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Article

Racial differences in weathering and its associations with psychosocial stress: The CARDIA study

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ABSTRACT

Biological age (BA) is a construct that captures accelerated biological aging attributable to “wear and tear” from various exposures; we measured BA and weathering, defined as the difference between BA and chronological age, and their associations with race and psychosocial factors in a middle-aged bi-racial cohort. We used data from the Coronary Artery Risk in Young Adults study (CARDIA), conducted in 4 U.S. cities from 1985–2016 to examine weathering for adults aged 48–60 years. We estimated BA via the Klemera and Doubal method using selected biomarkers. We assessed overall and race-specific associations between weathering and psychosocial measures. For the 2694 participants included, Blacks had a BA (SD) that was 2.6 (11.8) years *older* than their chronological age while the average BA among Whites was 3.5 (10.0) years *younger* than their chronological age (Blacks weathered 6.1 years faster than Whites). Belonging to more social groups was associated with less weathering in Blacks but not Whites, and after multivariable adjustment, lower SES and more depressive symptoms were associated with more weathering among Blacks than among Whites. We confirmed racial differences in weathering, and newly documented that similar psychosocial factors may take a greater toll on the biological health of Blacks than Whites.

1. Introduction

Race-based health disparities have been observed in many conditions including cardiovascular, inflammatory, upper respiratory diseases, and some cancers (Myers, 2009; Schneiderman et al., 2005). Specifically, Blacks are known to have a higher prevalence of risk factors for cardiovascular disease including hypertension, obesity, and diabetes (Gasevic et al., 2015). Blacks are also more likely to die from cardiovascular disease and stroke than Whites (Lloyd-Jones, Adams, Carnethon, De Simone, Ferguson & Flegal, 2009). Non-Hispanic Blacks (hereafter referred to as “Blacks”) have poorer health than non-Hispanic Whites (hereafter referred to as “Whites”) across the age spectrum, but differences are especially pronounced around middle-age (Fiscella & Williams, 2004; Geronimus, Hicken, Pearson, Seashols, Brown & Cruz, 2010). Race is a socially constructed category, not a biological one (LaVeist, 1994) and it is often a proxy for the unique stressors that minorities face, such as lower social and economic status, and worse access to and delivery of health care. Stressful lifetime events are more prevalent among Blacks and are associated with

cardiovascular disease (Brewer, Redmond, Slusser, Scott, Chamberlain & Djousse, 2018; Hagstrom, Norlund, Stebbins, Armstrong, Chiswell & Granger, 2018; Pedersen, von Kanel, Tully & Denollet, 2017), hypertension (Cuffee, Ogedegbe, Williams, Ogedegbe & Schoenthaler, 2014; Spruill, 2010), and inflammation (Gruenewald, Cohen, Matthews, Tracy & Seeman, 2009; Ranjit, Diez-Roux, Shea, Cushman, Seeman & Jackson, 2007). Blacks are more likely to experience chronic stress in the form of material hardship, interpersonal discrimination, structural discrimination, ambient stressors, segregated housing, and personal danger (Shadlen, Siscovick, Fitzpatrick, Dulberg, Kuller & Jackson, 2006). The “Weathering Hypothesis” (Geronimus, 1992) was proposed to explain the premature decline of health observed with age in African-American women exposed to stress, dangerous environments, and general social disadvantage, which are presumed to cause accelerated wear and tear.

The weathering hypothesis has been supported using biomarkers such as allostatic load (Geronimus, Hicken, Keene & Bound, 2006) and telomere length (Geronimus et al., 2010). Both of these methods illustrate the idea of weathering with Black individuals having a higher

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probability of high allostatic load score and middle-aged Black women showing more biological wear and tear through shorter telomeres. Although allostatic load and telomere length distributions are consistent with the weathering hypothesis, biological age, a construct that has been using in multiple scientific publications over the past decades (Cho et al., 2010), may be a more intuitive metric because it is expressed in years and thus more easily understood than allostatic load; and is derived from biomarkers that do not require an individual's DNA.

In this paper we propose biological age, or the “true global state” of an aging organism (Klemera & Doubal, 2006) to measure weathering and the association between psychosocial factors and weathering. Biological age is intended to measure multi-system change that can result in physiological dysfunction and quantify that change as an age that can be compared to one's chronological age. In this way, weathering can be measured by comparing chronological age at a given time (e.g. at onset of a disease or at time of death) with biological age at that same time point. In particular, a measure of weathering derived from biological age may allow us to better understand how psychosocial factors are associated with a cumulative measure of accelerated aging rather than with individual disease. Biological age has been operationalized using different methods (Cho et al., 2010). Here, we use the Klemera and Doubal method (KDM) (Klemera & Doubal 2006), which uses risk factors as the dependent variable in regressions on age and inverse transformations to return to the age scale, and has been found to be a better predictor of mortality (Levine, 2013; Levine & Crimmins, 2014) and work ability (Cho et al., 2010) than other methods. To our knowledge, the association between biological age and psychosocial factors has not been studied previously.

1.1. Current study

The primary aim of this manuscript is to investigate weathering and the relationship between psychosocial factors and weathering in a cohort of middle-aged Black or White individuals. We aim to extend previous research showing evidence of weathering through biological age by quantifying the association between weathering and psychosocial factors. We also queried whether there is a racial disparity in the strength of the relationship between weathering and psychosocial factors. We hypothesize that Blacks show evidence of weathering more than Whites; Blacks have higher levels of psychosocial distress; and psychosocial stressors are more strongly associated with weathering among Blacks than among Whites.

2. Methods

2.1. Study design

The Coronary Artery Risk Development in Young Adults study (CARDIA) is a multicenter longitudinal study of 5114 Black or White individuals aged 18 to 30 in 1985-86. Following the baseline examination at year 0 (Y_0) in 1985-86, follow-up examinations were conducted at Y_2 , Y_5 , Y_7 , Y_{10} , Y_{15} , Y_{20} , Y_{25} , and Y_{30} (2015-16). At baseline, CARDIA participants had to be free of long-term disease and disability and were selected by random sampling after stratification so that there would be approximately equal numbers of Blacks and Whites, men and women, age 18–23 vs. 24–30 and higher vs. lower educational attainment at each of the four CARDIA field centers in Birmingham, AL; Chicago, IL; Minneapolis, MN; and Oakland, CA. Recruitment at the sites other than Oakland was community based through telephone and mailing lists. Participants in Oakland were selected from among subscribers to Kaiser Permanente Medical Care Program. All participants provided informed consent and institutional review board approval was obtained at each field center (University of Alabama at Birmingham, Northwestern University, University of Minnesota, and Kaiser Permanente of Northern California) (Friedman, Cutter, Donahue, Hughes, Hulley & Jacobs, 1988). We excluded 2420 non-attendee

participants who did not have complete biological data at Y_{25} or Y_{30} for a sample size of 2694. Those who were missing any biological data were slightly younger, more likely to be Black, and were slightly more likely to have worse socioeconomic status.

2.2. Measurement

2.2.1. Biological age/weathering

Weathering (W) was defined as the difference between biological age (BA) and chronological age (CA) ($W = BA - CA$) so that a positive value indicates that a person is biologically older than their chronological age and conversely a negative value indicates that a person is biologically younger than their CA. BA was calculated with the Klemera & Doubal Method (KDM) (Klemera & Doubal, 2006), as a linear combination of selected biomarkers associated with age and derived as follows. “BA is equal to chronological age (CA) plus a random variable, R_{BA} , with a mean zero and variance of s_{BA}^2 ” (Levine, 2013). This method then minimizes the distance between m regression lines and m biomarker points, within an m dimensional space of all biomarkers through the following equation:

$$BA = \frac{\sum_{j=1}^m (x_j - q_j) \frac{k_j}{s_j^2} + \frac{CA}{s_{BA}^2}}{\sum_{j=1}^m \left(\frac{k_j}{s_j^2} \right)^2 + \frac{1}{s_{BA}^2}} \quad (1)$$

In Eq. (1), k_j is the slope of the regression of biomarker j on CA, q_j is the intercept, x_j is the value biomarker j , m is the number of biomarkers, and s_j is the root mean squared error of the regression of biomarker j on CA. This results in BA being a linear combination of the biomarkers included in the calculation.

In order to represent a wider age range we used multilevel mixed linear regression (clustered within-person, no age x risk factor interaction allowed), which accounts for repeated measures, to obtain k_j , q_j , and s_j . Rather than utilizing biological data solely from year 30 (where patients were aged 48–60) we included biological data beginning at year 15 when patients were as young as 33. This enabled us to use biomarkers that spanned the age range of 33 - 60 years, which is a similar age range to participants in previous research using the KDM method.

We selected 7 biomarkers from Y_{15} - Y_{30} based on general knowledge of their association with aging, availability in CARDIA, and significant association with CA in CARDIA: total and HDL cholesterol (mg/dL), glucose (mg/dL), waist-to-hip ratio (WHR), c-reactive protein (CRP) (mg/L), forced expiratory volume in 1 second ($FEV1/h^2$) (liters), and mean arterial pressure (MAP) (mmHg) (see Friedman et al., 1988) for more detail on biomarker measurement). We retained CRP even though its association with age was low because it is known to be disparate between Blacks and Whites, it has been previously used as biomarker in the biological age literature, and we wanted to include an inflammatory measure to avoid the biological age measure being composed of only cardiovascular, pulmonary, and metabolic markers.

We extended the age range by using biomarker data from years 15 - 30 as follows. In the first step of the KDM, where the individual biomarker is regressed on age to obtain the slope, intercept, and root mean squared error, we used multilevel linear regression to estimate the parameters while accounting for within person correlations between biomarkers at each year. Although we extended the age range to calculate BA, we only used BA at Y_{30} in subsequent analysis because we wanted to use BA data from individuals at their oldest chronological age in order to capture the longest period of accelerated aging possible.

2.2.2. Race

Race was self-reported as non-Hispanic Black/African American or non-Hispanic White/Caucasian.

2.2.3. Health behaviors

Alcohol was measured in mL/day. Tobacco use was measured as pack-years of cigarettes. Health behavior data used were from Y_{25} .

2.2.4. Socioeconomic status

Socioeconomic status (SES) included 7 categorical variables from Y_{25} : education level (less than high school [< 12 years], high school [9–12 years], undergraduate [13–16 years], graduate school [17–20 years]), difficulty paying for medical expenses (very hard to not very hard), difficulty paying for basics, income ($< \$5000$ to $> = \$100,000$ in \$10,000 increments), assets ($< = \$500$ to $> = \$500,000$ in \$10,000 increments), home status (owned or being bought to occupied without payment of money), and food eaten in home (often don't have enough food to have enough food and kinds of food). We utilized a factor score where a higher score indicated higher socioeconomic status. A more detailed description of the construction of the socioeconomic status score can be found in the online supplement.

2.2.5. Depression symptoms

The Center for Epidemiological Studies – Depression Scale (Radloff, 1977) (CES-D), a 20-question scale that asks about how often the respondent experienced symptoms of depression such as “feeling blue”, “weight changes”, and “sleep problems” was used to measure depression symptoms. Responses range from (0) “none of the time” to (3) “most or all of the time” and the score was modeled continuously. The CES-D has a score range of 0 to 60 and had good internal consistency within the sample ($\alpha = 0.88$). CES-D score was used from Y_{25} .

2.2.6. Discrimination

The Experiences of Discrimination Scale (Williams, Yan, Jackson & Anderson, 1997) was used to measure perceived discrimination. The scale asks about discrimination in seven domains—at school, finding a job, work, housing, medical care, home, and in public. The Experiences of Discrimination Scale has a score range of 0 to 7 for each subscale (race, gender, socioeconomic status, etc.). The race ($\alpha = 0.81$) and socioeconomic ($\alpha = 0.82$) subscales had good internal consistency in our sample. We

used only the racial and socioeconomic discrimination questions because they are more likely to be disparate by race. In keeping with previous analyses in CARDIA (Borrell, Kiefe, Diez-Roux, Williams & Gordon-Larsen, 2013) we modeled discrimination categorically. The discrimination variable was defined as endorsing 3 or more domains of discrimination, less than 3 domains, or none. The discrimination scale score assessed at Y_{25} was used.

2.2.7. Social participation

Social participation was measured from a questionnaire at Y_{25} that asked about the different types of groups that a participant may be a part of (e.g. church groups, unions, community groups, etc.). Social participation was defined as a continuous score that represented the number of groups that person indicated they were a part of (0–6).

2.3. Statistical analysis

All analyses used weathering (W, the difference between biological age and chronological age) at Y_{30} . We conducted multilevel linear regressions of each biomarker (from Y_{15} through Y_{30}) on age to be used in the KDM calculation of biological age. Each psychosocial variable was analyzed using the following steps: (1) Bivariate association through linear regression of W on continuous psychosocial variables and t-tests/ANOVAS for dichotomous and categorical variables; (2) linear regression of W on psychosocial variables controlling for sex, and race; (3) race stratified linear regression of W on psychosocial variables controlling for sex; and (4) linear regression of W on psychosocial variables including an interaction term defined as race*psychosocial variable and controlling for sex. These steps were repeated for each psychosocial

variable at Y_{25} . Each model was adjusted for site. Additionally, we included an overall model incorporating all psychosocial variables. We also utilized the “margins” command in Stata to obtain linear predictions for the interaction terms. All analyses were done with Stata 13 (StataCorp, 2013).

2.3.1. Sensitivity analysis

Our main analysis was a complete case analysis that included only those who had complete biological data at year 30. Since those who did not have data at year 30 were younger, more likely to be black, and more likely to have low SES, we completed a sensitivity analysis where we used multiple imputation to include those who were not available at year 30. We used multiple imputation, using the multivariate normal distribution, to impute missing biological and psychosocial variables for those who were lost due to attrition. The missing percentage was approximately 35%. We created 10 sets of imputed data and pooled the results across the 10 datasets. We then used the imputed datasets in the KDM calculations and in the linear regression models of psychosocial variables predicting weathering.

3. Results

3.1. Cohort description

We studied a bi-racial cohort of 2694 middle-aged adults (Table 1). The final sample of participants with complete biological data for Y_{30} consisted of 45% Blacks and 57% women. On average, Blacks had poorer mean biological markers with the exception of Blacks having a lower mean total cholesterol and a similar waist-to-hip ratio to Whites. Whites had higher SES score and Blacks reported consistently more racial and SES discrimination. Blacks also had a higher mean CES-D score than Whites. Mean pack-years in the sample was 26.8 (SD = 82.3) mean ML of alcohol/day was 11.5 (SD = 22.1). Mean pack-years was higher among Blacks (33.4, SD = 83.7) than Whites (21.5, SD = 81.9).

3.2. Overview of Tables and Figures

The values that went into the KDM calculation of BA are in Table 2. Table 3 displays associations between individual weathering and psychosocial variables overall (adjusted for sex and race) and stratified by race (adjusted for sex only). Table 4 shows findings from overall models testing independent associations of psychosocial variables with weathering. Fig. 1 displays graphically the unadjusted relationship between CES-D score and weathering, by race. Figs. 2 and 3 display graphically the interactions between race and socioeconomic status and social participation, respectively, on weathering.

3.3. Weathering

Weathering (W), mean biological age minus mean chronological age, was found to be higher for Blacks (Table 1). Blacks had a mean BA of 57.1 years while Whites had a mean BA of 52.3 years. Mean W for Blacks was 2.6 years and -3.5 years for Whites, indicating at Y_{30} Blacks had a mean biological age that was larger than their mean chronological age whereas the opposite was seen in Whites ($t = 14.4$, $p < 0.001$).

3.4. Health behaviors

Analyses adjusted for sex and race showed that pack-years and alcohol consumption at Y_{25} were associated with higher weathering overall at Y_{30} . Interaction terms revealed no significant race-pack year or race-alcohol association (p value for interaction terms = 0.877 and 0.373, respectively). However, we also performed analyses stratified by race given our initial hypotheses and the limited power known to affect

Table 1
Mean Biological and Psychosocial Variables by Race: CARDIA, 2000–2016.

	Black (n = 1219)			White (n = 1475)			p-value
	n	mean or %	sd	n	mean or %	sd	
Chronological Age Y ₃₀ (CA)	1219	54.5	3.7	1475	55.8	3.4	< 0.001
Biological Age Y ₃₀ (BA)	1219	57.1	11.5	1475	52.3	9.9	< 0.001
Weathering (BA – CA)	1219	2.6	11.8	1475	-3.5	10.0	< 0.001
Female	741	61%		796	54%		< 0.001
Biological age Variables (Y₃₀)							
Cholesterol (mg/dL)	1219	189.0	39.0	1475	195.3	36.6	< 0.001
HDL-C (mg/dL)	1219	59.6	18.8	1475	60.2	18.9	0.452
Glucose (mg/dL)	1219	105.4	37.9	1475	99.5	22.9	< 0.001
WHR	1219	0.9	0.1	1475	0.9	0.1	0.408
CRP (mg/L)*	1219	4.3	6.5	1475	2.1	3.5	< 0.001
FE1HSQ (l/m ²)	1219	0.8	0.2	1475	1.0	0.2	< 0.001
MAP (mmHg)	1219	109.2	14.5	1475	101.4	12.5	< 0.001
Psychosocial Variables							
CES-D Score (Y ₂₅)	1274	10.0	8.1	1540	8.6	7.0	< 0.001
Racial Discrimination (Y ₂₅)							
None	469	39%		1219	83%		< 0.001
< 3 Domains	342	28%		214	15%		
> = 3 Domains	394	33%		36	2%		
SES Discrimination(Y ₂₅)							
None	791	66%		1209	82%		< 0.001
< 3 Domains	220	18%		197	13%		
> = 3 Domains	194	16%		64	4%		
SES Score (Y ₂₅)	1212	4.6	1.8	1470	6.1	1.6	< 0.001
Milliliters of Alcohol/week (Y ₂₅)	1210	8.8	21.0	1464	13.7	23.0	< 0.001
Pack-years cigarettes (Y ₂₅)	1197	32.9	83.2	1454	21.3	81.7	< 0.001
Number of social groups (Y ₂₅)	1204	1.8	1.5	1456	1.7	1.4	0.630

HDL-C = High Density Lipoprotein Cholesterol; WHR = Waist-to-Hip Ratio; CRP = C-Reactive Protein; FE1HSQ = Forced Expiratory Volume in 1 second/height²; MAP = Mean Arterial Pressure; CRP measured at Y₂₅

Table 2
Values from Multilevel Linear Regression of Biomarker on Chronological Age: CARDIA, 2000–2016.

	k _j (slope)	q _j (intercept)	s _j (rmse)	r
Total Cholesterol	0.60	160.71	23.67	0.11
HDL Cholesterol	0.61	26.64	7.49	0.20
Glucose	0.96	51.31	17.77	0.20
WHR	0.002	0.73	0.08	0.16
CRP	0.004	2.81	2.98	-0.01
FE1HSq	-0.01	1.52	0.22	-0.25
MAP	1.03	50.64	10.37	0.36

statistical tests of interaction. Pack-years of alcohol were associated with weathering only among Whites in race-stratified models (Table 3). Mean mL of alcohol/day was significantly associated with higher weathering among both races (Table 3). Due to the strong association between alcohol and tobacco use at Y₂₅ and weathering at Y₃₀ we created additional models of all psychosocial variables where we controlled for alcohol use and tobacco use.

3.5. Discrimination

Blacks reported racial discrimination in at least 3 domains significantly more often than Whites (33% vs. 2% - Table 1). Similarly, Blacks reported socioeconomic status discrimination in at least 3 domains significantly more often than whites (16% vs. 4%). Socioeconomic status discrimination was not significantly associated with weathering, overall or within racial groups, so we report results for only racial discrimination. Overall analyses between racial discrimination (number of domains endorsed) and weathering at Y₃₀, adjusted for sex only, showed higher weathering associated with endorsing less than three domains compared to no discrimination (1.28; 95% CI: 0.24, 2.33) and with endorsing three or more domains compared to no

Table 3
Linear Regression Coefficients (standard errors) for Weathering at Y₃₀ Regressed on each Psychosocial Variable at Y₂₅, Overall and by Race: CARDIA, 2000–2016.

	Overall	Black	White
Psychosocial Variables ^a			
mL Alcohol/week	0.09 (0.01)**	0.09 (0.02)**	0.09 (0.01)**
Pack-Years Cigarettes	0.01 (0.003)**	0.004 (0.004)	0.01 (0.003)**
Racial Discrimination ^b			
< 3 Domains	1.28 (0.53)**	0.15 (0.83)	-1.44 (0.72)*
≥ 3 Domains	3.93 (0.59)**	0.80 (0.81)	-2.23 (1.62)
CES-D Score	0.05 (0.03)	0.09 (0.04)*	0.01 (0.04)
SES Score	-0.37 (0.12)**	-0.76 (0.19)**	0.03 (0.16)
Number of Social Groups	-0.46 (0.14)**	-0.75 (0.22)**	-0.17 (0.18)

^a Each cell represents one model. All parameter estimates are from linear regression models adjusted for sex, site, and race overall (with the exception of racial discrimination which is only adjusted for sex and site overall), and for sex only within race only; weathering (biological age minus chronological age) at Y₃₀ is the dependent variable and each psychosocial variable at Y₂₅ is the independent variable.

^b compared to “none”

* p < 0.05

** p < 0.01

discrimination (3.93; 95% CI: 2.78, 5.09) (Table 3). The interaction term between race and racial discrimination was not significant. The addition of alcohol and tobacco use did not change the associations (results not shown). Stratified analyses did not reveal any significant associations among Blacks however endorsing racial discrimination in less than 3 domains compared to no discrimination was associated with less weathering among Whites (-1.44; 95% CI: -2.84, -0.03) (Table 3).

Table 4
Linear Regression Coefficients (standard errors) for Weathering (Biological Age – Chronological Age) at Y₃₀ simultaneously regressed on all Psychosocial Variables at Y₂₅, Overall and by Race: CARDIA, 2000–2016^a.

	Overall (n = 2694) β (SE)	Black (n = 1219) β (SE)	White (n = 1475) β (SE)
Alcohol per week (mL)	0.09 (0.01)**	0.07 (0.02)*	0.09 (0.02)*
Pack-Years Cigarettes	0.0003 (0.003)	-0.003 (0.004)	0.002 (0.003)
SES Score	-0.23 (0.14)	-0.55 (0.21) [†]	0.01 (0.18)
CES-D Score	0.01 (0.03)	0.02 (0.05)	0.005 (0.04)
Racial Discrimination ^b			
< 3 Domains	-0.14 (0.55)	0.91 (0.84)	-0.94 (0.72)
≥ 3 Domains	0.34 (0.66)	0.97 (0.82)	-1.70 (1.68)
Social Group Sum	-0.29 (0.15) [†]	-0.48 (0.24) [†]	-0.08 (0.18)
Sex (Male)	-5.59 (0.43)	-4.21 (0.72) [†]	-6.59 (0.51) [†]
Race (Black)	5.52 (0.51)	-	-

^a Each column represents one model. All parameter estimates are from linear regression models; weathering (biological age minus chronological age) at Y₃₀ is the dependent variable and each psychosocial variable at Y₂₅ is the independent variable.

^b compared to “none”

** p < 0.01

* p < 0.05

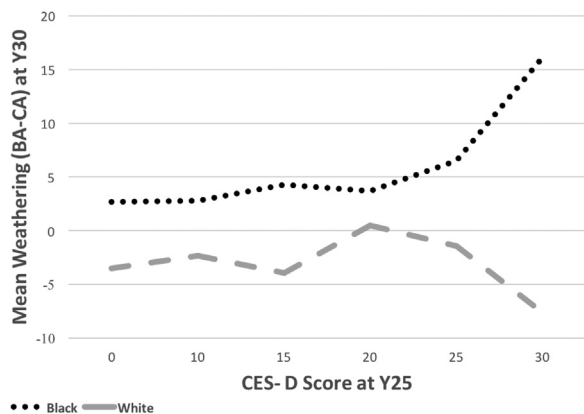


Fig. 1. Unadjusted Association between Weathering at Y₃₀ and CES-D at Y₂₅ score by Race: Coronary Artery Risk Development in Young Adults Study, 2000–2016.

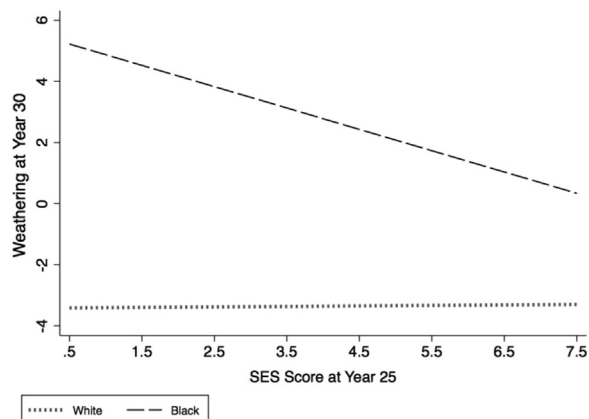


Fig. 2. Predicted Weathering at Y₃₀ by Race Accounting for Interaction of Socioeconomic Status and Race at Y₂₅ and: CARDIA, 2000–2016.

3.6. Depressive symptoms

Linear regression analysis adjusted for race and sex only, showed that, overall, a 1-point increment in CES-D score at Y₂₅ was associated

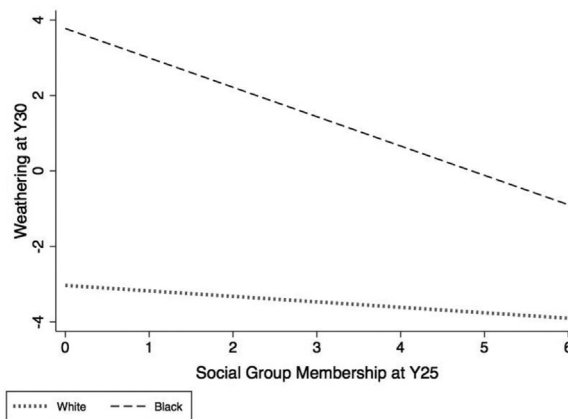


Fig. 3. Predicted Weathering at Y₃₀ by Race Accounting for Interaction of Social Participation at Y₂₅: CARDIA, 2000–2016.

with 0.05 year (95% CI: -0.004, 0.10) difference in weathering at year Y₃₀ (Table 3). Alcohol use per week and pack-years slightly attenuated the relationship but adding socioeconomic status to the stratified model attenuated the association such that it was no longer significant. (0.01, 95% CI: -0.06, 0.09). There was no statistically significant interaction between race and CES-D score on weathering.

Fig. 1 compares visually mean weathering by CES-D score for Blacks and Whites, unadjusted. Sex-adjusted stratified analyses showed that the association between weathering at Y₃₀ and depressive symptoms at Y₂₅ was driven by the significant linear association (test of linearity were performed and were consistent with linearity) among Blacks rather than among Whites (Table 3). Among Blacks, a one-unit increase in CES-D score at Y₂₅ was associated with 0.09-year higher weathering at Y₃₀ (95% CI: 0.01, 0.17) which amounts to an additional 33 days of age for each one-point increment in CES-D score.

3.7. Socioeconomic status

Linear regression analysis adjusted for race and sex only revealed significantly lower weathering at Y₃₀ as a function of SES at Y₂₅ (-0.37, 95% CI: -0.61, -0.13) (Table 3). Stratified analyses showed that an increase in SES at Y₂₅ was associated with a lower W at Y₃₀ for Blacks (-0.76; 95% CI: -1.12, -0.39) but not for Whites (0.03; 95% CI: -0.29 0.35) (Table 3). When alcohol use in the past year was added to the stratified model, the association between SES at Y₂₅ was slightly attenuated for both races, but the association among Blacks remained significant (-0.65; 95% CI: -1.02, -0.29) (results not shown). Pack-years slightly attenuated the association among blacks similarly to alcohol use (-0.75, 95% CI: -1.13, -0.37) (results not shown). The interaction between race and SES was significant so that higher SES was associated with lower weathering among Blacks, but not among Whites (-0.74, 95% CI: -1.22, -0.26) (Fig. 2).

3.8. Social participation

Overall analyses adjusted for race and sex only showed a significant association between number of social groups at Y₂₅ and weathering at Y₃₀ (-0.46; 95% CI: -0.73, -0.18) (Table 3). Inclusion of an interaction term revealed a significant difference by race (-0.63, 95% CI: -1.18, -0.09) (Fig. 3). Health behaviors slightly attenuated the association of the relationships between social participation and weathering (results not shown).

Stratified sex-adjusted analyses revealed that the significant association between number of social groups at Y₁₅ and W at Y₃₀ was driven mainly by the association among Blacks (-0.75; 95% CI: -1.18, -0.32) (Table 3).

3.9. Full model

We also developed full models with all psychosocial variables included in order to test for any independent associations. We ran three full models, one with race included as a covariate and two others stratified by race (Table 4). The first model, with race included as a covariate showed an independent association between milliliters of alcohol/day and higher weathering (0.09 95% CI: 0.07, 0.10). Stratified models revealed that the significant increase in weathering associated with increased milliliters of alcohol remained significant among both races (Table 4). Among Blacks, the only other independent associations were socioeconomic status score (-0.55, 95% CI: -0.97, -0.12) and social participation (-0.48, 95% CI: -0.95, -0.02). Among Whites, there were no independent predictors.

3.10. Findings from a sensitivity analysis using multiple imputations (data not shown)

After multiple imputation to include those who were missing biological data at year 30 due to attrition, the sample represented more Blacks and a larger range of SES scores. The imputed results showed the same significant associations between psychosocial factors and weathering for Blacks but also revealed significant associations among Whites for depression and social participation, before multivariable adjustment. In the fully adjusted model depressive symptoms were no longer independently associated with weathering in Whites and SES scores were no longer independently associated with weathering in Blacks nor Whites. Associations between psychosocial factors and weathering were consistently stronger for Blacks than for Whites.

4. Discussion

4.1. Biological age and weathering

In a bi-racial cohort of 2694 middle-aged adults we calculated biological age and used it to study weathering. In our chronologic age range of 48 to 60 years, Blacks weathered by approximately 6 years more than Whites, on average. We observed expected associations between psychosocial variables and weathering. Remarkably, however, we found that these associations were stronger for Blacks than Whites, suggesting that similar levels of psychosocial “wear and tear” are associated with more premature aging in Blacks than in Whites.

The finding of greater weathering in Blacks compared to Whites is in keeping with the findings of both Geronimus and Levine (Geronimus et al., 2010; Levine and Crimmins, 2014) who measured accelerated aging among Blacks and Whites in NHANES. Levine and Crimmins also used the KDM definition of weathering to measure accelerated aging among Blacks and Whites. The KDM has been validated through computer simulations and has been shown to be superior in predicting mortality and morbidity in both Blacks and Whites in multiple studies (Belsky, Caspi, Houts, Cohen, Corcoran & Danese, 2015; Cho et al., 2010; Jia et al., 2017; Klemra & Doubal, 2006; Levine & Crimmins, 2014). Our most striking findings regarding psychosocial variables and weathering were among the Black participants. Specifically, among Blacks, symptoms of depression were associated with higher weathering and, in the main models, among Blacks only, social participation and socioeconomic status were inversely related to weathering. Thus, it appears that any pathway by which psychosocial hardship may lead to worse wear and tear effects on health may have more explanatory power in Blacks than in Whites.

4.2. Weathering and depression symptoms

The association of symptoms of depression and weathering is not unexpected, However, this association being more significant in Blacks compared to Whites is unexpected, and previous reports on this theme

have been inconsistent. Although previous research has shown differential effects of race and sex with depressive symptoms on aortic calcification (Lewis, Everson-Rose, Colvin, Matthews, Bromberger & Sutton-Tyrrell, 2009), relationships specifically to weathering have not been shown. It is well-known that depression is associated with poor health, both prospectively (Moise, Khodneva, Jannat-Khah, Richman, Davidson & Kronish, 2018) and retrospectively, but relatively little is known about racial differences in these associations. One observational study found that retrospective and prospective associations between depressive symptoms and number of chronic medical conditions were present for Whites, but not Blacks (Assari et al., 2015) Other recent observational studies have found that depressive symptoms were more predictive of mortality in Whites than Blacks (Assari, 2018; Assari, Moazen-Zadeh, Lankarani & Micol-Foster, 2016) but a different observational study found that depressive symptoms were associated with incident coronary heart disease in Blacks but not Whites (Sims, Redmond, Khodneva, Durant, Halanych & Safford, 2015). A different study found no significant racial differences in the association between maternal antenatal depression and preterm birth risk (Ncube et al., 2017). Thus, disentangling the complex relationships between depressive symptoms, health, and race/ethnicity is in much need of further scrutiny. Our findings suggest psychosocial hardship is not only associated with poor health in general, but differentially more so in Blacks than in Whites. We also conducted a race and sex stratified analysis (not shown) in order to assess the results in regards to the intersection of race and sex. We found that Black men stood out with CES-D score remaining as a significant predictor of higher weathering whereas Black women were similar to White men and women. There is a well-known gap in the literature regarding depression in Black men but what has been found is consistent with our results (Watkins, Green, Rivers & Rowell, 2006).

Also of particular interest is the attenuation of effect in the model that controlled for SES. The attenuation of the association between depression and weathering by the addition of SES, supports the contention that race is often a proxy for SES and social inequality (Hayward, Toni, Crimmins & Yang, 2000; Spence et al., 2011). Further research that explores weathering stratified by race and SES is warranted to gain a better understanding of the intersection between race and SES. Interestingly, again, depression symptoms did not significantly predict weathering among Whites in any of the main models (there was an association in the imputed sensitivity analysis). It is worth mentioning that the association between depression symptoms and weathering disappeared in the fully adjusted model. This indicates that other factors such as health behaviors, socioeconomic status, and sex may be involved in the depression-weathering association that was found in the individual model. In particular, there is a complicated relationship between alcohol use and depression (Grant, Goldstein, Saha, Chou, Jung & Zhang, 2015; Sullivan et al., 2005). Since most research is on diagnosed depression it is unclear if this would be a factor when utilizing a measure of depressive symptoms only, such as in this paper. Recent research has shown a temporal relationship between smoking, depression, and alcohol use (Ruggles, Fang, Tate, Mentor, Bryant & Fiellin, 2017) indicating that a mediation may be at play. Due to this relationship the inclusion of alcohol and smoking in our models may represent over-adjustment.

4.3. Weathering and socioeconomic status

Socioeconomic status is well known to differ by race. In fact, race is often a proxy for socioeconomic status. Our finding that increases in socioeconomic status are inversely associated with weathering among Blacks appears to contradict the documented “diminished return” concept, whereby minorities have smaller health gains from similar improvements in socioeconomic and psychosocial resources than the majority group (Assari, 2017). In contrast, findings are consistent with other studies that show that increased SES is associated with better

physical health. It is possible that our findings are due, in part, to a threshold effect. Nearly 40% of Blacks, but only 13% of Whites are within the lowest quartile of SES score. This association may be due to the much smaller number of Whites represented in the lower levels of SES score. Our sensitivity analysis where we did multiple imputation to include those who were missing biological data at year 30 due to attrition showed that when a larger range of SES was represented among Whites and when Blacks and those of lower SES weren't differentially represented, higher SES was associated with less weathering among Whites as well. Our results should be replicated among a sample of Blacks and Whites with similarly high SES indicators. There is a possibility that our results were contrary to the minority's "diminished return" concept because our sample had consistently higher SES among Whites than among Blacks so a comparison at similar SES levels was difficult. We conducted a sensitivity analysis where we repeated the weathering-SES analysis on only those participants who had SES scores above the mean and found that among Blacks there remained a decrease in weathering with increased SES score, but the result was no longer significant (results not shown).

4.4. Weathering and social participation

We were particularly interested in social mechanisms that could affect weathering. It is well known that Blacks, especially older Blacks are more religious than Whites and that much of their social support tends to be religion based (Krause, 2002). Among older Blacks especially, both religious and secular support are associated with a lower depression and psychological distress (Assari & Moghani Lankarani, 2018) though this is also evident among younger Blacks (Lincoln et al., 2003). Utilizing support from social participation to deal with chronic stress and its effect on mental health are commonly reported in the stress literature, however the way social participation affects physical health is less commonly considered. Our results show that among Blacks especially, number of social groups is strongly protective when it comes to weathering. This finding persisted in every model with the exception of the full model. This is keeping with the limited literature regarding social support and physical health, particularly that church-based social support reduces the impact of financial strain on physical health among Blacks. This finding indicates that a more extensive look into social participation in regards to weathering is warranted. Religious coping among Blacks is not uncommon however membership in other social groups (e.g. parent groups, unions, etc.) are not as commonly studied.

4.5. Limitations and strengths

Our research has some limitations. First, we used only those participants who had complete biological data at year 30 so those who were less likely to remain in the study for 30 years (Black, less healthy, lower SES) may not have been represented as well in the analysis. In a sensitivity analysis where we used multiple imputation to fill in the missing values for those who were missing biological data due to attrition we found that the main findings remained the same for Blacks but that they also became significant among Whites, though to a lesser degree than among Blacks. Although the qualitative interpretation, that the associations are stronger among Blacks, didn't change, the significance among Whites found in the analysis may be an avenue for further study in the future. Second, our sample was relatively healthy, which may obscure the weathering effect accounting for the somewhat attenuated weathering that we found among Blacks compared to others' findings. Further, since CARDIA were free of long-term disease or disability at baseline and the sample is not nationally representative, the generalizability is limited compared to NHANES. Third, although we found an association between symptoms of depression and weathering, neither race on average had symptoms severe enough to warrant a diagnosis of even minor depression (though 12% of Whites and 18% of Blacks had

scores high enough to suggest a diagnosis of dysthymia) so our analysis might yield different results in a sample with more clinical depression. Fourth, there are multiple methods to calculate biological age (BA). Although we used a validated method, BA can be computed with many different biomarkers. It would be prudent to test different versions of BA in different samples to gain a better understanding of the best combination of biomarkers for predicting future health. Finally, this analysis was time-lagged (depressive symptoms at Y_{25} , weathering at Y_{30}), but used only one time-point. A longitudinal analysis may show different results when some psychosocial variables are allowed to vary with time.

The strengths of our study include that we used a validated and comprehensive equation to calculate biological age. We used data from a large biracial cohort with considerable biological and psychosocial data. Finally, we measured weathering in a biological age framework which is inherently easier to understand when compared to chronological age.

4.6. Concluding comment

To our knowledge, this is the first study to show the association between psychosocial stressors and weathering in a biological age framework. Important implications are found in the stark Black-White disparity in biological age and perhaps even more importantly, the associations between psychosocial stress and weathering among Blacks. The associations emphasize the disparity in health, not in a certain disease, but in overall aging that affects everyone. Our findings regarding discrimination, depression, SES, and social participation and weathering among Blacks warrants further within-race research to better understand these associations. It is increasingly obvious that social gradients affect physical health and that they are especially dangerous for minority populations. If we are to remedy the issue, we must have a better understanding of the problem.

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Ethics approval

Study protocols at each site were approved by their local IRB. Ethical approval was not required for this analysis because it utilized de-identified secondary data analysis. The primary author and Dr. Kiefe did complete and sign a Data and Materials Distribution Agreement with CARDIA prior to receiving data.

References

Assari, S. (2017). Unequal gain of equal resources across racial groups. *International*

- Journal of Health Policy and Management*, 7, 1–9.
- Assari, S. (2018). Depressive symptoms increase the risk of mortality for white but not black older adults. *Healthcare (Basel)*, 6.
- Assari, S., Burgard, S., & Zivin, K. (2015). Long-term reciprocal associations between depressive symptoms and number of chronic medical conditions: Longitudinal support for Black-White health paradox. *Journal of Racial and Ethnic Health Disparities*, 2, 589–597.
- Assari, S., Moazen-Zadeh, E., Lankarani, M. M., & Micol-Foster, V. (2016). Race, depressive symptoms, and all-cause mortality in the United States. *Frontier in Public Health*, 4, 40.
- Assari, S., & Moghani Lankarani, M. (2018). Secular and religious social support better protect Blacks than Whites against depressive symptoms. *Behaviour Science*, 8.
- Belsky, D. W., Caspi, A., Houts, R., Cohen, H. J., Corcoran, D. L., Danese, A., et al. (2015). Quantification of biological aging in young adults. *Proceedings of the National Academy of Sciences of the United States of America*, 112, E4104–E4110.
- Borrell, L. N., Kiefe, C. I., Diez-Roux, A. V., Williams, D. R., & Gordon-Larsen, P. (2013). Racial discrimination, racial/ethnic segregation, and health behaviors in the CARDIA study. *Ethnicity & Health*, 18, 227–243.
- Brewer, L. C., Redmond, N., Slusser, J. P., Scott, C. G., Chamberlain, A. M., Djousse, L., et al. (2018). Stress and achievement of cardiovascular health metrics: The American Heart Association Life's Simple 7 in Blacks of the Jackson Heart Study. *Journal of the American Heart Association*, 7.
- Cho, I. H., Park, K. S., & Lim, C. J. (2010). An empirical comparative study on biological age estimation algorithms with an application of Work Ability Index (WAI). *Mechanisms of Ageing and Development*, 131, 69–78.
- Cuffee, Y., Ogedegbe, C., Williams, N. J., Ogedegbe, G., & Schoenthaler, A. (2014). Psychosocial risk factors for hypertension: An update of the literature. *Current Hypertension Reports*, 16, 483.
- Fiscella, K., & Williams, D. R. (2004). Health disparities based on socioeconomic inequities: Implications for urban health care. *Academic Medicine*, 79, 1139–1147.
- Friedman, G. D., Cutter, G. R., Donahue, R. P., Hughes, G. H., Hulley, S. B., Jacobs, D. R., Jr., et al. (1988). CARDIA: Study design, recruitment, and some characteristics of the examined subjects. *Journal of Clinical Epidemiology*, 41, 1105–1116.
- Gasevic, D., Ross, E. S., & Lear, S. A. (2015). Ethnic differences in cardiovascular disease risk factors: A systematic review of North American evidence. *Canadian Journal of Cardiology*, 31, 1169–1179.
- Geronimus, A. T. (1992). The weathering hypothesis and the health of African-American women and infants: Evidence and speculations. *Ethnicity & Disease*, 2, 207–221.
- Geronimus, A. T., Hicken, M., Keene, D., & Bound, J. (2006). "Weathering" and age patterns of allostatic load scores among blacks and whites in the United States. *American Journal of Public Health*, 96, 826–833.
- Geronimus, A. T., Hicken, M. T., Pearson, J. A., Seashols, S. J., Brown, K. L., & Cruz, T. D. (2010). Do US black women experience stress-related accelerated biological aging?: A novel theory and first population-based test of Black-White differences in telomere length. *Human Nature*, 21, 19–38.
- Grant, B. F., Goldstein, R. B., Saha, T. D., Chou, S. P., Jung, J., Zhang, H., et al. (2015). Epidemiology of DSM-5 alcohol use disorder: Results from the National Epidemiologic Survey on alcohol and related conditions III. *JAMA Psychiatry*, 72, 757–766.
- Gruenewald, T. L., Cohen, S., Matthews, K. A., Tracy, R., & Seeman, T. E. (2009). Association of socioeconomic status with inflammation markers in black and white men and women in the Coronary Artery Risk Development in Young Adults (CARDIA) study. *Social Science & Medicine*, 69, 451–459.
- Hagstrom, E., Norlund, F., Stebbins, A., Armstrong, P. W., Chiswell, K., Granger, C. B., et al. (2018). Psychosocial stress and major cardiovascular events in patients with stable coronary heart disease. *Journal of Internal Medicine*, 283, 83–92.
- Hayward, M. D. M., Toni, P., Crimmins, Eileen M., & Yang, Yu (2000). The significance of socioeconomic status in explaining the racial gap in chronic health conditions. *American Sociological Review*, 65, 919–930.
- Jia, L., Zhang, W., & Chen, X. (2017). Common methods of biological age estimation. *Clinical Interventions in Aging*, 12, 759–772.
- Klemera, P., & Doubal, S. (2006). A new approach to the concept and computation of biological age. *Mechanisms of Ageing and Development*, 127, 240–248.
- Krause, N. (2002). Church-based social support and health in old age: Exploring variations by race. *The Journals of Gerontology Series B Psychological Sciences and Social Sciences*, 57, S332–S347.
- LaVeist, T. A. (1994). Beyond dummy variables and sample selection: What health services researchers ought to know about race as a variable. *Health Services Research*, 29, 1–16.
- Levine, M. E. (2013). Modeling the rate of senescence: Can estimated biological age predict mortality more accurately than chronological age? *The Journals of Gerontology Series B Psychological Sciences and Social Sciences*, 68, 667–674.
- Levine, M. E., & Crimmins, E. M. (2014). Evidence of accelerated aging among African Americans and its implications for mortality. *Social Science & Medicine*, 118, 27–32.
- Lewis, T. T., Everson-Rose, S. A., Colvin, A., Matthews, K., Bromberger, J. T., & Sutton-Tyrrell, K. (2009). Interactive effects of race and depressive symptoms on calcification in African American and white women. *Psychosomatic Medicine*, 71, 163–170.
- Lincoln, K. D., Chatters, L. M., & Taylor, R. J. (2003). Psychological distress among black and white Americans: Differential effects of social support, negative interaction and personal control. *Journal of Health and Social Behavior*, 44, 390–407.
- Lloyd-Jones, D., Adams, R., Carnethon, M., De Simone, G., Ferguson, T. B., Flegal, K., et al. (2009). Heart disease and stroke statistics–2009 update: A report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*, 119, 480–486.
- Moise, N., Khodneva, Y., Jannat-Khah, D. P., Richman, J., Davidson, K. W., Kronish, I. M., et al. (2018). Observational study of the differential impact of time-varying depressive symptoms on all-cause and cause-specific mortality by health status in community-dwelling adults: The REGARDS study. *BMJ Open*, 8, e017385.
- Myers, H. F. (2009). Ethnicity- and socio-economic status-related stresses in context: An integrative review and conceptual model. *Journal of Behavioral Medicine*, 32, 9–19.
- Ncube, C. N., Enquobahrie, D. A., & Gavin, A. R. (2017). Racial differences in the association between maternal antenatal depression and preterm birth risk: A prospective cohort study. *Journal of Women's Health (Larchmt)*, 26, 1312–1318.
- Pedersen, S. S., von Kanel, R., Tully, P. J., & Denollet, J. (2017). Psychosocial perspectives in cardiovascular disease. *European Journal of Preventive Cardiology*, 24, 108–115.
- Radloff, L. S. (1977). The CES-D Scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement*, 1.
- Ranjit, N., Diez-Roux, A. V., Shea, S., Cushman, M., Seeman, T., Jackson, S. A., et al. (2007). Psychosocial factors and inflammation in the multi-ethnic study of atherosclerosis. *Archives of Internal Medicine*, 167, 174–181.
- Ruggles, K. V., Fang, Y., Tate, J., Mentor, S. M., Bryant, K. J., Fiellin, D. A., et al. (2017). What are the patterns between depression, smoking, unhealthy alcohol use, and other substance use among individuals receiving medical care? A longitudinal study of 5479 participants. *Aids and Behavior*, 21, 2014–2022.
- Schneiderman, N., Ironson, G., & Siegel, S. D. (2005). Stress and health: Psychological, behavioral, and biological determinants. *Annual Review of Clinical Psychology*, 1, 607–628.
- Shadlen, M. F., Siscovick, D., Fitzpatrick, A. L., Dulberg, C., Kuller, L. H., & Jackson, S. (2006). Education, cognitive test scores, and black-white differences in dementia risk. *Journal of the American Geriatrics Society*, 54, 898–905.
- Sims, M., Redmond, N., Khodneva, Y., Durant, R. W., Halanych, J., & Safford, M. M. (2015). Depressive symptoms are associated with incident coronary heart disease or revascularization among blacks but not among whites in the Reasons for Geographical and Racial Differences in Stroke study. *Annals of Epidemiology*, 25, 426–432.
- Spence, N. J., Adkins, D. E., & Dupre, M. E. (2011). Racial differences in depression trajectories among older women: Socioeconomic, family, and health influences. *Journal of Health and Social Behavior*, 52, 444–459.
- Spruill, T. M. (2010). Chronic psychosocial stress and hypertension. *Current Hypertension Reports*, 12, 10–16.
- StataCorp (2013). *Stata Statistical Software: Release*. College Station, Tx: StataCorp LP13.
- Sullivan, L. E., Fiellin, D. A., & O'Connor, P. G. (2005). The prevalence and impact of alcohol problems in major depression: A systematic review. *American Journal of Medicine*, 118, 330–341.
- Watkins, D. C., Green, B. L., Rivers, B. M., & Rowell, K. L. (2006). Depression and black men: Implications for future research. *The Journal of Men's States Health and Gender*, 3, 227–235.
- Williams, D. R., Yan, Y., Jackson, J. S., & Anderson, N. B. (1997). Racial differences in physical and mental health: Socio-economic status, stress and discrimination. *Journal of Health Psychology*, 2, 335–351.