Wealth/Income Quartile:
First        Fourth
4            8            12            16

SDI: 10th percentile
90th percentile

Predicted DPoAm Aging

Yannatos, I. In preparation
Opportunities

• Use of decomposition to quantify how factors contribute to disparities in biological aging

• Further work to determine which social determinants influence vulnerability to PM2.5 exposure
  • Need for measures of psychosocial stress

• Need for longitudinal data

• Multidisciplinary questions:
  • Which aspects of neighborhood are salient for health?
  • How is the environment translated to health?
  • How does health operate as a resource or stressor?
  • Protective individual and neighborhood factors?
Environmental Health Disparities Framework

Race is a proxy for historical and structural systems
How to measure racism?

Which factors influence exposure and vulnerability to pollutants?
Need for psychosocial data to better measure stress

How does environment influence individual stress, behaviors?

How does health influence individual and community stress?

What neighborhood and individual factors are protective?

Causality and life-course: need for longitudinal data