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Perspective

The interface of geroscience with longitudinal health disparities research: a 20-year retrospective of the Healthy Aging in Neighborhoods of Diversity across the Life Span study

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Abstract

Geroscience may be the juggernaut that coalesces the pathways of biologic knowledge to expand our understanding beyond describing differences in rates of aging to feasible interventions for improving quality of life as we age. To accomplish this, geroscience must interdigitate with long-standing immutable factors about health. As early as the 17th century, physicians and early demographers like John Graunt, Percival Potts, Bernardino Ramazzini, and Rudolf Virchow identified the importance of differences in health trajectories and outcomes for individuals, and underlying aspects of health disparities. These differences in health status relate to numerous social determinants of health as they interact with biological risk factors and the environment. These populations and the psychosocial factors that influence health and longevity must be considered as an integral part of geroscience. Longitudinal studies that examine factors influencing the development of age-related health differences over time should be a key component of geroscience. The HANDLS study provides a useful demonstration project showing the value of studying aging in urban dwelling American adults, some of whom face significant social adversity based on race, socioeconomic status, and other factors.

Keywords: Aging, Perceived discrimination, Gene expression, Health disparities, Longitudinal studies

Introduction

Aging affects everyone, but the determinants of its progression vary among demographic groups. A large body of literature support the notion of "weathering" or accelerated aging among African American individuals.[1] Several societal subgroups experience health disparities based on race, ethnicity, sexual orientation, socioeconomic status, geographic setting, education, psychological states, and adverse behaviors.[2–4] By 2040, people over 65 will make up 22% of the US population, with racial and ethnic minorities over 65 increasing from 25% in 2022 to 34%.[5] Thus, the concept of healthy aging across all demographic groups should be a priority for policymakers and healthcare providers. Estimates suggest that delaying the onset of age-related diseases could yield significant monetary savings for countries.[6]

Understanding the effects of societal factors on aging, including the underlying biological mechanisms, is the first step toward developing effective clinical interventions. Geroscience is dedicated to identifying the biological drivers of the aging process, leading to the development of therapeutics and protective measures that delay age-related chronic diseases.[7,8] In age-related health disparity research, geroscientists have focused on the interplay between the social determinants and the biology of aging. In this context, various biological approaches identified the mechanisms through which adverse social experiences faced by minority groups lead to disproportional health outcomes.

Social and environmental disadvantages underlying health disparities often begin in childhood and persist into adulthood. Therefore, lifelong unequal environmental and social exposures should be considered when assessing health disparities in older adults.[9–11] Compared with longitudinal cohorts, cross-sectional cohorts are inadequate for accurately modeling how adverse life experiences affect health outcomes. Additionally, study cohort homogeneity remains a concern, as the clinical data currently used in aging research mostly consist of individuals of European ancestry, with limited data available for underrepresented populations.[12] An important challenge in the field of geroscience is the incorporation of underrepresented populations into aging research both as researchers and as participants.

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The Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) study is an ongoing population-based longitudinal cohort of African American and White adult participants. HANDLS was initiated in 2004 to investigate how racial and socioeconomic factors affect health disparities separately or synergistically with the goal of identifying biological factors underlying interactions among behavioral, psychosocial, and environmental factors over time.[13] In this review, we present a summary of research achievements from HANDLS.

Early onset frailty

Frailty is an age-associated clinical syndrome that is typically studied in elderly, mostly White populations. Data from HANDLS was used to examine frailty at midlife in African American and White participants aged 35- to 64-year old at initial assessment with overall mortality.[14] The known association of increasing frailty prevalence with age differed across race with White participants having higher prevalence at younger ages. Our findings indicate that frailty commences at midlife and is a risk factor for mortality in both African American and White adults. Understanding early onset of frailty at midlife may be an excellent surrogate for weathering or accelerated aging. Weathering initially described by Geronimus, is socially induced accelerated aging.[15] However, it is difficult to examine the relevant transduction factors of the resultant health effects of race-related stress. Using the surrogate clinical phenotype of early onset frailty for weathering, we pursued different biologic transduction pathways important in frailty overall and in health disparities. We focused on frailty and gene expression, DNA damage and repair, and extracellular vesicles as a molecular biomarker. This work characterizes early onset frailty as an important clinical entity in middle age influenced by demographic factors (Figure 1).

Gene expression

The epidemiologic findings of race and frailty led us to investigate whether genomic differences between African American and White adults were associated with frailty status in middle-aged adults.[16] We analyzed frailty-associated, genome-wide transcriptional changes by employing next generation RNA sequencing using total RNA from peripheral blood mononuclear cells (PBMCs). We identified 5082 genes differentially expressed with frailty. Frailty altered gene expression patterns and biological pathways differently across race, including pathways related to inflammation and immunity. Validation of gene expression revealed an interaction between frailty and race for the cytokine *IL1B* and the transcription factor *EGR1*. Other genes were lower with frailty including glucose transporter, *SLC2A6*, the neutrophil receptor, *FCGR3B*, and the accessory protein, *C17orf56*. These results suggest that there may be demographic dependent, divergent biological pathways underlying frailty in middle-aged adults.

DNA damage

We also examined DNA oxidation damage and inflammatory markers with frailty, since evidence suggests that DNA oxidation damage, DNA repair capacity (DRC) and inflammation are associated with aging and age-related conditions. We used a high throughput CometChip assay to quantify baseline and hydrogen peroxide (H_2O_2)-induced DNA oxidation damage, DRC in PBMCs and serum cytokines levels in nonfrail and frail middle-aged African American and White individuals living above and below poverty.[17] Baseline DNA damage levels do not differ across frailty status, poverty, race, or sex; however, differences in H_2O_2-induced DNA damage and DRC were detectable. Among those living above poverty, nonfrail individuals displayed higher H_2O_2-induced DNA damage compared to frail individuals. Additionally, among women, those

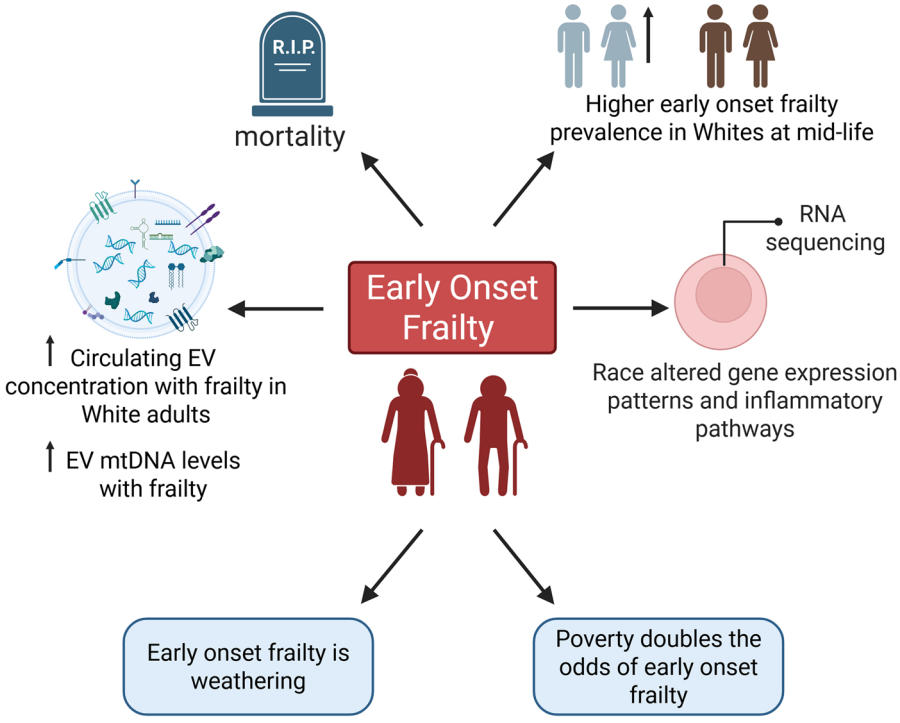

Figure 1. Early onset frailty is an important clinical entity in middle-age. EV, Extracellular Vesicles; mtDNA, mitochondrial DNA.

who were nonfrail displayed lower DRC than those who were frail. Among men, participants living below poverty displayed higher DRC than those living above poverty. Baseline DNA damage, H_2O_2-induced DNA damage as well as DRC were associated with serum cytokine levels. These data suggest that frailty, sex, and the social determinant of health (SDOH) poverty, interact to effect DNA damage and repair at midlife, which may contribute to health disparities observed later in old age.

Extracellular vesicles

The third molecular marker we focused on in the context of frailty was extracellular vesicles (EVs), which are small (30-400 nm), lipid-bound vesicles released by cells into biofluids that shuttle proteins including inflammatory proteins, nucleic acids, and lipids as part of intercellular communication systems.[18] EVs also carry circulating cell-free mtDNA (ccf-mtDNA),[19] which is a damage associated molecular pattern (DAMP) molecule. EVs were isolated from nonfrail and frail middle-aged African American and White HANDLS participants living above and below poverty.[20] Plasma EV levels were highest in frail White participants and EV mtDNA levels were higher in frail participants than nonfrail. EV inflammatory proteins were associated with frailty, race, sex, and poverty. Our findings suggest that EVs may carry DAMPs, such as mtDNA, as well as inflammatory proteins in frail individuals providing clues to molecular mechanisms that may underlie frailty and that race and poverty status influences the inflammatory cargo of EVs.

Perceived discrimination

Kidney function

Perceived discrimination is a form of chronic stress associated with psychosocial distress and adverse health outcomes. Using HANDLS longitudinal data on kidney function based on estimated glomerular filtration rate (eGFR), perceived racial and gender discrimination were associated with lower eGFR.[21] Among White women, greater experience with discrimination was associated with lower baseline eGFR, but in African American women, both perceived racial discrimination and discrimination experience were linked to lower follow-up kidney function.

Cardiovascular risk

HANDLS African American participants who reported high levels of discrimination and depressive symptoms had increased atherosclerosis assessed by carotid intimal-medial thickness (IMT).[22] In cross-sectional analyses, there were two interactions in African Americans: more frequent discrimination across various social statuses and a higher lifetime discrimination burden were related to thicker carotid IMT in participants with greater depressive symptoms. No significant findings were observed in White participants.

Religious coping mitigates the effects of racial discrimination on cardiovascular risk for African American men but not women.[23] Among men who experienced racial discrimination, religious coping was negatively related to systolic blood pressure and HbA1c. However, in men reporting no prior discrimination, religious coping was positively related to most cardiovascular risk factors. Among women who had experienced racial discrimination, greater religious coping was associated with higher HbA1c and body mass index. The lowest levels of cardiovascular disease risk were observed among women who seldom used religious coping but experienced discrimination.

In HANDLS cross-sectional data, religiously affiliated African American men reporting the lowest and highest experienced discrimination had heightened risk for subclinical cardiovascular disease assessed by pulse wave velocity, a measure of arterial stiffness and indicator of subclinical cardiovascular disease.[24] There was a significant three-way interaction of discrimination with religious affiliation status and sex on pulse wave velocity. Simple effect analyses showed a U-shape relation for only religiously affiliated men such that lower and higher levels of discrimination were related to greater pulse wave velocity. No such relations emerged among unaffiliated men or women.

Brain structure

Experience of lifetime discrimination was related to MRI-assessed white matter lesion volume in HANDLS African American participants[25] (Figure 2A). In this subsample of African American participants for whom MRI scans were available, there were significant interactive relations of age and quadratic lifetime discrimination burden and quadratic racial discrimination with white matter lesion volume. Among older African American participants, increases in lifetime discrimination burden and racial discrimination were associated with increases in white matter lesion volume; in younger African American participant, decreasing levels of racial discrimination were related to increases in white matter lesion volume.

Telomere length

Exposure to various forms of discrimination is related to cellular aging as assessed by telomere length.[26] In HANDLS cross-sectional data on White participants, younger and older men reporting greater racial discrimination had shorter and longer telomeres, respectively. In African American participants, shorter telomere lengths were found in women reporting greater lifetime burden of discrimination, racial, or gender discrimination; higher socioeconomic status African American participants reporting greater lifetime burden or racial discrimination; and younger African American participants reporting greater exposure to multiple sources of discrimination.

Molecular pathways

In HANDLS cross-sectional data, there was evidence for identifiable cellular pathways by which racial discrimination amplifies cardiovascular and other age-related disease risks.[27] Oxidative stress is the process by which reactive oxygen species damage cellular components including DNA, proteins, and lipids, and is likely associated with psychological stress. Racial discrimination was significantly associated with red blood cell oxidative stress after adjusting for age, smoking, high-sensitivity C-reactive protein (hsCRP) level, and obesity. When stratified by race, discrimination was not associated with oxidative stress in White participants but was associated significantly in African American participants. The biological transduction pathway through which discrimination results in oxidative stress may relate to changes in gene expression patterns. We found that gene expression associates with discrimination in White and African American adults.[28] Discrimination alters gene

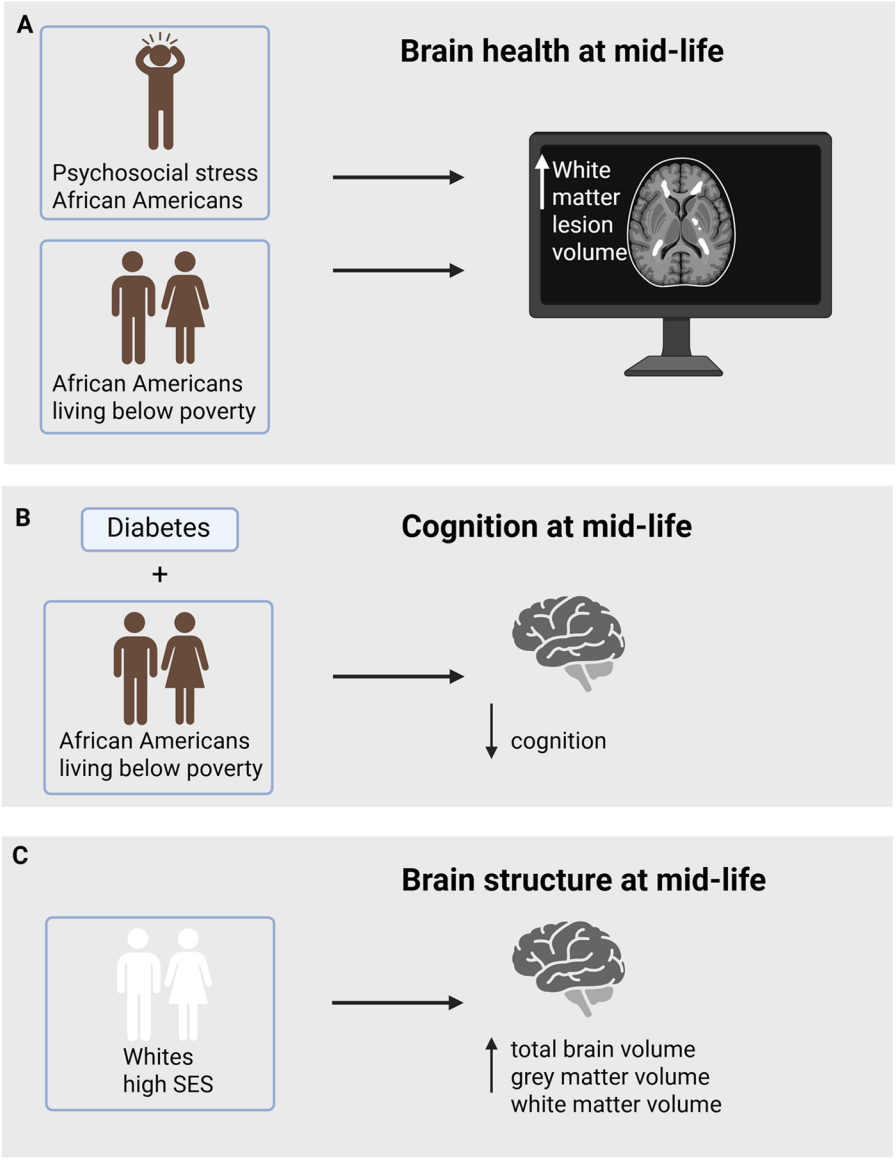

Figure 2. Social determinants of health and chronic disease affect brain health, cognition, and brain structure at mid-life. SES, socioeconomic status.

expression in inflammatory and immune response genes and pathways. The relationship between perceived discrimination and obesity trajectory differed by race.[10] In HANDLS longitudinal data, higher baseline perceived discrimination was associated with a positive body mass index trajectory in African American participants but not in White participants. Racial discrimination was associated with more mental health symptoms, which in turn was associated with intimate partner violence perpetration.[29] The negative effect of discrimination on mental health was stronger for African American women than African American men and for African American participants with household incomes below poverty.

Medical mistrust

Mistrust of the health care system is associated with underutilization of medical services and poor self-reported health. However, in HANDLS longitudinal data, poverty status and health literacy did not influence the association between medical mistrust and self-rated health but perceived discrimination did.[30] Stratified analyses by race found that White participants exhibited greater influence from medical mistrust and perceived discrimination on self-rated health than African American participants.

Cognition and brain structure

Age-associated cognitive differences and change

Individual differences in cognitive performance by age and sex is well known. Less well known is whether individual differences vary by socioeconomic status and race. In cross-sectional data from the HANDLS first wave, diabetes was associated with poorer verbal memory, working memory, and attention among only African American participants with household incomes below poverty[31] (Figure 2B). No consistent differences between diabetic and nondiabetic individuals were found for African American and White participants above poverty.

In HANDLS longitudinal data, the relationships between carotid IMT—a well-established measure of marker of

atherosclerosis—and cognitive performance differed as a function of race and socioeconomic status especially for measures of attention, executive function, and memory.[32] Notably, greater IMT was generally associated with worse cognitive performance, but the disadvantage was most pronounced among White participants above poverty.

Telomere length was differentially associated with aspects of attention, executive functioning, and memory among individuals below poverty, who may be uniquely vulnerable to adverse effects of shorter telomeres.[33] In White participants below poverty, shorter telomere length was associated with worse short-term memory. Regardless of race, shorter telomere length was also associated with worse performance on immediate visual memory and executive performance.

Plasma neurofilament light (NfL) is a marker for neurodegenerative diseases. In HANDLS longitudinal data, initial plasma NfL level was associated with a faster decline on normalized mental status scores in Whites only and in those >50-year old.[34] Annualized increase in NfL was associated with a greater decline in verbal fluency in men. NfL was also associated with a slower decline in verbal memory among individuals above poverty.

Systemic inflammation affects cognitive performance over time. In HANDLS longitudinal data, hsCRP—an inflammatory marker—was linked to poorer baseline mental status among younger women and poorer attention in older women and African American participants.[35] Erythrocyte sedimentation rate—another inflammatory marker—was related to faster decline on verbal memory among older men, with poorer performance on attention and executive function among African American participants.

Reading ability is associated with cognitive performance especially for African American participants in HANDLS.[36] Reading literacy, but not education, was associated with all but one cognitive measure in African American participants and below poverty Whites. In contrast, both education and reading scores were associated with many cognitive measures in above poverty White participants. These findings provide evidence that reading ability better predicts cognitive functioning than years of education and suggest that disadvantages associated with racial minority status and low SES affect the relative influence of literacy and years of education on cognition.

Brain structure

In an ancillary substudy, HANDLS examined the relationships of MRI-assessed global brain outcomes with a composite measure of socioeconomic status (SES) that combined educational attainment and poverty status. African American participants with low SES had significantly greater white matter lesion volumes than White participants with low SES[37] (Figure 2A). In addition, dorsolateral prefrontal cortex volume significantly mediated the association between SES and executive function in White participants but not African American participants.[38]

HANDLS investigators also found SES, but no race differences, in measures of white matter integrity using diffusion tensor imaging to estimate regional fractional anisotropy.[39] Relative to the high SES group, low SES was associated with poorer white matter integrity. In a separate study using brain volumes assessed by T1-weighted MP-RAGE, there were SES by race interactions for right and left medial prefrontal cortexes, left medial prefrontal cortex, left orbital prefrontal cortex, and left anterior cingulate cortex.[40] Nevertheless, higher SES Whites had greater volumes than all other groups (Figure 2C). Overall, higher SES participants had greater right and left hippocampal and amygdala volumes; White participants had greater right and left hippocampal, right orbital prefrontal cortex, and right anterior cingulate cortex volumes than African American participants (Figure 2C).

The relationship between SES and executive function was mediated by the integrity of the anterior limb of the internal capsule (ALIC), external capsule (EC), superior longitudinal fasciculus (SLF), and cingulum.[41] Lower SES was related to poorer cognitive performance and white matter integrity. Lower executive function performance was related to poorer integrity of the ALIC, EC, and SLF.

Social determinants of health influence biomarkers and disease risk

Biological aging

Aging involves a diverse set of molecular changes including epigenetic alterations. DNA methylation adds a methyl group to the fifth carbon of a cytosine at Cytosine-Phosphate-Guanine (CpG) sites, forming 5-methylcytosine. Analyzing changes in DNA methylation (DNAm) patterns at CpG sites with age is a commonly used method for predicting epigenetic age, also known as the "epigenetic clock."[42] The deviation between epigenetic age and chronological age can predict the rate of accelerated aging in individuals which is associated with adverse health outcomes. Using HANDLS cross-sectional data, Tajuddin et al. examined the association between race, poverty, and sex with epigenetic age acceleration in African Americans and White adults.[43] Using the Horvath epigenetic aging clock, both African American and White male participants had faster age acceleration compared to African American and White female participants. There was no association between poverty status and epigenetic age acceleration.[43] Since the Horvath clock is trained solely on DNAm changes with chronological aging rather than lifespan biomarkers, it is not as predictive of the effects of adverse socioeconomic stressors on accelerating epigenetic aging.[44] Using the DunedinPACE epigenetic clock, which estimates the ongoing rate of decline in system integrity,[45] Shen et al. reported that living below poverty and African American race were associated with a higher rate of accelerated aging in a longitudinal cohort from HANDLS[46] (Figure 3). While living below poverty in White participants was associated with faster epigenetic aging, African Americans regardless of poverty status demonstrated accelerated aging (Figure 3). The higher pace of epigenetic aging among African American adults is not unexpected. The weathering hypothesis posits that health and aging disparities in African American individuals are the product of cumulative socioeconomic disadvantage.[1] Even as it appears that the DunedinPACE score is sensitive to adverse life experience, it cannot disentangle the effects of race from other socioeconomic factors. Therefore, to incorporate epigenetic aging measures to develop inclusive anti-aging therapies, these measures must stem from diverse population cohorts that account for genetic variation and ancestry.

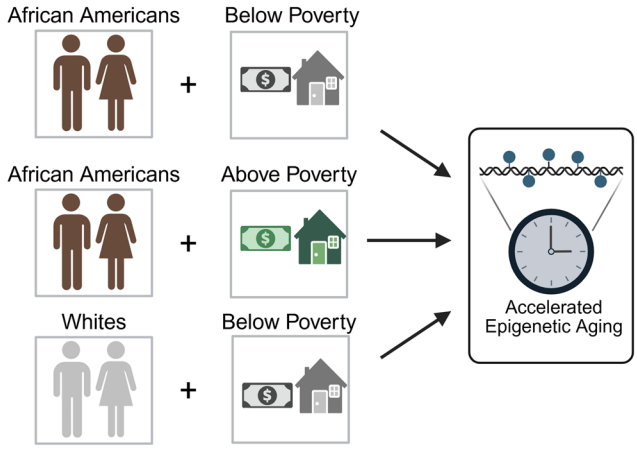

Figure 3. African American race and living below poverty accelerate epigenetic aging.

Chronic disease

The chronic disease burden is increasing in the United States and areas with greater socioeconomic disadvantage show the highest prevalence.[47] Using the HANDLS cohort which spans race and SES, we have examined how various social determinants of health (SDOH) are related to chronic disease. After the first wave of data were collected, we endeavored to disentangle the role of race and SES in chronic kidney disease (CKD) prevalence across African American and White adults living above and below poverty.[48] While overall, low SES was associated with a greater odd of CKD, when stratifying by race, low SES was only associated with an increased odds of CKD for the African American participants.

There are many avenues in which SDOH can affect chronic disease risk. Poor sleep is a risk factor for CKD and other chronic diseases. Previous studies have demonstrated sleep disparities by race, although many studies do not have participants enrolled from similar environments.[49] In the HANDLS cohort, there were no significant racial group differences in sleep duration. The study did find that almost a quarter of this urban-dwelling cohort reported having an inadequate amount of sleep compared with recommendations.[50] Another aspect of SDOH is the local environment, which can have direct and indirect effects on health. We used the HANDLS cohort to examine how the specific neighborhood factor of crime was related to CVD risk factors.[51] The results indicated no association between crime rates and risk factors for White participants or African American men. However, African American women had significant associations between overall crime rates and higher fasting glucose, and between violent crime rates and higher blood pressure, independent of SES. African American women may be particularly vulnerable to health consequences of living in an area with high crime due to concerns regarding personal safety. These findings highlight the importance of examining risk factors across race and SES in similar environments.

Molecular genetics

Vitamin D

We used a molecular genetics approach to investigate the biological transduction pathways that may contribute to the accelerated aging phenotype and health disparities. Our first approach was to address racial differences in vitamin D insufficiency. Although African American individuals generally have lower 25-hydroxyvitamin D (25D) than White individuals, they have higher bone mineral density and lower risk of osteoporosis. We reported that African American adults in HANDLS had similar levels of bioavailable 25D than White adults, due to low levels of both 25D and vitamin D-binding protein, which may be partly explained by racial differences in the prevalence of genetic polymorphisms in the vitamin D-binding protein gene.[52] Furthermore, African American individuals had lower levels of a 25D metabolite, 24,25-DihydroxyvitaminD[24,25(OH)2D], but a similar vitamin D metabolite ratio (VMR) to White individuals.[53] These studies provide evidence that total vitamin D measurements may not be suitable for assessment of vitamin D status in African American individuals.

Hypertension

We examined potential molecular drivers that may contribute to the racial health disparities observed in hypertension, as African American adults have the highest hypertension prevalence and mortality due to CVD.[7] By transcriptionally profiling PBMCs, we identified novel hypertension and race-related mRNA-microRNA pairs that may contribute to disparities in hypertension.[54] We also examined EVs in hypertensive and nonhypertensive HANDLS participants. There were no differences in EV characteristics with hypertension, but we did observe that both EV and plasma ccf-mtDNA were higher in African American participants compared with White participants.[55] Incorporating genetic ancestry, we found that EV mtDNA levels were highest in self-identified African American participants with African mtDNA haplogroup. These studies revealed that gene expression differences may underly racial hypertension disparities but that EVs may be altered with race and ancestry.

Mortality

To identify biological mechanisms that underlie premature mortality, we examined whether EVs could be used as molecular markers of mortality. Our initial study examined plasma EVs characteristics and protein content in a cross-sectional cohort of African American and White participants.[56] EV levels of apoptotic proteins were higher in White participants compared to African American participants. Importantly, EV concentration in this middle-aged cohort was analyzed in the context of clinical markers of mortality and was significantly associated with hsCRP, homeostatic model assessment of insulin resistance, alkaline phosphatase, body mass index, waist circumference and pulse pressure. These data led us to further explore whether EVs and their associated cargo can be utilized as novel markers of mortality. We isolated plasma EVs from HANDLS participants who died within a 5-year period and matched to surviving participants.[57] There were no differences in EV concentration or EV mtDNA levels with mortality status, but we did observe higher levels of inflammatory proteins in EVs with mortality. We found that differences in EV inflammatory protein levels were associated with poverty, race and sex. Our studies of socioeconomically diverse African American and White adults at middle age suggest that EVs and their protein cargo may be able to identify individuals at risk for premature mortality.

Poverty

Given our previous work demonstrating high mortality rates among African American men living below poverty in HANDLS,[58] we aimed to identify biologic pathways through which poverty possibly triggered premature mortality. Since we previously found race and hypertension-related differential expression for miRNAs, we examined another class of noncoding RNAs, long noncoding RNAs (lncRNAs), in HANDLS men. Profiling of lncRNAs and mRNAs from PBMCs from young and old White and African American men living above or below poverty revealed changes in both lncRNAs and mRNAs with age and poverty status in White men, but not in African American men.[59] In younger men, mitochondrial function and response to DNA damage and stress were pathways enriched. In men living above poverty, response to stress, viral infection, and immune signals were pathways enriched. Thus, in this study we found that age and poverty influence lncRNA expression, which may help us further understand molecular pathways underlying how SDOH and aging can affect disparities in aging and disease.

Conclusion

In summary, our work with the HANDLS cohort highlights the influence of SDOH on biological transduction pathways that may lead to the accelerated aging phenotype and health disparities in a mid-life cohort of African American and White residents of Baltimore. From our perspective, there are five immutable issues that geroscience must consider: representation matters among study populations as well as among researchers, the SDOH especially poverty influences health outcomes throughout the lifespan, as our work in a mid-life cohort exemplifies. Race is a freighted term in this society and does not represent biology but the disadvantage or privilege it conveys in society. Ancestry should be addressed in geroscience studies of the future. Algorithms and prediction models must be examined in all populations to assess accuracy and scientific value. Few population-based studies include mid-life or early adulthood individuals, especially minority populations in aging/geroscience research.[4] Thus, geroscience needs to prioritize examining representative cohorts in future studies including a focus on the SDOH. This is especially important given the demographic shifts in the aging population.[4] Representative studies are essential to avoid bias in clinical trials of senolytics and senomorphics and in epidemiologic and genomic studies. We are only beginning to understand how biologic, psychosocial, socioeconomic, and environmental factors contribute to an accelerated aging phenotype in low SES individuals and in minority populations. Thus, the inclusion of these populations into future clinical studies should be prioritized.

Our data highlight the difficulty in identifying simple prescriptions for understanding and addressing health disparities. This is not entirely unexpected because there are large individual differences within groups defined by intersecting demographics. Our research finds larger individual differences within groups than between groups, despite important mean differences often attributed to SDOH. In addition to replicating our longitudinal data in other representative samples, it is not too early to conceptualize studies that may resolve some of the apparent complexities identified so far. New research designs are required to address rapidly changing cohort effects, which we must separate from longitudinal trends. One design that might contribute to this effort is a representative family study in which groups of first-degree relatives are followed from birth to death with appropriate assessments of environmental and biological effects. Such a design would contribute to our understanding of the relative contributions of social, economic, genetic, epigenetic, and nutritional factors, among others.

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Conflict of interest

None declared.

Author contributions

Nicole Noren Hooten and Nicolle A. Mode contributed equally to this work Conceptualization: Nicole Noren Hooten, Michele K. Evans, Shafagh Valipour; Methodology: Nicole Noren Hooten, Michele K. Evans; Writing—original draft: Nicole Noren Hooten, Nicolle A. Mode, Shafagh Valipour, Alan B. Zonderman; Writing—review & editing: Nicole Noren Hooten, Nicolle A. Mode, Alan B. Zonderman, Shafagh Valipour, Michele K. Evans; Data curation: Nicolle A. Mode, Alan B. Zonderman; Formal Analysis: Nicolle A. Mode, Alan B. Zonderman; Supervision: Michele K. Evans, Alan B. Zonderman; Funding acquisition: Michele K. Evans; Resources: Michele K. Evans; Project administration: Michele K. Evans, Alan B. Zonderman. All authors read and approved the final manuscript.

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Data availability statement

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request through the HANDLS website https://handls.nih.gov/.

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