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NEIGHBORHOOD STRUCTURAL DISADVANTAGE AND BIOLOGICAL AGING IN A SAMPLE OF BLACK MIDDLE AGE AND YOUNG ADULTS

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Abstract

Objectives: Research on the social determinants of health has suggested that neighborhood disadvantage may undermine healthy aging and is particularly relevant for understanding health disparities. Recently, this work has examined deoxyribonucleic acid methylation (DNAm)-based measures of biological aging to understand the risk factors for morbidity and mortality. However, it is unknown whether neighborhood disadvantage is related to different indices of DNAm-based aging among Black Americans and whether such neighborhood effects vary as a function of age or gender.

Methods: Our analyses of a Black American sample included 448 young adults and 493 middle-aged adults. We measured neighborhood disadvantage using the Area Deprivation Index at the census block group level. DNAm-based accelerated aging indices were measured using established procedures. Regressions with clustered standard errors were used for the analysis.

Results: Neighborhood disadvantage was independently associated with acceleration in PhenoAge, GrimAge, and DunedinPoAm, among young and middle-aged adults. Further, there was no evidence that gender conditioned the effects of neighborhood disadvantage on the aging indices.

Conclusions: Regardless of age groups or gender, accelerated biological aging among Black Americans is partly rooted in differences in neighborhood disadvantage. From a policy standpoint, our findings suggest that programs that decrease neighborhood disadvantage are likely to increase healthy aging, especially among Black Americans.

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Authors' Contributions

MKL led design and analysis, participated in the construction of measures, and drafted the manuscript; MTB participated in the design of the study and drafting of the manuscript; RLS and SRHB conceived of the study and made substantive contributions to the manuscript regarding interpretation of findings.

Keywords

Neighborhood disadvantage; DNA methylation-based age; gender; age groups; Black Americans

1. Introduction

Aging is a lifelong process that begins in childhood with implications for health and life expectancy (Kuh et al., 2003). According to Kennedy et al. (2014: 709), aging is a "predominant risk factor for most diseases and conditions that limit health span." Given that neighborhood quality is linked to dimensions of well-being (Aneshensel et al., 2016), stressors found in the residential neighborhood have been identified as potentially relevant for understanding human aging. Prolonged exposure to neighborhood socioeconomic disadvantage theoretically fosters an adverse physiological response that damages cells and induces oxidative stress, which increases risk for biological aging. The body of evidence on neighborhood effects is particularly relevant for understanding the health burden of Black Americans. Indeed, relative to majority groups, Black Americans are more likely to reside in places affected by concentrated poverty, high rates of unemployment, and single-parent families (Peterson & Krivo, 2010). Moreover, Black Americans have historically had higher morbidity and mortality from chronic illness than majority groups (Geronimus et al., 2016; Williams, 2012). Knowing whether adverse neighborhood conditions increase aging among Black Americans is, therefore, crucial for understanding disparities in morbidity that oftentimes do not manifest until later decades in life.

Recently, research has become increasingly aware of the associations between deoxyribonucleic acid methylation (DNAm) and aging. These biological aging indices have been developed to predict morbidity and time-to-mortality risk, including a DNAm-based measure of the pace of aging (Belsky et al., 2020; Levine et al., 2018; Lu et al., 2019). Several studies have also reported associations between adverse socio-environmental conditions and these different indices of aging (Raffington et al., 2021; Schmitz et al., 2021; Simons et al., 2021). However, a recent systematic review by Evans et al. (2021: 8) indicated that comparatively few studies of biological aging have accounted for the potential explanatory role of neighborhood conditions. Thus, it is important to examine whether neighborhood disadvantage is associated with biological aging, as measured by DNAm in samples of Black Americans—a population disproportionately affected by adverse neighborhood conditions. Moreover, while gender differences in aging are evident (Crimmins et al., 2021; Zhao et al., 2019) and there is some evidence that neighborhoods might be more consequential for women's physical health (see Bishop et al., 2020; Lippert, 2016), it is not clear whether neighborhood disadvantage has different links to the aging process of men and women. More generally, epigenetic biomarkers of aging are powerful tools to assess a key component of physical health. The more widely used self-report measures of health outcomes are affected by multiple limitations and biases of human memory (see Bollen et al., 2021; Harris & Schorrp, 2018; Widom, 2019). To address these voids in this literature, the current study examines the extent to which neighborhood disadvantage predicts three different indices of epigenetic aging and whether these effects differ by gender and periods of the lifespan.

1.1. Assessing variation in physical health

Although many studies have identified linkages between social environmental factors and physical health, much of this research relies on traditional measures derived from self-reports rather than objective assessments. While useful, such self-report indices provide limited information on the biological processes that precede the manifestations of disease. Asymptomatic conditions go unmeasured. Furthermore, and perhaps more importantly, subjective reports of health confound "physiological with psychological and emotional well-being" (Harris & Schorpp, 2018: 362). Studies have found that self-reports may better reflect an individual's emotional state or perceived health than their actual physical health status (see Bollen et al., 2021), which raises fundamental questions about their reliability. This is because many types of self-reported measures of health (e.g., self-rated health, chronic symptoms) and life social circumstances are vulnerable to known limitations (e.g., forgetting, projection) and biases (e.g., distortions, reconstruction) of human memory that are known to bias estimates of health (see, Widom, 2019).

Health research is undergoing a shift in focus, however, and new biomarkers of aging have been developed that provide stronger evidence of a link between environmental factors and physical health (Jylhävä, Pedersen, & Hägg, 2017). Objective biomarkers are not vulnerable to such subjective errors and, furthermore, they capture pre-disease pathology regardless of symptoms. Among these, epigenetic biomarkers of cellular aging have attracted a good deal of scientific attention (Kennedy et al., 2014).

1.2. Biological aging as an indicator of weathering

Scores of studies have found that chronic exposure to stressful situations results in more frequent activations of biological responses to stress, leading to wear and tear on bodily systems that are associated with biological weathering and premature aging (Geronimus, 2013). Increasingly research has used DNAm to quantify biological weathering, a form of accelerated biological aging. Specific DNAm sites scattered across the human genome gradually become less methylated (i.e., down-regulated), whereas others become more methylated (i.e., up-regulated) with advanced age. That is, some genes are being turned off with age while others are turned on. The classic biological aging measures developed by Horvath (2013) and Hannum et al. (2013) were designed based on the association between DNAm and chronological age; however, these measures were not found to be consistently associated with the early onset of chronic illness (Jylhävä et al., 2017). In addition, these two measures were developed by the Infinium 450K array. About 5 to 8 percent of the required loci are not available on the EPIC array, which may not accurately assess biological aging.

To overcome these limitations, Levine and colleagues (2018) using the Infinium EPIC array developed the "PhenoAge" index to capture clinical measures to increase the accuracy of morbidity predictions. Lu and colleagues (2019) measure known as the "GrimAge" index uses plasma protein predictors to identify 1,030 sites that forecast time-to-death due to all-cause mortality. GrimAge has been validated with large Black American samples (Lu et al., 2019). A study by Hillary et al. (2020) revealed that both accelerated PhenoAge and GrimAge provide useful objective markers of elevated risk for morbidity and mortality (Hillary et al., 2020).

Recently, an aging index has been developed using DNAm at 46 sites (Belsky et al., 2020). The resulting The Dunedin(P)ace(o)f (A)ging(m)ethylation index, labeled "DunedinPoAm," uses methylation signatures to capture within-individual variation in the pace of aging of health-relevant systems (Belsky et al., 2020). This index allows the rate of biological aging to be quantified at any stage of life and to forecast the early onset of chronic illness, as well as premature mortality (Belsky et al., 2020). However, given that three aging indices (i.e., PhenoAge, GrimAge, DunedinPoAm) are designed to capture different mechanisms and risk potentials, it is unclear whether neighborhood socioenvironmental stressors have similar or different relationships with the aging indices.

1.3. Neighborhood disadvantage and biological aging

A plethora of research has reported linkages between social stressors and physical health (Snyder-Mackler, 2020). While dietary and lifestyle factors have a small to moderate effect on accelerated aging, recent studies (Brody et al., 2016; Zannas et al., 2015) have shown that the social environment may exert a relatively strong influence. These empirical observations fit with the predictions of theories of the stress process. Specifically, the "neighborhood stress process model" (Aneshensel et al., 2016) posits that the distress of living under disadvantaged neighborhoods promotes physiological distress, which may lead to biological weathering across bodily systems and premature death. This phenomenon is especially relevant for Black Americans who, on average, are more likely than whites to reside in disadvantaged neighborhoods (Peterson & Krivo, 2010), which are characterized by the spatial clustering of material deprivation, poor quality housing and schools, and limited labor force opportunities (Aneshensel et al., 2016).

1.4. Age and gender variation in neighborhood effects

Some studies have reported a relationship between neighborhood disadvantage and DNAm-based aging (e.g., Lawrence et al., 2020; Martin et al., 2021; Raffington et al., 2021). Consistent with the weathering hypothesis, they have found that residing in a disadvantaged neighborhood has an accelerating effect on PhenoAge, GrimAge, and DunedinPoAm after controlling for individual socioeconomic and health-related variables. However, such studies have been conducted exclusively with white samples (e.g., Lawrence et al., 2020; Raffington et al., 2021) and are based on either children or elderly adults (e.g., Martin et al., 2021; Raffington et al., 2021). Whether the effects of neighborhood disadvantage on accelerated aging generalize to non-whites and are evident at different stages of the adult life course remains unclear. In addition, only a single study has investigated the link between neighborhood disadvantage and DunedinPoAm (Raffington et al., 2021).

Among Black Americans, untested to date is whether neighborhood disadvantage is associated with three measures of DNAm-based aging and whether associations vary for different age groups. Strands of the life course and stress process literature indicate that psychosocial stressors in the neighborhood environment may have age-invariant effects such that adults, regardless of their position in the lifespan, will experience physiological responses that impair the integrity of different bodily stems (Pearlin et al., 2005). In fact, epigenetic alterations linked to environmental triggers, including psychosocial stressors across social domains, have been observed at different life-course stages (Zannas &

Chrousos, 2017; Zannas, 2019). This work provides some support for the possibility of age-invariant effects of stressors on biological aging processes. In addition, studies of older and younger adult health have found that various proximate stressors (e.g., combat trauma, incarceration exposure, financial hardship) are associated with accelerated biological aging (Berg et al., 2021, Austin et al., 2018; Hughes et al., 2018).

In addition, it is largely unknown whether the presumed influence of neighborhood disadvantage on biological aging differs between males and females. This is an important research gap. The nature of gender differences in biological aging is the subject of research on the gender disparities in premature mortality and morbidities. Women, on average, live longer than men (Nakamura & Miyao, 2008), and there are well-documented gender differences in age-related morbidities, including the pathophysiology and symptoms of chronic diseases and illnesses such as cancer and cardiovascular disease (e.g., hypertension) (Ostan et al. 2016). Empirical work has suggested that women respond differently from men to stress-induced responses that forecast accelerated biological aging (e.g., Needham et al., 2014). However, theories of social ecology and human behavior suggest that neighborhood effects on health may be invariant among gender groups (Shaw & McKay, 1942). According to a recent systematic review (Minh et al., 2017: p. 171), studies of gender differences in neighborhood effects on health outcomes is scarce, and only rarely have such studies modeled biomarkers. Studies of adolescents and emerging adults find that associations between local poverty on obesity are typically stronger for men than women (Chang et al., 2009; Lippert, 2016). Answers to the question of whether there are gender differences in neighborhood effects, especially among Black Americans, therefore, remain inconclusive. As of now, no study to date has tested whether the nature of the presumed association between neighborhood disadvantage and biological aging varies between men and women.

1.5. The present study

Based upon the weathering hypothesis and the neighborhood stress process model, we first hypothesize that living in a disadvantaged neighborhood would be independently associated with biological aging measures across age groups. Further, we test if the effects of neighborhood disadvantage on the speed of biological aging by gender. To strengthen confidence in the validity of the instruments, we tested our models using three recently developed biological aging indices among two age groups: young (29 years old) and middle-aged adults (49 years old).

2. Method

2.1. Participants

We tested hypotheses using data from the Family and Community Health Study (FACHS). The FACHS sample included 889 Black families who were recruited randomly from neighborhoods in both Georgia and Iowa when the target youths were, on average, ten years of age. FACHS interviewed both children and their adult caregivers from the first wave onward. Details regarding the recruitment are described by Gibbons and colleagues (2004) and Simons and colleagues (2021). Analyses use data collected from the *young-adult* portion of the FACHS sample, who were re-interviewed in 2015–2016, retaining 62.5% of

the original sample, and yielding N = 449 young adults (172 men and 277 women), and who provided both self-report and a blood sample. Young adults participating were, on average, aged 28.67 (SD = .792) for the 2015–2016 data collection. In the current study, there is one missing case for missing geo-coordinates. The final analyses of young adult outcomes are based on 448 individuals (171 women and 277 men). Comparisons of those who were not included in this study (n = 108) versus those who were (n = 448) did not reveal any significant differences in key study variables (Supplementary Table S1).

We also examine aging outcomes among older adults using the caretaker sample. Of the adult caregivers interviewed in FACHS at Wave 1, 77% were interviewed again in 2009–2010. Their mean chronological age was about 49 years. For the present study, the adult caretakers are deemed hereafter as the *middle-aged group*. Roughly 80% of these individuals agreed to provide blood and successful assaying for DNA methylation (n = 506). After eliminating missing cases for missing geo-coordinates, complete data were available for 493 middle-aged Black Americans (367 women and 126 men). Comparisons of individuals in the middle-age sample with those were not included in this study did not reveal any significant differences across key study variables (Supplementary Table S2).

2.2. Procedures

The protocol and all study procedures were approved by the University Institutional Review Board (Title: FACHS weathering – Protocol study number 00006152). Computer-assisted interviews were administered in the respondent's home and took on average about two hours to complete. The instruments were presented on laptop computers. Questions appeared in sequence on the screen, which both the researcher and participant could see. The researcher read each question aloud, and the participant entered an anonymous response using a separate keypad. Participants were also asked to provide a blood sample at age 29 for the young adult age group and age 49 for the middle-age group. The phlebotomist drew four tubes of blood (30 mL) from each participant; these were shipped on the same day to a laboratory for preparation. Whole blood DNA was prepared using cold protein precipitation, quantified with a NanoDrop photometer (Thermofisher, 168 Third Avenue Waltham, MA, USA), and stored at −20°C until use (Lahiri & Nurnberger Jr, 1991).

DNA methylation-based assessments were conducted with the Illumina Infinium (Sequenom, Inc., San Diego, CA, USA) HumanMethylationEPIC 850 BeadChip. This array contains 865,918 probes recognizing CpG positions of known transcripts, potential transcripts, or CpG islands. Participants were randomly assigned to 16 sample "slides/chips" with groups of eight slides being bisulfite converted in a single plate, resulting in two "batches/plates." A replicated sample of DNA was included in each plate to aid in assessment of batch variation and to ensure correct handling of specimens. The replicate sample was examined for average correlation of beta values between plates and was found to be greater than 0.99. Quantile normalization methods were used, with separate normalization of Type I and Type II assays, as this approach has been found to produce marked improvement for the Illumina array in detection of relationships by correcting distributional problems inherent in the manufacturers default method for calculating the beta value. The beta value at each CpG locus was calculated as the ratio of the intensity of

the methylated probe to the sum of intensities of the methylated and unmethylated probes. Finally, beta values after quantile normalization were used to calculate DNAm-based aging indices. Details regarding the preparation of the methylation data are described by Simons and colleagues (2021).

2.3. Measures

DNA methylation (DNAm)-based aging index.—We assessed DNAm-based aging using established procedures to calculate the previously established DNAm-based clocks, including the PhenoAge and GrimAge. All indices were analyzed using the online "New Methylation Age Calculator" with the Advanced Analysis option and the "normalize data" option. To transform each DNAm-based age into accelerated aging, we formulated a measure of accelerated aging using the unstandardized residual scores from the regression of DNAm-based age on chronological age (Simons et al., 2021) and denoted as *PhenoAgeAccel* and *GrimAgeAccel*. These residuals had a mean of zero and represented both positive and negative deviations from chronological age (in years), with positive scores indicating accelerated aging.

In addition to epigenetic clock, pace of aging was measured by *DunedinPoAm* and calculated using the algorithm provided by Belsky et al. (2020). Based on methylation at 46 CpG sites, DunedinPoAm is a rate measure that estimates how fast aging is occurring (the pace of aging) during the years leading up to the assessment. The index is denominated in years of physiological decline occurring per 12 months of calendar time. Therefore, a .01 increment of DunedinPoAm corresponds to a one percentage point increase in an individual's pace of aging.

Neighborhood disadvantage.—A measure of neighborhood disadvantage was assessed using the 2013 and 2015 *Area Deprivation Index* (ADI) that was geocoded with participants' residential addresses at the time of the blood draw in 2009 for middle-aged adults and 2015 for middle-aged adults. The ADI was developed by Singh (Singh, 2003) and was updated by Kind et al. (Kind et al., 2014) at the University of Wisconsin School of Medicine and Public Health. The 2013 and 2015 ADI versions were created using five-year estimates of 2009–2013 and 2011–2015 American Community Survey (ACS) at the census block group level. The ADI included 17 measures of socioeconomic status and housing quality (all items shown in Table 1). To facilitate comparison between neighborhoods, the ADI is provided in national percentile rankings at the block group level ranging from 1 to 100. The percentiles are constructed by ranking the ADI from low to high at the national level and then grouping block groups corresponding to each 1% range of the ADI. A block group with a ranking of 1 indicates the lowest level of area disadvantage, while an ADI with a ranking of 100 indicates the highest level of disadvantage.

Cell-type composition—Cell-type composition was estimated using the "EstimateCellCounts" function in the "minfi" Bioconductor package, which is based on the reference-based method developed by Houseman and colleagues (Houseman et al., 2012). Using this approach, we estimated cell-type proportions in whole blood for CD4+ T cells, CD8+ T cells, Natural Killer cells, B cells, and monocytes. These cell-type proportions were

controlled to examine associations between DNAm-based aging measures and predictors that were relatively free of potentially confounding cell-type variation influences. In this way, the associations reflect "intrinsic" accelerated aging measures that are relatively independent of cell-type differences between individuals.

Covariates.—To account for variables that could provide plausible rival explanations, all analyses controlled for socioeconomic covariates at the time of the blood draw. *Annual household income* was assessed by asking participants to report their income in the past year. Some skew is evident, so we take the natural log to reduce skew in the multivariate analysis. *Binge drinking* was measured using an item that asked whether, during the prior 12 months, respondents had three or more drinks of alcohol, ranging from 0 (never) to 5 (every day). *Cigarette use* was assessed with an item, "In the past month, how much did you smoke cigarettes?" with responses on an item of 0 (none at all) to 6 (about 2 packs a day). *Healthy diet* was assessed using two items that asked about the frequency of fruit and vegetable consumption during the previous 7 days [0 (none) to 4 (twice a day or more)]. Respondents reported whether they had *relocated to a different neighborhood* in the past 12 months (yes = 1).

2.4. Analytic strategy

All cross-sectional analyses were conducted using Stata 16. Although individuals were clustered within neighborhoods, we did not use multilevel modeling because more than 80% of census blocks had less than two participants. Instead, to avoid overestimating the significance of results due to non-independent samples, we used regression models with robust clustered standard errors [the vce(cluster blocks) option in Stata] to adjust standard errors for all analyses and account for the nested nature of the data (Nichols & Schaffer, 2007). Then, given that respondents are not randomly assigned to residential addresses, we employed inverse-probability-of-treatment weighting (IPTW) to adjust for a potential neighborhood selection bias (Robins, 2000). Accordingly, participants who are underrepresented in exposure assignment are given proportionately higher weights, while those who are highly represented in exposure assignment are given proportionally lower weights. Finally, we used two-way interaction terms to test for gender differences in the effect of neighborhood disadvantage.

3. Results

3.1. Initial findings

Table 2 shows the descriptive statistics. The first row of the table indicates chronological age for a young adult sample ($\bar{x}$ = 29.16 years, *SD* = .75) and a middle-aged sample ($\bar{x}$ = 48.30 years, *SD* = 8.35). The second row shows neighborhood disadvantage, which was assessed by national percentile rankings of Area Deprivation Index (ADI, range 0 to 100). Of the 448 young adults and 493 middle-aged adults, the mean ADI percentiles were 67.97 and 70.40, respectively. Further, 81% and 89% of our participants lived in neighborhoods at or above the median (50th percentile) of national percentile rankings of neighborhood disadvantage. Consistent with previous studies (Peterson & Krivo, 2010), blacks tend to predominate within the upper range of the distribution of neighborhood disadvantage measure. Compared

to young adults, middle-aged adults had higher incomes and were more likely to use cigarettes and relocation. In contrast, middle-aged adults were less likely to report a healthy diet and binge drinking than young adults.

3.2. Effects of neighborhood disadvantage on biological aging

We began our analyses by conducting regression models with inverse probability of treatment weighting (IPTW) to examine the impact of neighborhood disadvantage on three biological aging indices. All of these regressions controlled for income, gender, binge drinking, cigarette use, healthy diet, residential relocation, and cell-type composition. Due to nonrandom assignment of participants into neighborhoods, we used the IPTW to minimize potential selection bias. The IPTW was calculated using a regression model with cluster-adjusted standard errors to estimate each participant's probability of receiving the treatment of exposure to neighborhood disadvantage. That is, neighborhood disadvantage was regressed on covariates. Similar to propensity score matching (Jin et al., 2021), IPTW can provide unbiased estimations of treatment effects. As shown in Supplementary S3 and S4, income in young adult sample and cigarette use in middle-aged sample was significantly associated with neighborhood disadvantage. Such self-selection may result in the overestimation of neighborhood effects if not properly accounted for in the regression equations.

To examine the robustness of the results and avoid an extreme variation of weights, we first checked the variance of IPT weights. The unstabilized IPTW was associated with substantial variability (young adult samples: $SD = 722.43$; middle-aged sample: $SD = 301.59$), whereas this variability was eliminated by using stabilized IPTW (young adult samples: $SD = .19$; middle-aged sample: $SD = .14$). Given that extreme weights can bias standard errors, all models were weighted by stabilized IPTW (Hernán et al., 2000).

The first three columns in Table 3 show the results of the regressions with IPTW for the young adult sample. After adjusting for stabilized IPTW, Table 3 shows that neighborhood disadvantage, measured by ADI index, has an effect on PhenoAgeAccel ($b = .490$, $p = .018$), GrimAgeAccel ($b = .571$, $p < .001$), and DunedinPoAm ($b = .006$, $p = .042$). For example, the results suggest that a standard deviation increase in neighborhood disadvantage was associated with .490 years increase in PhenoAge.

Turning to the models with stabilized IPTW for a middle-aged sample, the results of the last three columns in Table 3 are the same as those just discussed for the young adult sample. The findings indicate that, after controlling for a variety of covariates, neighborhood disadvantage was significantly associated with PhenoAgeAccel ($b = .677$, $p = .005$), GrimAgeAccel ($b = .365$, $p = .040$), and DunedinPoAm ($b = .007$, $p = .011$). Across two samples, our findings are consistent with the hypothesis that individuals living in disadvantaged neighborhoods show significantly accelerated biological aging, suggesting an increased risk of morbidity and mortality for both the young adult and middle-age groups.

3.3. Gender differences in DNA Methylation-Based Aging by Neighborhood Disadvantage

The direct effects of gender across the aging indices are somewhat mixed. Among the younger sample, males age slower than women as indexed by the PhenoAge measure.

In both samples, males age more quickly than women on the GrimAgeAccel, whereas on the middle-aged sample, males age more rapidly on the DunedinPoAm measure. On balance, gender is a rather important determinant of aging patterns. However, of particular interest here is the extent to which the influence of neighborhood disadvantage on the aging measures varies among males and females. To test for gender differences, we added the multiplicative interaction term formed by multiplying neighborhood disadvantage by gender. As shown in Table 4, their interaction effects were not significant in any of the aging indices. Consistent with neighborhood structuralist theories (Shaw & McKay, 1942), these findings do not indicate there are gender differences in the effect of neighborhood disadvantage on biological aging. Rather, for men and women, exposure to neighborhood disadvantage has similar effects on the speed of biological aging.

3.4. Sensitivity Analysis

We conducted sensitivity analyses to test the robustness of these findings. First, without adjusting for stabilized IPTW, the results were virtually identical to those obtained with IPTW (Supplementary Tables S5 and S6). Further, the inconsistencies in the literature regarding the determinants of aging may differ in whether studies control for likely individual differences in cell-type composition. Intrinsic accelerated aging captures properties of aging that are independent of cell-type variation. In contrast, extrinsic accelerated aging likely reflects both epigenetic variation and individual differences in the cell-type composition of blood (Horvath et al., 2016). Thus, to control for individual differences in cell type variation to generate an “intrinsic” aging measure that is less influenced by individual differences in composition of blood across individuals. These individual differences may confound the association between DNAm aging and phenotypes (Lei et al., 2020). Although it may be useful to control for cell-type composition when comparing effects across different aging indices, we repeated all analyses to ensure the robustness of the results, excluding cell-type compositions. The results show no change in the pattern of effects reported earlier (Supplementary Tables S7 and S8).

4. Discussion

Recent research has provided evidence that the social environment plays an important role in the speed of epigenetic aging (Brody et al., 2016; Simons et al., 2021; Zannas et al., 2015) and that such aging is a stronger predictor of morbidity and mortality (Belsky et al., 2020; Harris & Schorpp, 2018; Levine et al., 2018). This research on the social determinants of aging is especially important for understanding the health burden of Black Americans because they are disproportionately exposed to disadvantaged neighborhoods (Evans et al., 2021). Residing in disadvantaged neighborhoods is thought to get “under the skin” to increase potential biological precursors of elevated morbidity and mortality (Lei et al., 2019; Simons et al., 2021). Indeed, many social scientists have looked to neighborhood environments as potential explanations for racial and ethnic disparities in poor health (Morenoff et al., 2004; Sampson, 2003). Yet, it is unclear if neighborhood disadvantage is predictive of biological aging, measured by methylation measures, and whether such patterns vary substantially across age groups and gender.

Consistent with prior studies using epigenetic measures of aging (Lawrence et al., 2020; Martin et al., 2021), we found evidence of an association between neighborhood disadvantage and biological aging. Going beyond previous studies, however, we assessed effects on three recently developed DNAm aging indices among two age groups. Importantly, the aging measures were originally developed to capture increased risk of morbidity (AgeAccelPheno), and mortality (AgeAccelGrim), and to quantify the rate of aging across body systems (DunedinPoAm). The findings suggest that the effects of the neighborhood social environment on different measures of accelerated aging are consistent among the age periods under investigation.

Further, consonant with the finding that males demonstrate earlier onset of mortality (Simons et al., 2021; Zhao et al., 2019), we found that, with some exceptions, males generally showed a faster pace of aging than females. However, there was no evidence that gender conditioned the effects of neighborhood disadvantage on biological aging for either group of respondents. To our knowledge, this is the first study to examine such a possibility in the context of accelerated biological aging. These findings are consistent with previous literature on the link between neighborhood and physical health, suggesting that exposure to neighborhood disadvantage has similar effects on the physical health state of males and females.

While the present study overcame some of the limitations of past research, it also contained limitations. To begin, our sample was exclusively Black American. In one sense, this might be considered a strength given the high rates of disadvantage, accelerated aging, and poor health suffered by this population (Geronimus et al., 2016; Williams, 2012). Still, our model must be tested with more ethnically and racially diverse samples. Second, while we contained a series of potential confounders that have been previously reported to be associated with neighborhood disadvantage and DNAm-based aging, our results may have been influenced by unobserved confounders that violated the assumption of IPTW. Accordingly, findings should be viewed as tentative pending replication with other samples and sets of covariates. Third, this study did not test the classic original clocks (i.e., Horvath, 2013; Hannum et al., 2013) because the Illumina Infinium MethylationEPIC array did not include 19 of Horvath's original 353 sites and 6 of the 71 Hannum clock CpG sites, which may result in underestimated biological clocks. Although the classic original clocks were not included in this study, previous studies using the Illumina Infinium HumanMethylation 450k array have provided evidence of a significant link between neighborhood disadvantage and both the Hannum and Horvath clocks (e.g., Lawrence et al., 2020; Lei et al., 2019; Martin et al., 2021). Finally, the current study assessed methylation status at only one point in time. The cross-sectional analysis precludes causal interpretations and the estimation of a non-recursive model. Support for our causal arguments would be more compelling if we had longitudinal assessments of aging. This would have enabled us to examine whether changes in neighborhood context are associated with an alteration in the speed of aging. Future studies should focus on longitudinal changes in DNAm-based aging. This would be useful information for clinicians when designing treatments and interventions.

5. Conclusions

Our findings support the hypothesis that speed of aging might be partly rooted in differences in neighborhood structural characteristics, particularly in adverse conditions such as poverty, poor quality housing, and joblessness. Indeed, our analyses indicate that going beyond individual socioeconomic status and lifestyle factors, the speed of biological aging is a weathering process fostered by the quality of residential environments. Further, as noted, such effects of neighborhood disadvantage do not appear to vary by gender nor age period. From a social policy standpoint, programs that decrease neighborhood disadvantage are likely to have beneficial effects on the prospects of healthy aging, especially among Black Americans (Firebaugh & Acciai, 2016; Wilson, 2013). The current findings suggest that neglecting to invest in such programs could very well result in long-term societal costs due to an increased number of individuals suffering from accelerated aging and ultimately elevated morbidity and mortality. There is an opportunity to decrease health disparities by attending to the economic and material conditions that reproduce neighborhood disadvantage.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights:

- Neighborhood disadvantage is related to three indices (PhenoAgeAccel, GrimAgeAccel, and DunedinPoAm) of epigenetic aging.
- The effects of neighborhood disadvantage on epigenetic aging do not appear to vary by age period (young adult and middle age).
- No gender differences in the effects of neighborhood disadvantage on epigenetic aging.
- Identifying social determinants of aging will guide intervention efforts.

Table 1

Components of the Area Deprivation Index (ADI)

1	Percent of population aged >= 25 years with < 9 years of education
2	Percent of population aged >= 25 years with < a high school diploma
3	Percent of employed persons >=16 years of age in white-collar occupations
4	Median family income
5	Income disparity (Defined as the log of 100 * the ratio of the number of households with <$10,000 in income to the number of households with $50,000 or more in income.)
6	Median home value
7	Median gross rent
8	Median monthly mortgage
9	Percent owner-occupied housing units (home ownership rate)
10	Percent of civilian labor force population >= 16 years of age unemployed
11	Percent of families below the poverty level
12	Percent of population below 150% of the poverty threshold
13	Percent of single-parent households with children < 18 years of age
14	Percent of households without a motor vehicle
15	Percent of households without a telephone
16	Percent of occupied housing units without complete plumbing
17	Percent of households with more than one person per room (crowding)

Table 2

Descriptive statistics for study variables

	Young adulthood (*N* = 448)			Middle age (*N* = 493)		
Variables	**% or Mean**	***SD***	**Range**	**% or Mean**	***SD***	**Range**
Chronological age	29.154	0.753	27 – 31	48.300	8.350	26 – 92
Neighborhood disadvantage	67.968	17.940	7 – 99.33	70.398	16.050	19.5 – 98
PhenoAgeAccel	0.000	5.430	−19.59 – 18.58	0.000	5.741	−18.11 – 21.90
GrimAgeAccel	0.000	4.221	−9.27 – 19.27	0.000	4.780	−9.55 – 17.04
DunedinPoAm	1.025	0.078	.83 – 1.27	1.040	0.079	.87 – 1.28
CD8+ T cells	0.100	0.509	0 – .42	0.101	0.048	0 – .31
CD4+ T cells	0.148	0.055	0 – .31	0.178	0.070	0 – .46
Natural killer cells	0.008	0.022	0 – .15	0.022	0.037	0 – .28
B cells	0.042	0.031	0 – .15	0.061	0.059	0 – .94
Monocytes	0.056	0.025	0 – .14	0.057	0.027	0 – .16
Gender (1 = Males)	0.380	0.486	0 – 1	0.260	0.437	0 – 1
Income	21237.960	16443.722	0 – 83136	41085.193	37343.697	0 – 200000
Binge drinking	0.784	1.143	0 – 5	0.381	0.661	0 – 4
Cigarette use	0.478	0.999	0 – 4	0.880	1.343	0 – 6
Healthy diet	2.327	1.210	0 – 5	1.702	1.033	0 – 3
Relocation	0.136	0.343	0 – 1	0.353	0.478	0 – 1

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Table 3.

Robust regression models with inverse-probability-of-treatment weighting examining the effects of neighborhood disadvantage on epigenetic aging

	Young adulthood (*N* = 448)			Middle age (*N* = 493)		
	PhenoAgeAccel *b*/(*SE*)	**GrimAgeAccel *b*/(*SE*)**	**DunedinPoAm *b*/(*SE*)**	**PhenoAgeAccel *b*/(*SE*)**	**GrimAgeAccel *b*/(*SE*)**	**DunedinPoAm *b*/(*SE*)**
Neighborhood disadvantage	.490 * (.207)	.571 ** (159)	.006 * (.003)	.677 ** (.243)	.365 * (178)	.007 * (.003)
Males	−1.982 ** (.486)	2.358 ** (.456)	.012 (.007)	−.681 (670)	2.410 ** (.380)	.017 * (.007)
Log income	−.094 (.059)	−.081 (.058)	−.002 * (001)	.066 (059)	−.032 (051)	−.001 (.001)
Binge drinking	.256 (199)	.141 (.191)	.006 * (.003)	.172 (.374)	.077 (.274)	−.007 (.004)
Cigarette use	.322 (.228)	.986 ** (176)	.021 ** (.003)	.330† (180)	1.894 ** (116)	.028 ** (.002)
Healthy diet	−.190 (191)	.022 (.161)	−.002 (.003)	.053 (193)	.032 (.137)	.003 (.003)
Relocation	−.171 (671)	−.034 (.541)	−.001 (010)	−.062 (.543)	.421 (.350)	.001 (.005)
CD8+ T cells	−16.884 ** (4.608)	−13.313 ** (3.642)	−.573 ** (067)	−22.258 ** (5.239)	−11.635 ** (3.641)	−.409 ** (.049)
CD4+ T cells	−32.259 ** (5.473)	−6.845† (3.933)	−.311 ** (.060)	−3.828 ** (3.823)	−19.311 ** (2.717)	−.408 ** (051)
Natural killer cells	5.732 (8.101)	−2.377 ** (7.457)	−.364 * (153)	6.218 (7.789)	−17.628 ** (4.650)	−.504 ** (.062)
B cells	−5.616 (8.441)	−1.756 * (5.296)	−.403 ** (105)	1.466 (8.593)	−5.898† (3.448)	−.231 ** (.042)
Monocytes	26.054 * (11.470)	8.433 (7.909)	−.022 (141)	1.283 (11.703)	6.397 (7.686)	−.125 (129)
Constant	6.722 ** (1.426)	1.542 (1.238)	1.147 ** (.020)	6.102 ** (1.635)	2.797 * (1.317)	1.160 ** (019)
R-squared	.247	.216	.376	.238	.485	.487

Note: Unstandardized (*b*) coefficients shown with robust clustered standard errors in parentheses; income is log-transformed, and neighborhood disadvantage is standardized by z-transformation (mean = 0 and *SD* =1).

* $p \leq .05$;

** $p \leq .01$ (two-tailed tests).

Table 4

Robust regression models with inverse-probability-of-treatment weighting examining the effects of neighborhood disadvantage on epigenetic aging, controlling for sociodemographic covariates, health-related covariates, and cell-types

	Young adulthood (*N* = 448)			Middle age (*N* = 493)		
	PhenoAgeAccel *b*/(*SE*)	**GrimAgeAccel *b*/(*SE*)**	**DunedinPoAm *b*/(*SE*)**	**PhenoAgeAccel *b*/(*SE*)**	**GrimAgeAccel *b*/(*SE*)**	**DunedinPoAm *b*/(*SE*)**
Neighborhood disadvantage	.507 † (.284)	.432 * (186)	.005 (.004)	.579 * (.240)	.328 (194)	.006 * (.003)
Males	−1.983 ** (.486)	2.364 ** (.443)	.012 (.007)	−.680 (681)	2.410 ** (.382)	.017 * (.007)
Neighborhood disadvantage × Males	−.043 (.400)	.355 (.360)	.004 (.007)	.416 (.553)	.160 (.372)	.004 (.006)
Constant	6.726 ** (1.420)	1.506 (1.245)	1.146 ** (.020)	6.149 ** (1.642)	2.815 * (1.307)	1.161 ** (019)
R-squared	.247	.218	.377	.239	.485	.487

Note: Unstandardized (*b*) coefficients shown with robust clustered standard errors in parentheses; neighborhood disadvantage is standardized by z-transformation (mean = 0 and *SD* =1).

† $p \leq .10$;

* $p \leq .05$;

** $p \leq .01$ (two-tailed tests).