Neighborhood Opportunity and Biological Aging: Results From the Midlife in the United States

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Objective: To quantify the association between neighborhood opportunity and biological aging as measured by epigenetic clocks.
Methods: This cross-sectional study pooled data from 1205 participants in the Midlife in the United States Biomarker Projects (2004-2016). Neighborhood opportunity was measured continuously based on the Childhood Opportunity Index 3.0, which evaluates census tract conditions across educational, health and environment, and social and economic domains. Biological aging was measured using 3 validated DNA methylation-based indicators: the DunedinPACE, GrimAge2, and PhenoAge. Analyses controlled for the confounding effects of age, sex, race, educational attainment, household income, marital status, perceived neighborhood quality, smoking status, past month alcohol consumption, and body mass index (BMI).
Results: Participants living in neighborhoods with low overall opportunity showed a faster pace of aging with DunedinPACE (0.06 SD increase, 95% CI = 0.01, 0.12; p = .029). Similar effects occurred for the health and environment (0.05 SD increase, 95% CI = 0.01, 0.10; p = .023) and social and economic (0.07 SD increase, 95% CI = 0.01, 0.12; p = .026) domains of the overall opportunity score. GrimAge2 and PhenoAge showed similar associations, but those were attenuated after adjusting for sociodemographic characteristics and health behaviors.
Conclusions: Low neighborhood opportunity, particularly in health and environment and social and economic domains, is associated with accelerated biological aging. Health behaviors may contribute to these effects, and additional mechanisms need to be examined in future research.

Key Words: accelerated aging, DNA methylation, place-based health, biological embedding, residential environment

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Abbreviations: **BMI** = body mass index, **COI** = Childhood Opportunity Index, **GED** = general educational development, **MIDUS** = Midlife in the United States, **SES** = socioeconomic status

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INTRODUCTION

The neighborhood in which people live is a strong determinant of health.[1–4] Individuals residing in disadvantaged areas face increased risks of various health conditions, including cardiovascular disease,[5] diabetes,[6] mortality,[7] poor mental health,[8,9] and low cancer survival.[10] While this association is well-established, the precise biological mechanisms underlying the impact of adverse neighborhood conditions on disease development remain poorly understood. To better understand how neighborhood disadvantage becomes biologically embedded and contributes to disease risk, researchers have increasingly turned to biomarkers of aging. Recent advances in epigenetics have provided valuable tools for investigating the biological effects of environmental factors on human health. DNA methylation, a key epigenetic modification, has emerged as a promising biomarker for quantifying the pace and progress of biological aging.[11] Epigenetic clocks were initially developed using machine learning algorithms to predict chronological age[12] and subsequently refined to enhance their prediction of morbidity and mortality[13–15] based on biological age acceleration (ie, the difference between biological age vs chronological age). Epigenetic age acceleration has been linked to numerous diseases, including cardiovascular disease and cancer.[16–18]

This epigenetic measure of biological aging is increasingly recognized as a marker of adverse environmental conditions. Growing research has linked specific neighborhood-level factors, such as socioeconomic position (eg, low income, education, and employment)[19–22] and exposure to pollutants like benzene[23–26] to accelerated biological aging. While previous studies highlight the effects of specific environmental features on biological aging [eg, neighborhood socioeconomic status (SES) or exposure to pollutants], these focused analyses risk underestimating the multifaceted impacts of neighborhood environments.

The Childhood Opportunity Index (COI)[27,28] offers a relatively comprehensive framework for quantifying the

effects of neighborhood context by considering a wide range of neighborhood factors crucial for human development. While it is important to acknowledge that the Neighborhood Opportunity Index shares correlations with other neighborhood indices,[29] it differentiates itself through its broader scope. Compared with narrower measures like the Area Deprivation Index,[30] which primarily captures concentrated disadvantage through markers of socioeconomic hardship (eg, poverty, low education, and poor housing quality), the COI[31] reflects the presence of contextual assets that support health and development, including access to quality education (eg, standardized test scores), health care infrastructure (eg, clinic density), safe environments (eg, fewer hazardous waste sites), and social capital (eg, ties to high-SES individuals within low-SES communities). Though both indices address neighborhood context, they are not conceptual opposites; each captures distinct, complementary dimensions of neighborhood environments. Yet, this opportunity-focused measure includes promotive and protective factors often not captured by deprivation-based metrics. While initially designed to assess child health and development, the index is equally relevant to understanding adult health outcomes. One study found that features of the index, particularly toxic chemical releases, green space, and concentration of employment opportunities, were indirectly related to cortical tissue volume in adults through cardiometabolic risk.[32] Features of neighborhoods captured by this index make it possible to detect health outcomes beyond those associated with conventional indicators of neighborhood disadvantage. The overall index captures a wider range of contextual exposures that may help explain variation in adult health outcomes.

Opportunities within neighborhoods are not randomly distributed but are the product of structural forces. Both historical and contemporary policy decisions have played a critical role in determining access to resources and exposure to risk.[4,33,34] For example, in the 1930s, redlining policies labeled many Black and immigrant neighborhoods as too risky for investment, restricting access to home loans and triggering decades of disinvestment.[35] Many of these same neighborhoods remain economically disadvantaged today, continuing to experience poor housing conditions, limited access to green space, and elevated exposure to pollutants, all of which increase the risk of disease.[2,35–37] Moreover, contemporary zoning laws continue to allow the concentration of industrial facilities in these underresourced areas, exposing residents to environmental hazards while limiting access to green space, quality schools, and other health-promoting infrastructure.[38–41] Diez Roux and Mair[1] provide a widely used framework for understanding how neighborhood environments contribute to health inequalities. They highlight that unequal distribution of resources across neighborhoods can reinforce and perpetuate disadvantage, particularly racial residential segregation. Aside from its direct influence on health, such as exposure to pollutants, the quality of the built environment can also shape social interaction and collective efficacy. Poorly maintained or unsafe public spaces can weaken social cohesion, undermining the capacity of residents to organize and advocate for neighborhood improvements. Neighborhood conditions can also adversely influence health behaviors, as limited access to nutritious food, safe spaces for physical activity, and quality health care constrains individuals' ability to maintain health and well-being. In addition, living in low-opportunity neighborhoods may heighten exposure to chronic stress. Yet, how neighborhood opportunity directly relates to biological aging in adults remains poorly understood.

To understand better how the social fabric of a neighborhood contributes to biological aging processes, we examined the relationship between neighborhood opportunity and biological aging in middle-aged adults, using 3 epigenetic clocks. We explored potential mechanistic pathways by controlling for sociodemographic factors and further adjusting for health behaviors.

METHODS

Study Design and Setting

The Midlife in the United States (MIDUS) is a nationally representative prospective cohort study designed to assess the influence of sociodemographic, psychosocial, and behavioral factors on health.[42] The University of Wisconsin Institutional Review Board approved the MIDUS study protocol, which used random digit dialing to recruit potential study participants. From 1995 to 1996, MIDUS enrolled 7108 noninstitutionalized English-speaking adults aged 25 to 74. A follow-up assessment was conducted in 2006 to 2008 (MIDUS 2), during which an additional sample of 592 African American adults from Milwaukee, WI, was enrolled to increase racial diversity. From 2011 to 2014, an additional 4085 noninstitutionalized English-speaking adults aged 25 to 74 were recruited into the MIDUS Refresher Study. This study included an oversample of 508 African Americans from Milwaukee, WI.

The MIDUS team initiated biomarker studies for subsamples of individuals from the MIDUS 2 cohort [MIDUS Biomarker Project (2004-2009; n = 1255)] and the MIDUS Refresher Study cohort [MIDUS Refresher Biomarker Study (2012-2016; n = 863)]. Participants were eligible if they had completed the core telephone interview and self-administered questionnaire, were part of the Main Random Digit Dialing (MainRDD) sample, and resided in the continental United States. The biomarker protocol involved a 2-day clinic visit that included collection of biological indicators (eg, inflammatory, neuroendocrine, cardiovascular markers), physical exams, medical histories, and medication reviews.[43] Both MIDUS 2 and MIDUS Refresher followed identical protocols. All study individuals provided informed consent before participating in phone interviews, completing self-administered questionnaires, and providing biomarker measurements. Further details of the MIDUS protocols have been described elsewhere.[44,45] The New York University Institu-

tional Review Board considered this cross-sectional study exempt because the data were deidentified and publicly available. This study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[46]

Analytic Sample

We pooled cross-sectional data from the MIDUS Biomarker Project (n = 1255) and the MIDUS Refresher Biomarker Study (n = 863; Figure 1). Of these 2118 participants, we excluded 808 individuals without epigenetic age measurements at the time of data release in 2023. We excluded 105 participants with missing outcome information (n = 1) and covariates (n = 104). The final analytic sample comprised 1205 study participants.

Measures

Biological Aging

Blood samples were collected from participants in the MIDUS study (2004-2016). Whole blood DNA was extracted and subjected to genome-wide methylation profiling using Illumina Methylation EPIC microarrays. After quality control, DNA methylation data were used to calculate second and third-generation clocks that are known for the predictive power for morbidity and mortality and sensitivity to social determinants of health: GrimAge2,[47] DunedinPACE,[15] and PhenoAge.[13] GrimAge2 is an epigenetic clock trained to predict mortality and has demonstrated improved predictive performance compared with the original GrimAge model (GrimAge1).[47,48] To calculate age acceleration scores for GrimAge2 and PhenoAge were regressed on chronological age, with the resulting residuals representing deviations from expected biological age based on chronological age. DunedinPACE directly reflects the rate of biological aging. All biological aging measures were standardized for subsequent analyses (mean = 0, SD = 1). Detailed information on data collection and processing is found in the MIDUS Colectica Portal.[49]

Neighborhood Opportunity

Participants' census tract data were merged to the Childhood Opportunity Index (COI) 3.0.[31] The COI is a composite structural racism index measuring the level of an individual's neighborhood opportunity.[31] This index comprised 44 indicators across content areas such as postsecondary education, pollution, and wealth. We analyzed nationally normed 2010 COI scores for 3 subdomains (education domain, health and environment domain, and social and economic domain) and an overall composite score (COI). Each measure score ranged from 1 to 100, with higher values indicating higher neighborhood opportunity. We reverse-coded these values such that higher values indicated lower neighborhood opportunity. Additional technical information about the index is described elsewhere.[31] The linking of the COI to MIDUS participants required permission and was conducted exclusively by the MIDUS Geocode team to protect participant privacy.

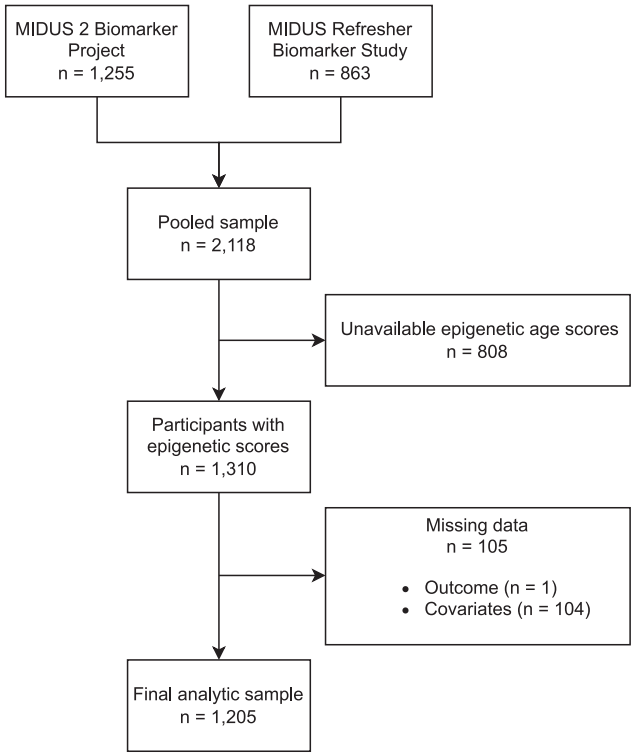

FIGURE 1. Analytic sample selection of participants from the Midlife in the United States (MIDUS) Study.

Covariates

We controlled for several key covariates, including age (measured continuously), sex (male or female), race (white, black, and other), educational attainment (< high school, high school/GED, or some college and above), annual household income (< $50,000, $50,000 to $100,000, and $100,00+), marital status (married, divorced/separated/widowed, or never married), perceived neighborhood quality (measured continuously), smoking status (never, past, and current), past month alcohol consumption (never, < 1 day a week, 1 to 2 days a week, 3 to 4 days a week, 5 to 6 days a week, everyday), and body mass index (BMI; measured continuously). Due to small sample sizes, we included those who identified as Hispanic, Native American/Alaska Native, Asian, or Native Hawaiian/Pacific Islander in the other race category. Perceived neighborhood quality[50] was assessed using 4 items: "I feel safe being out alone in my neighborhood during the daytime," "I feel safe being out alone in my neighborhood at night," "I could call on a neighbor for help if I needed it," and "People in my neighborhood trust each other." Response options ranged from 1 (not at all) to 4 (a lot). Responses were averaged such that higher mean values indicated higher perceived neighborhood quality (Cronbach $\alpha = 0.72$).

Statistical Analysis

Multivariable linear regression models quantified the relationship between neighborhood opportunity and bio-

logical age acceleration. Primary analyses (model 1) controlled for any confounding effects of chronological age and sex. Secondary analyses, in addition, controlled for any effects of race, educational attainment, household income, marital status, and perceived neighborhood quality (model 2). To determine the role of health behaviors in the relation between neighborhood opportunity and biological age acceleration, we conducted a final analysis that, in addition, controlled for smoking status, past month alcohol consumption, and BMI (model 3).

We conducted a series of exploratory analyses. First, we examined the interaction between neighborhood opportunity and race on biological age acceleration. Then we examined the associations between neighborhood opportunity and other epigenetic aging clocks: Horvath and Hannum.[12,51] For all multivariable analyses, we standardized the neighborhood opportunity measures such that the regression coefficients reflected the SD-change in biological age acceleration per 1-SD increase in neighborhood opportunity score. Analyses used R version 4.4.1 (R Core Team, R Foundation for Statistical Computing), with statistical significance assessed as 2-sided $p < .05$.

RESULTS

Data come from 1205 middle-aged adults (Table 1; mean = 51 y, SD = 12), 55% female, 68% white, and 58% never smoked cigarettes. Zero-order correlations are presented in Table 2. In primary analyses (controlling for age and sex; Table 3), individuals living in lower opportunity neighborhoods—according to the COI—showed accelerated epigenetic aging across all measures: DunedinPACE (0.34 SD increase, 95% CI = 0.29, 0.39, $p < .001$), GrimAge2 (0.14 SD increase, 95% CI = 0.11, 0.17, $p < .001$), and PhenoAge (0.03 SD increase, 95% CI = 0.01, 0.06, $p = .021$). When analyses, in additon, controlled for race, educational attainment, household income, marital status, and perceived neighborhood quality in model 2, COI effect sizes showed substantial attenuation: DunedinPACE effects decreased by approximately two-thirds (0.11 SD increase, 95% CI = 0.05, 0.17, $p = .001$) and GrimAge2 effects decreased by nearly 80% (0.03 SD increase, 95% CI = 0.00, 0.06, $p = .063$). The COI effect for PhenoAge remained unchanged in magnitude but lost statistical significance (0.03 SD increase, 95% CI = −0.01, 0.06, $p = .141$). Further controlling for health behaviors (smoking status, past month alcohol consumption, and BMI) in model 3 resulted in additional modest attenuation across all aging measures: DunedinPACE effects were reduced by an additional 45% (0.06 SD increase, 95% CI = 0.01, 0.12, $p = .029$), while GrimAge2 and PhenoAge effects became negligible (GrimAge2: 0.01 SD increase, 95% CI = −0.02, 0.04, $p = .439$; PhenoAge: 0.02 SD increase, 95% CI = −0.02, 0.05, $p = .305$). We did not find statistically significant interactions between overall neighborhood opportunity and race for any aging measure (Supplemental Tables S1, S5, S9, Supplemental Digital Content, http://links.lww.com/PSYMED/B111).

TABLE 1. Characteristics of 1205 Individuals From the Midlife in the U.S. Study

Characteristic	N = 1205
Age, mean (SD)	50.9 (12.4)
Sex, N (%)	
Male	539 (45)
Female	666 (55)
Race, N (%)	
White	822 (68)
Black	297 (25)
Other	86 (7)
Educational attainment, N (%)	
< High school	65 (5)
High school/GED	201 (17)
Some college and above	939 (78)
Annual household income ($), N (%)	
100,000+	265 (22)
50,000-100,000	334 (28)
< 50,000	606 (50)
Marital status, N (%)	
Married	718 (60)
Divorced/separated/widowed	265 (22)
Never married	222 (18)
Perceived neighborhood quality, mean (SD)	3.4 (0.6)
Smoking status, N (%)	
Never	697 (58)
Past	344 (29)
Current	164 (14)
Past month alcohol consumption, N (%)	
Never	391 (32)
< 1 d a week	324 (27)
1-2 d a week	216 (18)
3-4 d a week	130 (11)
5-6 d a week	65 (5)
Everyday	79 (7)
Body mass index, mean (SD)	28.9 (6.7)
Childhood Opportunity Index, mean (SD)	54.7 (30.0)
Education domain, mean (SD)	53.5 (33.0)
Health and environment domain, mean (SD)	60.3 (25.8)
Social and economic domain, mean (SD)	53.6 (28.8)
DunedinPACE, mean (SD)	1.0 (0.1)
GrimAge2, mean (SD)	62.3 (10.7)
PhenoAge, mean (SD)	43.2 (12.9)

To determine which components of neighborhood opportunity contributed most to epigenetic age acceleration, we conducted parallel analyses of the education, health and environment, and social and economic domains. For DunedinPACE, all 3 domains showed strong initial associations in model 1, with the education (0.33 SD increase) and social and economic (0.34 SD increase) domains demonstrating the largest effect sizes compared with the health and environment domain (0.17 SD increase; See Tables S2-S4, Supplemental Digital Content, http://links.lww.com/PSYMED/B111). However, the education domain showed the greatest sensitivity to confounding, with effects decreasing by 76% in model 2 (0.08 SD increase, 95% CI = 0.02, 0.15, $p = .011$) and becoming nonsignificant in model 3 (0.04 SD increase, 95% CI = −0.02, 0.10, $p = .193$).

For GrimAge2, the education and social and economic domains showed similar moderate effect sizes in model 1 (0.13 and 0.14 SD increases, respectively), while the health and environment domain showed a smaller ef-

TABLE 2. Correlations Among All Variables

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1. Age	1.00	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
2. Sex	−0.09*	1.00	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
3. Race	−0.16***	0.09**	1.00	—	—	—	—	—	—	—	—	—	—	—	—	—	—
4. Educational attainment	−0.02	−0.07*	−0.15***	1.00	—	—	—	—	—	—	—	—	—	—	—	—	—
5. Annual household income	0.21***	0.12***	0.19***	−0.23***	1.00	—	—	—	—	—	—	—	—	—	—	—	—
6. Marital status	−0.23***	0.16***	0.34***	−0.15***	0.37***	1.00	—	—	—	—	—	—	—	—	—	—	—
7. Neighborhood quality	0.20***	−0.09**	−0.28***	0.18***	−0.17***	−0.32***	1.00	—	—	—	—	—	—	—	—	—	—
8. Smoking status	0.06*	−0.01	0.07*	−0.25***	0.24***	0.15***	−0.16***	1.00	—	—	—	—	—	—	—	—	—
9. Alcohol consumption	0.08**	−0.19***	−0.17***	0.06*	−0.10***	−0.07*	0.11***	0.15***	1.00	—	—	—	—	—	—	—	—
10. Body mass index	−0.03	0.03	0.14***	−0.19***	0.16***	0.16***	−0.09**	0.05	−0.17***	1.00	—	—	—	—	—	—	—
11. Childhood Opportunity Index	−0.13***	0.07*	0.36***	−0.26***	0.34***	0.30***	−0.35***	0.18***	−0.18***	0.23***	1.00	—	—	—	—	—	—
12. Education domain	−0.13***	0.06	0.38***	−0.25***	0.30***	0.31***	−0.36***	0.18***	−0.15***	0.23***	0.93***	1.00	—	—	—	—	—
13. Health and environment domain	−0.05	−0.02	0.10***	−0.09**	0.18***	0.09**	−0.15***	0.13***	−0.10***	0.11***	0.65***	0.52***	1.00	—	—	—	—
14. Social and economic domain	−0.13***	0.08**	0.35***	−0.26***	0.34***	0.30***	−0.35***	0.16***	−0.20***	0.23***	0.98***	0.85***	0.58***	1.00	—	—	—
15. DunedinPACE	0.19***	−0.02	0.24***	−0.28***	0.32***	0.20***	−0.15***	0.39***	−0.07*	0.35***	0.31***	0.30***	0.16***	0.30***	1.00	—	—
16. GrimAge2	0.87***	−0.13***	−0.05	−0.17***	0.31***	−0.09**	0.08**	0.34***	0.10***	0.07*	0.02	0.02	0.03	0.01	0.53***	1.00	—
17. PhenoAge	0.89***	−0.09**	−0.13***	−0.05	0.21***	−0.19***	0.17***	0.12***	0.10***	0.03	−0.09**	−0.08	−0.02	−0.09**	0.36***	0.88***	1.00

*$p < .05$.
**$p < .01$.
***$p < .001$.
Pearson correlations with p-values generated using 2-tailed significance tests.

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TABLE 3. Primary Analyses Relating Neighborhood Opportunity Indices to Biological Aging in the Midlife in the United States Study

	Model 1			Model 2			Model 3		
Characteristic	**Beta**	**95% CI**	***p***	**Beta**	**95% CI**	***p***	**Beta**	**95% CI**	***p***
DunedinPACE									
COI	**0.34**	**0.29, 0.39**	**<.001**	**0.11**	**0.05, 0.17**	**.001**	**0.06**	**0.01, 0.12**	**.029**
Education domain	**0.33**	**0.27, 0.38**	**<.001**	**0.08**	**0.02, 0.15**	**.011**	0.04	−0.02, 0.10	.193
Health and environment domain	**0.17**	**0.11, 0.22**	**<.001**	**0.09**	**0.04, 0.14**	**<.001**	**0.05**	**0.01, 0.10**	**.023**
Social and economic domain	**0.34**	**0.28, 0.39**	**<.001**	**0.11**	**0.04, 0.17**	**.001**	**0.07**	**0.01, 0.12**	**.026**
GrimAge2									
COI	**0.14**	**0.11, 0.17**	**<.001**	0.03	0.00, 0.06	.063	0.01	−0.02, 0.04	.439
Education domain	**0.13**	**0.11, 0.16**	**<.001**	0.02	−0.01, 0.06	.190	0.00	−0.03, 0.03	.997
Health and environment domain	**0.07**	**0.05, 0.10**	**<.001**	**0.04**	**0.01, 0.06**	**.008**	0.02	−0.01, 0.04	.147
Social and economic domain	**0.14**	**0.11, 0.16**	**<.001**	0.03	0.00, 0.06	.096	0.01	−0.01, 0.04	.346
PhenoAge									
COI	**0.03**	**0.01, 0.06**	**.021**	0.03	−0.01, 0.06	.141	0.02	−0.02, 0.05	.305
Education domain	**0.03**	**0.01, 0.06**	**.019**	0.03	−0.01, 0.06	.115	0.02	−0.02, 0.05	.318
Health and environment domain	**0.03**	**0.01, 0.06**	**.023**	0.03	0.00, 0.05	.057	0.02	−0.01, 0.05	.155
Social and economic domain	**0.03**	**0.01, 0.05**	**.040**	0.02	−0.01, 0.05	.265	0.01	−0.02, 0.05	.410

COI = Childhood Opportunity Index.
Bold indicates statistical significance at $p < .05$.
p-values were generated using multivariable linear regression.
Model 1 controlled for age and sex.
Model 2 controlled for age, sex, race, educational attainment, annual household income, marital status, and perceived neighborhood quality.
Model 3 controlled for age, sex, race, educational attainment, annual household income, marital status, perceived neighborhood quality, smoking status, past month alcohol consumption, and body mass index.

fect (0.07 SD increase). The education and social and economic domains demonstrated marked attenuation in model 2, with effects decreasing by ∼85% and losing statistical significance (education: 0.02 SD increase, $p = .190$; social and economic: 0.03 SD increase, $p = .096$). In contrast, the health and environment domain showed more gradual attenuation, with effects decreasing by 43% in model 2 (0.04 SD increase, 95% CI = 0.01, 0.06, $p = .008$) and becoming nonsignificant only in the fully adjusted model 3 (0.02 SD increase, 95% CI = −0.01, 0.04, $p = .147$). By model 3, all domain-specific associations with GrimAge2 became negligible (all ≤0.02 SD; See Tables S6-S8, Supplemental Digital Content, http://links.lww.com/PSYMED/B111).

For PhenoAge, all 3 domains showed small but significant associations in model 1 (all 0.03 SD increases), with effects remaining unchanged in magnitude but losing statistical significance in model 2 (education: $p = .115$; health and environment: $p = .057$; social and economic: $p = .265$). In the fully adjusted model 3, all domain-specific associations with PhenoAge remained small and nonsignificant (all 0.01 to 0.02 SD increases, all $p > .15$; See Tables S10-S12, Supplemental Digital Content, http://links.lww.com/PSYMED/B111).

Tables S13 and S14 (Supplemental Digital Content, http://links.lww.com/PSYMED/B111) present the exploratory analyses relating overall neighborhood opportunity to other epigenetic aging clocks (Horvath and Hannum). Controlling for age and sex, lower overall neighborhood opportunity was associated with a 0.01 SD decrease in Hannum in model 1 (95% CI = −0.03, 0.02, $p = .605$; Table S14, Supplemental Digital Content, http://links.lww.com/PSYMED/B111). This association strengthened to a 0.03 SD increase (95% CI = 0.01, 0.06, $p = .019$) when further controlling for race, educational attainment, household income, marital status, and perceived neighborhood quality in model 2. It remain unchanged and statistically significant [0.03 SD increase (95% CI = 0.01, 0.06, $p = .036$)] in model 3 (in addition, controlling for smoking status, past month alcohol consumption, and BMI). We did not find any evidence of statistically significant associations between overall neighborhood opportunity and Horvath across all models (all $p > .13$; Table S13, Supplemental Digital Content, http://links.lww.com/PSYMED/B111).

DISCUSSION

We investigated the relationship between neighborhood opportunity, as measured by the Childhood Opportunity Index (COI), and biological aging. Our findings indicate that individuals residing in low-opportunity neighborhoods exhibited both a faster pace of aging (DunedinPACE) and greater epigenetic age acceleration (GrimAge2 and PhenoAge). For DunedinPACE specifically, the association between low neighborhood opportunity and biological aging was observed across nearly all COI domains, including the health and environment and social and economic domains. Approximately half of the relationship between neighborhood opportunity and DunedinPACE was explained by smoking status, past month alcohol consumption, and BMI. When accounting for sociodemographic characteristics and health behaviors, GrimAge2 and PhenoAge associations were attenuated to nonsignificant levels.

Our findings align with prior research linking deprived neighborhoods to accelerated biological aging.[19,20,52,53] Importantly, our study highlights the key influence of different domains of neighborhood oppor-

tunity. Within DunedinPACE, the health and environment and social and economic domains emerged as having particularly strong relations to biological aging, even after adjusting for smoking status, alcohol consumption, and BMI. These findings suggest that neighborhoods characterized by limited economic and social capital, heightened exposure to environmental pollutants, and restricted access to health care may accelerate biological aging processes. In contrast, the education domain appeared less relevant for adult populations, which may be attributable to the index's original design for assessing environments critical to child development. For instance, one indicator within this domain, the percentage of teachers in their first or second year, may hold greater relevance for child outcomes than for adults. This observation suggests that the relationship between educational opportunity and biological aging may vary across different life stages. Future research should replicate these findings across the life course to examine whether the influence of neighborhood domains on biological aging differs by age cohort. Such studies could offer valuable insights into the timing through which neighborhood environments exert their effects on aging.

The quantitative associations between neighborhood opportunity and biological age were attenuated by approximately half in analyses that controlled for smoking status, alcohol consumption, and BMI. This attenuation was expected, as these variables likely capture a range of health-relevant behavioral pathways that mediate the relationship between neighborhood opportunity and biological aging. Neighborhoods divested of opportunities often lack access to supermarkets and recreational facilities and are disproportionately targeted by tobacco companies.[54,55] Consequently, individuals living in such neighborhoods are more likely to have high BMI and engage in smoking, partially accounting for the statistically significant relationship between neighborhood opportunity and biological aging. Despite this significant attenuation, sociodemographic factors also played a significant role in explaining these relationships. It is possible that low-opportunity neighborhoods limit individual socioeconomic mobility,[56,57] and in turn, activate stress pathways and contribute to behavioral responses, such as alcohol consumption, that further accelerate aging. Future research should aim to identify additional mechanisms, including stress-related inflammation and other health behaviors, to better understand how these processes intersect with neighborhood context to influence biological aging.

Consistent with findings from a prior MIDUS study,[58] the relationship between neighborhood opportunity and biological aging was most pronounced when assessed using the DunedinPACE clock. Unlike GrimAge2 and PhenoAge, which captures the cumulative effects of aging across the life course, DunedinPACE focuses on the current rate of aging. As hypothesized by Cuevas et al,[58] this distinction may explain the heightened sensitivity of the DunedinPACE measure to current environmental conditions. Low-opportunity neighborhoods may exert more immediate effects on the pace of aging rather than on cumulative lifespan aging metrics. We also examined whether neighborhood opportunity was associated with other epigenetic clocks and found a consistent association with the Hannum clock across all models. This may be because the Hannum clock was specifically trained on whole blood[59] and is particularly sensitive to variations in blood cell composition,[60] which could be influenced by neighborhood conditions. As such, the Hannum clock may be especially responsive to the types of exposures captured by COI. Further research is needed to explore how other epigenetic clocks respond to other distinct neighborhood characteristics and to evaluate the long-term effects of prolonged residence in low-opportunity neighborhoods on biological aging trajectories.

This study is not without limitations. The cross-sectional design limits our ability to draw causal inferences about the relationship between neighborhood opportunity and biological aging. Neighborhood opportunity was assessed at a single time point, which does not account for changes over time. People relocate, neighborhoods undergo dynamic transformations, and individuals may adapt to their neighborhood environments, all of which could have significant implications for downstream epigenetic aging processes. Future research should examine how cumulative exposure to low-opportunity neighborhoods or fluctuations in neighborhood conditions over time influence biological aging. In additon, while the COI is among the most comprehensive indices available of neighborhood conditions, it does not account for all relevant dimensions of neighborhood environments, nor does it incorporate historical and structural factors that have shaped neighborhood opportunity.[61] For instance, the long-term effects of systemic inequities, such as redlining or the legacy of Jim Crow laws,[37,53] are not explicitly represented. Incorporating novel indices alongside this current index could provide a better understanding of how neighborhoods influence biological aging. Lastly, the linking of the COI to MIDUS participants required permission and was conducted exclusively by the MIDUS Geocode team to protect participant privacy. We did not have direct access to granular geographic identifiers such as census tract information. Therefore, we could not assess the extent of participant clustering within specific census tracts or conduct multilevel models that account for spatial dependencies.

CONCLUSION

Our results reveal that individuals residing in low-opportunity neighborhoods exhibit accelerated epigenetic aging, and that variations in health behavior (eg, smoking, alcohol consumption, and adiposity) may mediate approximately half of that total effect. These insights provide a basis for future research to explore the pathways linking neighborhood opportunity to biological aging and accelerated biological aging may serve as one potential mechanism that contribute to the elevated health risks observed in low-opportunity neighborhoods.

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