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Racial discrimination, Educational Attainment, and Biological Dysregulation Among Midlife African American Women

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Abstract

Objective: To examine the association between self-reported racial discrimination and allostatic load, and whether the association differs by socioeconomic position.

Methods: We recruited a purposive cross-section of midlife (ages 30–50) African American women residing in four San Francisco Bay area counties (n=208). Racial discrimination Was measured using the Experience of Discrimination scale. Allostatic load was measured as a comPosite of 15 biomarkers assessing cardiometabolic, neuroendocrine, and inflammatory activity. We calculated four composite measures of allostatic load and three system-specific measures of biological dysregulation. Multivariable regression was used to examine associations, while adjusting for relevant confounders.

Results: In the high education group, reporting low (b=−1.09, *P*=.02, 95% CI=−1.99,−0.18) and very high (b=−1.88, *P*=.003, 95% CI=−3.11,−0.65) discrimination was associated with lower allostatic load (reference=moderate). Among those with lower education, reporting low (b=2.05, *P*=.008, 95% CI=0.55,3.56) discrimination was associated with higher allostatic load. Similar but less consistent associations were found for poverty status. Associations were similar for cardiometabolic functioning, but not for neuroendocrine or inflammatory activity.

Conclusions: Racial discrimination may be an important predictor of cumulative physiologic dysregulation. Factors associated with educational attainment may mitigate this association for African American women and other groups experiencing chronic social stress.

Keywords

Racial Discrimination; African American; Race/ethnicity; Stress; Allostatic Load; Socioeconomic Position

1. INTRODUCTION

In the U.S., experiences of social stress associated with race and gender intersect to perpetuate and exacerbate poor health outcomes for women of color, particularly African Americans (Geronimus, 1996; Jackson, 2005; Jackson et al., 2001). African American (AA) women are disproportionately burdened by the simultaneous dysregulation of multiple physiologic systems (Chyu and Upchurch, 2011; Duru et al., 2012; Geronimus et al., 2006; Upchurch et al., 2015), commonly referred to as allostatic load or cumulative biological risk. Allostatic load has been associated with numerous negative health outcomes including decreased cognitive and physical function, heart disease, stroke, diabetes, and mortality (Beckie, 2012; Borrell et al., 2010; Habib et al., 2001; McEwen, 1998; Seeman et al., 1997). The association between social stress and cumulative biological risk is now well accepted. Though early studies focused on age-related changes in physiologic function (Crimmins et al., 2003; Karlamangla et al., 2002; Seeman et al., 2001; Seeman et al., 1997), more recent studies have demonstrated associations with explicit forms of social stress that appear to be

unrelated to chronological age. In particular, numerous studies show an association between chronic (i.e., ongoing or repeated) social stress and allostatic load, which may help explain the heightened risk of poor health among AA women (Beckie, 2012; Borrell et al., 2010; Carlson and Chamberlain, 2005; Habib et al., 2001; Kessler et al., 1999; McEwen, 1998; Seeman et al., 1997).

Chronic stress plays a critical role in the progression of multiple disease states via prolonged activation of the hypothalamic-pituitary-adrenal (HPA) axis and the sympatho-adrenal-medullary (SAM) axis, the body's primary stress response systems (Borrell et al., 2010; Karlamangla et al., 2002; McEwen, 1998; Seeman et al., 1997). Activation of these neuroendocrine systems results in a cascade of physiologic events including the secretion of pro-inflammatory cytokines, catecholamines, and acute phase proteins, all of which have deleterious effects on the body with sustained elevation (Karlamangla et al., 2002; McEwen, 1998; Seeman et al., 1997). When stress exposure is *chronic*, the negative feedback loops that typically shut-off the neuroendocrine stress response are dysregulated resulting in a chronic pro-inflammatory state (Karlamangla et al., 2002; Seeman et al., 1997), heightened and extended autonomic reactivity (Karlamangla et al., 2002; McEwen, 1998; Seeman et al., 1997), and a variety of other impairments (e.g., tissue damage, receptor desensitization) (Crimmins et al., 2003; McEwen, 1998; Miller et al., 2002). Although helpful in the short term (i.e., when responding to more mild and transient forms of stress) chronic hyperactivity of various systems can compromise the body's ability to regulate the internal physiologic environment resulting in cumulative biological dysregulation (Karlamangla et al., 2002; McEwen, 1998; Seeman et al., 1997).

Perception of mistreatment has been associated with pronounced and sustained arousal across a number of physiologic systems including the HPA axis, autonomic nervous system, immune, metabolic and cardiovascular systems (Adam et al., 2015; Busse et al., 2017; Cooper et al., 2009; Cunningham et al., 2012; Dickerson et al., 2009; Friedman et al., 2009; Fuller-Rowell et al., 2012; Hill et al., 2017; Hoggard et al., 2015; Huynh et al., 2017; Lewis et al., 2010; Mays et al., 2007; Mendes et al., 2008; Myers, 2009; Wagner et al., 2015; Zeiders et al., 2014). Studies have also provided evidence of a more buffered stress response among those reporting chronic unfair treatment. For example, numerous studies have shown associations between reports of unfair treatment and a blunted cortisol response as well as overall poor HPA flexibility (e.g., flatter diurnal slope), especially among AAs (Adam et al., 2015; Busse et al., 2017; Fuller-Rowell et al., 2012; Hill et al., 2017; Huynh et al., 2016; Skinner et al., 2011; Zeiders et al., 2014). This heightened dysregulation observed among AAs may be at least partially explained by their histories of past exposures and their perception of the potential impact of these events (Zeiders et al., 2014)—getting hired and work settings, more generally, are among the most commonly reported sources of discrimination among AAs (Brondolo et al., 2011; Karlsen and Nazroo, 2002; Krieger et al., 2011).

Several studies show that the majority of AA women report racial discrimination as a unique and chronic social stressor (Cunningham et al., 2012; Fuller-Rowell et al., 2012; Krieger and Sidney, 1996; Lewis et al., 2010), evoking negative affective states that have been linked with biological alterations characteristic of the stress response (Nuru-Jeter et al., 2009;

Tomfohr et al., 2016). Moreover, it is generally widely accepted that the nature of the threat matters for evoking particular stress responses (Dickerson et al., 2009; Kemeny, 2003; Miller et al., 2007; Plummer and Slane, 1996). Social evaluative threat, such as that experienced with racial discrimination, is a particular form of stress that studies show is associated with heightened inflammation via dysregulation of both the HPA and SAM axes (Kemeny, 2003). A strong body of research has shown adverse effects of discrimination on mental health outcomes including depression, anxiety, psychological distress, hypervigilance, and various health behaviors (Borrell et al., 2006; Brown et al., 2000; Landrine and Klonoff, 1996; Lorenzo-Blanco et al., 2011; Robinette et al., 2016; Sellers et al., 2006; Tomfohr et al., 2016; Williams and Mohammed, 2013; Williams et al., 1997), all of which have been linked with subsequent poor physical health outcomes via neurobiological stress responses (Brown et al., 2000; Chae et al., 2012b; Gee et al., 2006; Pieterse et al., 2012). Those neurobiological pathways include, among others, impaired hippocampal learning and activity, which has deleterious effects on HPA functioning; a hyperactive amygdala, which compromises memory and the body's ability to predict threat and prepare the body for adaptive regulation (i.e., allostasis); and overall reduced neuroplasticity which promotes wear and tear due to the inability of the brain to respond adaptively to both anticipated and unanticipated stressors (Berger and Sarnyai, 2015; Carlson and Chamberlain, 2005; Fossion and Linkowski, 2007; Logan and Barksdale, 2008; Lucas et al., 2016; Lupien et al., 2015; McEwen, 2003; McEwen et al., 2015; Ziabreva et al., 2003). One of the amygdala's primary roles is to regulate the fight or flight response. Notably, studies have shown enhanced amygdala activity—especially the left amygdala, which is associated with recall of events—among women than among men, suggesting that women may be more vulnerable to emotionally threatening events (Hamann, 2005).

Evidence suggests that rather than having uniform effects on physiology, stressors are met with integrated cognitive, affective, and behavioral responses that determine the psychobiological response to stress (Kemeny, 2003). In particular, studies suggest that how people appraise and cope with specific stressors differs by socioeconomic position (SEP). Lower socioeconomic groups are more likely to minimize attributions to discrimination and internalize their discrimination experiences (Crocker et al., 1991), both of which have been associated with poorer health (Chae et al., 2012a). Lower socioeconomic groups also report greater stress exposure, and hence may face depletion of health-protective resources and a lower sense of control over stressful life situations, increasing the likelihood of appraising stressors as threatening (Gallo and Matthews, 2003).

Geronimus proposed the "weathering hypothesis" to explain the accelerated physiologic deterioration experienced among black women due to the repeated stress associated with cumulative social disadvantage, including chronic experiences of racial discrimination (Geronimus, 1996; Geronimus et al., 2006). Several studies show heightened allostatic load among AA women relative to other race-gender groups (Chyu and Upchurch, 2011; Duru et al., 2012; Geronimus et al., 2006; Upchurch et al., 2015), which may help explain their elevated risk of poor health especially during midlife where differences are most pronounced (Borrell et al., 2010; Chyu and Upchurch, 2011). However, no studies to our knowledge have examined whether racial discrimination may account for the higher levels of allostatic load observed among this group. The purpose of this study was two-fold: To (1) examine the

association between level of reported racial discrimination and allostatic load among a community-sample of midlife AA women, and (2) assess whether two commonly used indicators of SEP (i.e., educational attainment and poverty status) modify this association. We hypothesized that the association between racial discrimination and allostatic load would be greatest among lower socioeconomic groups.

2. METHODS

2.1 Study Design

Data are from the African American Women's Heart & Health Study, an observational cross-sectional study designed to examine associations between social-environmental stressors and cardiometabolic risk among a community sample of midlife (ages 30–50) AA women residing in the San Francisco Bay area (n=208). The SF Bay area is a major metropolitan area in the state of California. Study recruitment was conducted by the 1st and 5th author and took place March 2012 through March 2013. According to the 2010 U.S. Census, the nine-county San Francisco Bay area was: 52.5% white, 23.3% Asian, 6.7% AA, 16% other or two or more races, and 23.5% Latino (Census, 2010). Given their relatively low proportion compared to other groups, recruitment efforts targeted counties with the highest percent of AAs: Solano (14.7%), Alameda (12.6%), Contra Costa (9.3%), San Francisco (6.1%).

Purposive sampling was used to maximize variability on key exposures and covariates (e.g., racial discrimination, socioeconomic factors) and included: targeted neighborhood sampling (e.g., low vs. high percent AAs per census tract), venue-based (e.g., nail/hair salons, churches, transportation hubs), event-based (e.g., arts concerts/performances, festivals, black college expo) and organization-based sampling (e.g., non-profits serving either low- or high-income AA women). We also recruited via social media and traditional media outlets. Potential study participants were screened for the following eligibility criteria: 1) self-identified AA and female gender since birth, 2) ages 30–50, 3) US-born, 4) parent(s)/primary caregiver(s) US-born AA, 5) can read/write English. Women who were pregnant or lactating and/or self-reported a physician-diagnosed inflammatory (e.g., HIV) or auto-immune disease (e.g., Lupus) were excluded to avoid misclassification. Study participation consisted of two visits: 1) interviewer-administered questionnaire and computer-assisted self-interview, 2) physical exam (i.e., height, weight, resting blood pressure, waist and hip circumference, body fat percent and body mass index) and fasting venous blood draw. Participants incentives included a $70 gift card, t-shirt, 8 heart healthy cookbook, and a packet of health promotion materials. The study was approved by the Committee for the Protection of Human Subjects at the University of California, Berkeley.

2.2 Measures

Allostatic Load (AL) was operationalized as a composite of 15 biomarkers assessing functioning of the HPA axis (cortisol), SAM axis (epinephrine and norepinephrine), inflammation (Interleukin-6 (IL-6) and C-reactive protein (hsCRP)), and cardiometabolic function (diastolic and systolic blood pressure, waist circumference, body mass index, glucose, glycosylated hemoglobin, high and low-density lipoprotein, triglycerides, and total

cholesterol) (Borrell et al., 2010; Geronimus et al., 2006; McEwen, 1998; Seeman et al., 1997; Seplaki et al., 2005).

Resting diastolic and systolic blood pressure (DBP and SBP, respectively) were measured from the sitting position using an automated oscillometric blood pressure monitor, after an initial 5-minute rest. Four consecutive measures were taken in 1-minute intervals; the first measure was discarded and the average of the last 3 measures was recorded (Pickering et al., 2005). Waist circumference was measured just above the top of the iliac crest with a tape measure, arms/hands down at the sides after one normal exhalation (NHLBI Obesity Education Initiative, 2000). Body mass index was measured via bioelectrical impedance using a handheld body fat analyzer. Fasting venous blood specimens were collected and stored at −80°C. Assays for hsCRP, cortisol, epinephrine and norepinephrine were performed by Quest Diagnostics. All other labs were assayed by the Client Services Laboratory at the UC Davis Department of Pathology and Laboratory Medicine.

Cutpoints for each biomarker are displayed in Table 1. We used established clinically-based cutpoints where available (Crimmins et al., 2003). Most of the biomarkers with established cutpoints have thresholds for subclinical and clinical risk, permitting assessment of dysregulated systems that may not yet meet criteria for clinical diagnosis. For biomarkers without established cutpoints (IL-6, epinephrine, norepinephrine, and cortisol), risk assessment was based on the distribution of the study sample as described below (Geronimus et al., 2006; Karlamangla et al., 2002; Seeman et al., 1997; Seplaki et al., 2005).

We calculated four composite measures of AL to assess predictive ability across varying assessments and degrees of dysregulation (Seplaki et al., 2005): 1) sum of biomarkers for which the respondent is above the established cutpoint for subclinical risk (for biomarkers with established criteria) or above the 75th-percentile (for biomarkers without established criteria), 2) sum of biomarkers for which the respondent is above the established cutpoint for clinical risk or the 90th-percentile to assess more extreme dysregulation, 3) summary score based on established cutpoints for subclinical and clinical risk respectively or, correspondingly, the interquartile range (IQR), and 4) sum of z-scores for each biomarker. For the 75th-percentile/subclinical and 90th-percentile/clinical risk measures, each of the 15 biomarkers was categorized at the specified cutpoint (0=not at risk, 1=at risk) and summed with scores ranging from 0 to 15 where higher scores reflect higher levels of AL. The summary measure based on the IQR categorizes biomarkers at the 25th-percentile/ subclinical and 75th-percentile/clinical cutpoints to capture mor e of a gradient rather than establishing risk based only on the extremes of the distribution, and to avoid potential misclassification from combining all participants in the bottom 75th or 90th percentile as not at risk. Participants were categorized as low (0=bottom 25%), moderate (1=middle 50%), or high risk (2=top 25%); values were summed with scores ranging from 0 to 30 where higher values reflect higher levels of AL_{IQR}. Last, z-scores were calculated for each biomarker and summed to represent risk in standard deviation units.

We also calculated system-specific measures of physiologic dysregulation to examine whether certain systems were more or less responsive to stress. Scores for inflammation included CRP and IL-6, and were based on the IQR specification described above due to the

greater range of the summary scores (0–4 vs. 0–2) and to minimize the misclassification inherent in dichotomous risk assessment. Scores from the component biomarkers were summed and then categorized to reflect risk: none (both inflammatory markers in normal range), low (one biomarker in normal range and one in moderate range), moderate (two in moderate range, or one in high range and one in normal range), high (one biomarker in moderate range and one in high range, or both in high range). Scores for neuroendocrine dysregulation included cortisol, epinephrine and norepinephrine and was based on the 75^{th}-percentile scoring (0/1) since the majority of the biomarker values fell within the laboratory reference range and there was no distinction in level of risk between the 25^{th}- and 75^{th}-percentile cutpoints. Scores from the component biomarkers were summed and categorized to reflect low (all biomarkers in normal range), moderate (one elevated biomarker), and high risk (at least two elevated biomarkers). For cardiometabolic function, each of the 10 remaining biomarkers was categorized used the coding scheme described above for low, moderate, and high based on subclinical and clinical cut-points, respectively. Next, a summary score ranging from 0–20 was generated.

We decided to collapse cardiovascular and metabolic functioning into one cardiometabolic system-specific measure for several reasons: (1) blood glucose and various measures of lipid balance vary together and are determined by a common set of lifestyle factors (Basaranoglu et al., 2015; Sacks et al., 2014), (2) models of allostasis include many of the biomarkers reflected in our CV and metabolic system measures but do not separate them (McEwen and Rasgon, 2018) (3) the synergy of the metabolic and cardiovascular systems leave decisions about which biomarkers belong to which system equivocal and dependent upon the study aims. High density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides, and total cholesterol could easily be moved to the CV system measure leaving the metabolic system focused on carbohydrate metabolism (glucose, hemoglobin A1c (HbA1c), body mass index (BMI), waist circumference). Some studies have separated cardiovascular, lipid metabolism, and glucose metabolism (e.g., Ong et al., 2017; Robinette et al., 2016), which would also be acceptable for our study aims, (4) the metabolic syndrome (MS) has been characterized as a critical pathway to CVD as well as allostatic load (McEwen & Rasgon, 2018), (5) MS includes biomarkers from both our cardiovascular and metabolic system measures, and (6) recent studies are starting to link allostatic load and the stress response with cardiometabolic health (Nobel et al., 2017; Picard et al., 2014).

Racial discrimination was measured using a modified version of the widely used and previously validated Experiences of Discrimination (EOD) scale (Krieger et al., 2005), consisting of eight items asking whether respondents have ever experienced discrimination because of their race, ethnicity, or skin color in any of eight different domains (i.e., at school, getting hired/getting a job, at work, getting housing, getting medical care, getting credit/bank loans/mortgage, from police/courts, on the street/public setting). Reliability of the scale in our sample (α=.92) was higher than in the original validation study (α=0.81–0.87 among AA respondents). Responses were scored on a 5-point likert scale ranging from 1=“Never” to 5=“6 or more times”, summed across items, and categorized into: none, low, moderate, high, and very high levels of racial discrimination, given previous evidence of non-linear associations (Table 2).

We used moderate as the referent group given previous evidence indicating that moderate stress exposure is self-regulatory and provides optimal psychological and biological functioning (Aschbacher et al., 2013; Bush et al., 2011; Chatkoff et al., 2010; Del Giudice et al., 2011; Dooley et al., 2017; Gunnar et al., 2015; Seery et al., 2010). The standard approach of modeling racial discrimination continuously, rather than categorically, precludes an assessment of the potentially protective/buffering effects of moderate levels of racial discrimination. One exception is Krieger & Sidney (1996) who used moderate discrimination (experiencing 1 or 2 situations vs. none or 3+) as the referent category in a study of the association between EOD and blood pressure among young Black and White adults in the CARDIA study. Findings showed moderate discrimination to be protective against high blood pressure in most study subgroups defined jointly by race, gender, and class. In another study, O'Brien and colleagues (2017) examined hair cortisol and lifetime discrimination in a multi-ethnic sample of 180 adults. They found the mean level of lifetime discrimination (moderate) to be associated with lower hair cortisol concentration compared to 1 standard deviation (SD) above (high) or below (low) the mean. Based on this evidence, we treated moderate discrimination as the referent category in all analyses.

Educational attainment and poverty status were both dichotomous variables. Participants were asked to report the highest level of education completed. Responses ranged from "some grade school but did not graduate" to a "doctoral degree". Due to cell size, educational attainment was dichotomized as > versus ≤ a high school diploma (0/1). Participants were also asked to report their total monthly household income and the number of persons in the household. Poverty status was then operationalized as ≤ versus > 100% of the Federal Poverty Threshold (FPT) according to the 2011 FPT guidelines. Potential covariates included age in years, health insurance (0=yes, 1=no), marital status (married/domestic partner=0 vs. not married/no domestic partner=1), neuroticism based on a summary score from the 8-item neuroticism subscale of the Big 5 Inventory of personality traits, and medication use. For medication use, participants were asked if they were currently taking medication for "high blood pressure, hypertension, stroke, heart attack, blood circulation problems, hardening of the arteries, or any other heart or blood problem" and whether they were "currently taking medication to manage diabetes" (no/yes).

2.3 Statistical Analysis

Multivariable regression was used to quantify the change in AL per unit change in racial discrimination. Ordinary least squares and ordered logistic models were used, according to the specification of the dependent variable. First, we estimated the independent effect of racial discrimination on each outcome. Next, we performed two different sets of marginal effects models to examine effect modification: first by educational attainment, then by poverty status. Following recommendations outlined by Selvin (2004), we used a threshold of $P<0.2$ for interactions to prevent threats to validity resulting from false negatives or "wrong model bias". For all other estimates, significance was based on $P<.05$ and 95% confidence intervals (CIs). Models were adjusted for age, educational attainment and medication use regardless of significance to account for known confounders and ensure accurate risk assessment. Health insurance, poverty status adjusted for household size, marital status, and neuroticism were included in final models if significant at $P<.10$ to

account for potential confounding and reporting bias (see Table 2). Previous studies show associations between lifestyle behaviors and allostatic load. However, there is also literature suggesting that lifestyle behaviors may mediate the association between racial discrimination and allostatic load. Hence, we conceptualized lifestyle behaviors as mediators rather than moderators and therefore consistent with epidemiologic modeling (directed acyclical graph), did not include these variables as covariates in our analysis in order to avoid over-controlling and due to the cross-sectional nature of our data. Employment status was also conceptualized as a potential mediator and not included in our analysis.

Multiple imputation by chained equations was used to account for missing data (missing at random). Several biomarkers were log-transformed prior to imputation to correct for skewness and meet the normality assumptions of multiple imputation. Monte Carlo estimates were examined to confirm reproducibility of effect estimates across imputations. There were no significant departures from established criteria. Relative efficiency ranged from 98–100%, and relative variance increase and percent increase in standard error were both within 5%. One observation was excluded because it had missing data on both the right- and left-hand side of the imputation model, and therefore had missing data post-imputation (n=207). One additional outlying observation (> 3 SD beyond the IQR) was excluded from models estimating inflammation and neuroendocrine dysregulation (n=206). Additional post-estimation diagnostics included variance inflation factors to assess multicolinearity and tests of leverage and influence (Cook's D), multivariate normality (Doornik-Hansen omnibus test) and heteroskedasticity (Breusch-Pagan and Cook-Weisberg). Analyses were conducted using Stata/SE 14.0.

3. RESULTS

Sample characteristics are shown in Table 2. Mean age was 42 years. Two-thirds of the study sample had more than a high school diploma. Approximately 20% were below the federal poverty level, a little over half were employed (55%), 30% were married, and 73% had health insurance. Mean levels of AL were in the low to moderate range. Approximately 11% of the sample reported no experiences of racial discrimination, the majority (64%) reported low to moderate levels of discrimination (i.e., between 1 to 3 experiences of discrimination in at least 1 domain), and 25% reported high to very high levels of racial discrimination (i.e., 5 to 6+ experiences in at least 1 domain). Discrimination experienced "on the street or in a public setting" was the most common form reported followed by "from the police or in the courts", "at work", "getting hired or getting a job", and "at school": 73%, 67%, 67%, 65%, and 61% respectively.

Results showing the adjusted association between racial discrimination and AL are shown in Table 3. For three of the four composite measures of AL, associations varied by education (all except AL_{z_sum}). For simplicity, we display results for AL_{75} only (results for all composite measures is available online, supplementary Table 1). For AL_{75}: among those with higher education (> high school diploma), those reporting low (b=−1.09, P=.02, 95% CI= −1.99, −0.18), and very high (b=−1.88, P=.003, 95% CI= - 3.11, −0.65) levels of racial discrimination had lower levels of AL (ref=moderate). Among those with lower education, we found the opposite (Figure 1): those reporting low (b=2.05, P<.01, 95% CI= 0.55, 3.56)

racial discrimination had the highest levels of AL_{75}. Associations for high and very high racial discrimination did not reach statistical significance but are suggestive of a U-shaped relationship among those with lower education. For AL_{IQR}, a similar and statistically significant U-shaped pattern emerged among those with lower education, but with effect sizes roughly 1.5–2× greater than observed for AL_{75}. Among those with higher education, reporting very high levels of discrimination was associated with lower levels of AL_{IQR} (supplementary Figure 1). Fewer significant associations emerged for AL_{90}: among those with higher education, those reporting very high discrimination had lower AL. The opposite was observed among those with lower education, although the joint test of coefficients for the interaction did not reach statistical significance ($P>.2$) (Selvin, 2004). There were no significant differences by education for AL_{z_sum} and no significant main effects, although the direction of effect estimates is consistent with those observed using the other AL measures for the high education group. Interaction results for poverty were less consistent.

Only one of the composite AL measures, AL_{30}, showed significant differences between poverty-level groups (supplementary Table 2). Findings were consistent with the results for educational attainment (Figure 2): among those not in poverty, reporting very high (vs. moderate) racial discrimination was associated with lower levels of AL (b=−2.54, $P<.05$, 95% CI= −4.56, −0.52). Among those at or below 100% of the FPL, reporting no racial discrimination (vs. moderate) was associated with higher levels of AL (b=4.88, $P<.04$, 95% CI= 0.28–9.48).

Table 4 shows results for the interaction of racial discrimination and educational attainment in relation to each of our system-specific measures of physiologic dysregulation. Findings for cardiometabolic function mirrored those reported for AL_{75} and AL_{IQR} above (supplementary Figure 2). For neuroendocrine and inflammatory activity, no differences by education emerged. Instead, reporting very high levels of racial discrimination was associated with blunted physiologic activity, regardless of educational attainment. There were no significant interactions for poverty status: reporting very high levels of racial discrimination was associated with blunted cardiometabolic activity after adjusting for model covariates including education and poverty status (b=−1.61, $P=0.03$, 95% CI=−3.06, −0.15). For neuroendocrine activity, those reporting very high racial discrimination had lower odds of AL. However, these results did not reach statistical significance (OR=0.32, $P=.06$, 95% CI= 0.10, 1.05).

To determine if our results were being driven by particular biomarkers, we performed separate regressions on each individual biomarker. Given the direction, magnitude and statistical significance of associations, it does not appear that a few biomarkers are driving the results (supplementary Tables 3 and 4). For educational attainment, there were significant effects for two of the individual biomarkers: epinephrine and waist circumference. Among those in the low education group: reporting a high level of racial discrimination was associated with higher levels of circulating epinephrine (b=.63, $P=.03$, 95% CI=0.05, 1.2) and higher waist circumference (b=0.52, $P=.03$, 95% CI=0.05, 0.98). Among those in the higher education group: reporting low levels of racial discrimination was associated with lower waist circumference (b= −0.21, $P=.04$, 95% CI= −0.41, −0.01). For poverty status, there were no significant interaction effects for any of the individual

biomarkers. We also examined independent main effects for the remaining 13 biomarkers (excluding epinephrine and waist circumference). HbA1c was the only biomarker showing a significant main effect for racial discrimination: reporting very high racial discrimination was associated with lower HbA1c (b= −0.21, *P*=.04, 95% CI=−0.42, −.01).

4. DISCUSSION

We examined the association between racial discrimination and cumulative biological dysregulation among a community sample of midlife AA women in the San Francisco Bay Area. This is the first study to examine racial discrimination and AL among this group. This is also the first study to show that the association between racial discrimination and AL is moderated by educational attainment, and quite dramatically. This is not only a novel finding but a very informative one that points to potential differences in the mechanisms linking racial discrimination and AL between socioeconomic groups. The buffered pattern observed among both the higher education and higher income groups highlights the need to better understand the factors that may safeguard against the negative health outcomes associated with racial discrimination and potentially other forms of chronic social stress. The U-shaped pattern observed among the lower socioeconomic groups, particularly the inverse association among those reporting low (vs. high) levels of racial discrimination, raises questions that may help inform future research in this area such as potential reporting bias (i.e., underreporting) and the role of coping, racial identity and internalized racism (Chae et al., 2014; Krieger, 1990; Sellers et al., 2006), among other potential explanations. Additionally, although our findings do not appear to be driven by particular individual biomarkers, cardiometabolic function may be a primary driver and warrants further consideration as a mechanism underlying this association.

The buffered pattern observed among the higher socioeconomic groups is consistent with prior work suggesting that acknowledging racism is protective compared to internalizing those experiences and potentially engaging in self-blame (Chae et al., 2012a; Chae et al., 2014; Krieger and Sidney, 1996; LaVeist et al., 2001; Major et al., 2002). The U-shaped relationship observed among the lower socioeconomic groups is also consistent with previous research. Reporting lower levels of racial discrimination has been associated with worse cardiovascular health among low socioeconomic black women who respond to unfair treatment by accepting it and keeping it to themselves, suggesting that coping may influence how discrimination impacts biological functioning (Krieger and Sidney, 1996). This may reflect a tendency to deny, suppress, or otherwise passively cope with racial discrimination (Krieger and Sidney, 1996; Nuru-Jeter et al., 2009), which has been previously associated with poor health outcomes (Krieger and Sidney, 1996), and may suggest some degree of reporting bias among lower socioeconomic groups. Literature on stigma and attributions to discrimination reflect the need to better understand the factors that determine variability in responses to discrimination. It is now generally understood that vulnerability and resilience are both common responses to prejudice and discrimination (Major et al., 2002).

Other studies have, similarly, noted non-linearities in the racial discrimination-biology relationship (Fuller-Rowell et al., 2012; Krieger and Sidney, 1996; Skinner et al., 2011). Skinner (2011) found that AAs reporting low (vs. high) levels of racial discrimination have a

flatter diurnal cortisol rhythm, characteristic of poor HPA flexibility (i.e., dysregulation) (Skinner et al., 2011). Using data from the National Study of Midlife in the United States (MIDUS), Fuller-Rowell et al. examined associations by race and found that among African Americans, reporting low (vs.) high levels of discrimination (where 90% of AAs reported their discrimination experiences as due to race) was associated with lower waking cortisol (i.e., less HPA flexibility), and that this effect was greatest among lower socioeconomic groups (Fuller-Rowell et al., 2012).

The lack of consistent results for poverty are not surprising given previous findings that higher income does not protect blacks from higher levels of AL (Geronimus et al., 2006). Further studies suggest that neighborhood poverty may be a stronger predictor of AL than individual-level income. (Robinette et al., 2016; Schulz et al., 2012; Tan et al., 2017) Additionally, studies suggest that higher educated, but not necessarily higher income, AAs are more likely to live and work in settings where they are the minority, thereby increasing opportunities for experiencing racial discrimination (NPR/Robert Wood Johnson Foundation/Harvard T.H. Chan School of Public Health, 2017; Pew Research Center, 2016; Wilson et al., 2017). Hence, higher educated AAs may not only experience certain types of discrimination more but may also be better equipped to recognize it. Howard and Sparks (2015) found that among AAs, those with a college degree or higher had significantly lower AL compared to those with less than a high school diploma. Our study findings complement these results and provide preliminary evidence suggesting that reports of racial discrimination may be one factor helping to explain this disparity. Further research is needed to explicitly test this hypothesis.

Consistent with the concept of subclinical dysregulation, the association between racial discrimination and AL was strongest for measures capturing more moderate (i.e., AL_{75}, AL_{IQR}) vs. extreme levels of dysregulation (AL_{90}), which is especially salient given our sample of mostly healthy women not yet diagnosed with serious medical conditions

Several methodological considerations should be noted. This was an exploratory study intended to generate preliminary data and hypotheses about the potential role of social stress, in particular racial discrimination, for heightened biological dysregulation among AA women. However, we are unable to infer causality due to the cross-sectional nature of the study. We used a non-probability purposive sample intended to maximize variability in the primary exposure and ensure stable estimates across subgroups (Rothman et al., 2014). Compared to AA women in the 2013 American Community Survey ages 30–50 residing in the same Bay Area counties, our sample had a similar distribution of educational attainment, employment and marital status but a higher percent not insured and lower percent in poverty (data available upon request) (Ruggles et al., 2010). Although we used validated scales, our self-report measures are subject to the typical reporting bias inherent in all survey research. Biomarkers were assessed via one fasting venous blood draw and therefore do not capture circadian rhythm. Resting, rather than ambulatory, blood pressure was measured but taken to capture a true average and minimize white coat effect. A few of our models had power below 80% (i.e., inflammation=34%, neuroendocrine=65%). Hence, observed differences are likely under-estimates of the true effects. Educational attainment was dichotomized at high school diploma, also biasing our results toward the null vs. dichotomizing at college

degree. Last, detailed information about medication use was not available. Hence, we were unable to control for medications prescribed off-label.

This study also has several strengths. First, only one other study has, to our knowledge, examined the relationship between racial discrimination and AL among any population. Brody et. al. examined the association among AA adolescents ages 16–18 in the rural south (Brody et al 2014). Other studies have examined racial discrimination and health more broadly (e.g., birth outcomes, mental health outcomes, cardiovascular disease) (Dominguez et al., 2008; Lewis et al., 2014; Pieterse et al., 2012) and in relation to specific biomarkers (e.g., cortisol, CRH, CRP, catecholamines) (Albert et al., 2008; Braveman et al., 2015; Fuller-Rowell et al., 2012; Lewis et al., 2010; Wagner et al., 2013), though findings are mixed (Cohen et al., 2006; Huynh et al., 2016; Schmitt et al., 2014; Skinner et al., 2011; Wagner et al., 2013). However, previous studies indicate the need to study simultaneous dysregulation across multiple systems to better understand how psychosocial factors contribute to stress-related illness, given the importance of integrative biology for disease outcomes. In fact, some studies have shown significant associations between composite AL scores and subsequent poor health outcomes whereas individual biomarkers are not significant independent risk factors (Ong et al., 2017). Hence, studies point to the need to understand the “interconnected nature of biological stress systems including their co-occurring responses to social stressors” (Lucas et al., 2016).

There have also been studies examining more general unfair treatment (not attributed to race, ethnicity, skin color) in relation to specific biomarkers (e.g., IL-6, CRP, cortisol, coronary artery calcification) and one in relation to AL (Upchurch et al., 2015). These studies support previous findings suggesting that experiencing discrimination is more salient than the type of discrimination experienced (Huynh et al., 2016; Kershaw et al., 2016; Ong et al., 2017; Zeiders et al., 2014). However, other studies suggest that racial discrimination has particularly pernicious health effects among racial minority groups for whom such experiences are more frequent, more severe and occur across a wider range of situations; and among those with a particularly strong racial group identity (Crocker and Major, 1989; Major et al., 2002; Sellers et al., 2003). Racial discrimination is commonly reported by AA women, has been reported as a particularly salient form of social stress (Carter, 2007; Nuru-Jeter et al., 2009; Williams et al., 2012), and as distinct from other forms of social stress including other forms of unfair treatment. Our study is the first to examine whether *racial* discrimination is associated with multi-system physiologic dysregulation among AA women.

Prior research has shown considerable variation in reports of discrimination by race both in terms of frequency of reports and to what the discrimination was attributed (e.g., race, gender). The majority of AAs attribute their discrimination experiences to race and report more chronic experiences, whereas whites report non-racial forms of discrimination more frequently (Cozier et al., 2006; Karlamangla et al., 2002; Krieger and Sidney, 1996; Plummer and Slane, 1996; Williams et al., 2012). African Americans’ reports of racial discrimination have been further described as a form of historical trauma characterized by rumination, heightened vigilance, and the processing of contemporary experiences as re-experiencing historical oppression (Borders and Liang, 2011; Carter, 2007; Hicken et al.,

2013; Nuru-Jeter et al., 2009; Williams et al., 2012). On the contrary, whites commonly attribute their experiences to reverse racism such as being denied opportunities due to Affirmative Action policies (i.e., policies intended to protect and provide opportunities to groups that have faced historical discrimination) (Williams et al., 2012). Further work is needed to better understand differences in how different groups recognize and understand discrimination. However, these qualitative differences suggest the importance of not conflating the racial discrimination experiences of AAs and whites, and the importance of distinguishing between racial discrimination and other forms of unfair treatment. Taken together, this evidence was a primary motivation for limiting our study to African American women, in addition to evidence documenting significant gender disparities in AL by race (Chyu and Upchurch, 2011; Deuster et al., 2011; Duru et al., 2012).

Additionally, acknowledging the heterogeneity in reports of racial discrimination among AA women, our within group study was an attempt to better isolate racial discrimination as the exposure of interest. By restricting the sample to AA women, we avoid the misclassification and biases inherent in multi-ethnic studies vis a vis incommensurability of the exposure across groups (Howard and Sparks, 2015). Testing this association among AA women provides evidence suggesting that reported racial discrimination may be one risk factor associated with higher AL among this group; but that importantly, this association varies by level of educational attainment. Further, given that AAs report racial discrimination at a much higher frequency than whites, it follows that racial discrimination may help explain the higher rates of AL observed among this group. However, future studies examining differences between AA men and women is warranted. It is unclear whether this association is unique to AA women and thus explains the disparity observed among this group. If the association persists for AA women and men, it would suggest that racial discrimination is not an adequate explanation for heightened risk among AA women alone but rather may help explain why AAs, as a group, experience accelerated biological weathering relative to whites.

This is also the first study to examine the racial discrimination-AL association in adulthood, the period of life where race-gender disparities in AL become more apparent. Geronimus showed the gap in AL scores between race-gender groups becomes “especially pronounced after age 30” with AA women having the highest probability. Notably, although AA and white men and women start with the same intercept at age 18, the slope of the association between age and AL is greatest among AA women, suggesting that AA women experience biological “weathering” at an accelerated pace relative to other race-gender groups. We believe this distinction—the *racial* discrimination-AL association among *midlife* AA women—is an important one that may help explain the higher rates of AL observed in previous studies. Thus, while several studies have now shown that AA women have higher levels of AL relative to other groups, no previous studies to our knowledge, have specifically investigated the factors that may account for this particular vulnerability (heightened *multi-system* physiologic dysregulation during midlife among this group).

5. CONCLUSIONS

Racial discrimination may be an important predictor of biological dysregulation, increasing risk for poor health among AA women. Results suggest mechanisms that may buffer or exacerbate the effect of racial discrimination; and the need to further explore differences by socioeconomic position, particularly educational attainment. Findings provide new insights that may help explain the role of social determinants for disease pathogenesis, and offer direction for future research among socially disadvantaged groups and other groups experiencing more general forms of chronic stress. In the US, disparities by race have persisted over time and across health outcomes. African Americans are among the most socially disadvantaged groups in the US. However, after adjustment for socioeconomic factors, health behaviors, and access to and utilization of health care, health disparities persist. The role of social stress for adverse health outcomes is now widely accepted. Although de jure racial discrimination no longer exists, AAs report various forms of de facto racial discrimination (structural, institutional, personally-mediated) as a salient and ongoing source of life stress (Carter, 2007; Guyll et al., 2001; Nuru-Jeter et al., 2009; Williams et al., 2012; Williams and Mohammed, 2013). Geronimus' "weathering" hypothesis was developed as a framework for examining the early health deterioration observed among AA women, and suggests that this decline is a physical manifestation of the stress associated with being a member of a socially marginalized group and contending with various forms of recurring racial discrimination (Geronimus et al., 2006). Our findings have implications for AA women in the US and for socially marginalized groups more broadly. Studies show associations between racial discrimination and mental and physical health among many socially marginalized groups; for example, indigenous people of Australia, Native Hawaiians, Turkish immigrants in Germany, minority and immigrant women in New Zealand, Southeast Asian refugees and Korean immigrants in Canada, and "blacks and browns" in Brazil (Bastos et al., 2014; Berger et al., 2015; Fischer et al., 2017; Kaholokula et al., 2012; Larson et al., 2007; Thayer and Kuzawa, 2015). Importantly, these reports have included both observational and laboratory- based assessments, though attention to multi-system physiologic dysregulation is limited.

Further research using larger probability-based samples is needed to provide more precise risk estimates, improve generalizability, and determine causation. Additionally, studies examining lifestyle behaviors as potential mediators is also warranted. Though further research is needed, discrimination remains a unique and important stressor and may have relevance for identifying at-risk groups and help inform strategies to prevent, detect, and treat disease progression.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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A Allen, Principal Investigator, conceptualized the study, coordinated all logistics related to recruitment and data collection, designed and performed all statistical analyses (and takes responsibility for the integrity of the data analyzed), and took primary responsibility for drafting the manuscript; M Thomas assisted with the design of the analysis, specifically operationalizing study variables, as well as data interpretation, and drafting the manuscript; E Michaels assisted with design of the analysis, reviewing statistical code, data interpretation, and drafting the manuscript; AN Reeves assisted with data interpretation and drafting the manuscript; U Okoye assisted with data interpretation and editing of the manuscript; M Price was responsible for management of data collection, made contributions to the intellectual content of the manuscript and assisted with manuscript revisions; R Hasson assisted with laboratory data collection and manuscript revisions; SL Syme helped provided assistance with interpreting the study results and drafting the manuscript. DH Chae helped conceptualize the study and provided assistance with data interpretation and drafting the manuscript.

Abbreviations:

CV medication	cardiovascular medication

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Highlights

- There was a non-linear association between discrimination and allostatic load
- The association between discrimination and allostatic load varied by education
- A U-shaped relationship emerged among those with lower education
- High discrimination had a buffering effect among those with higher education
- Associations were found for allostatic load and in system-specific analyses

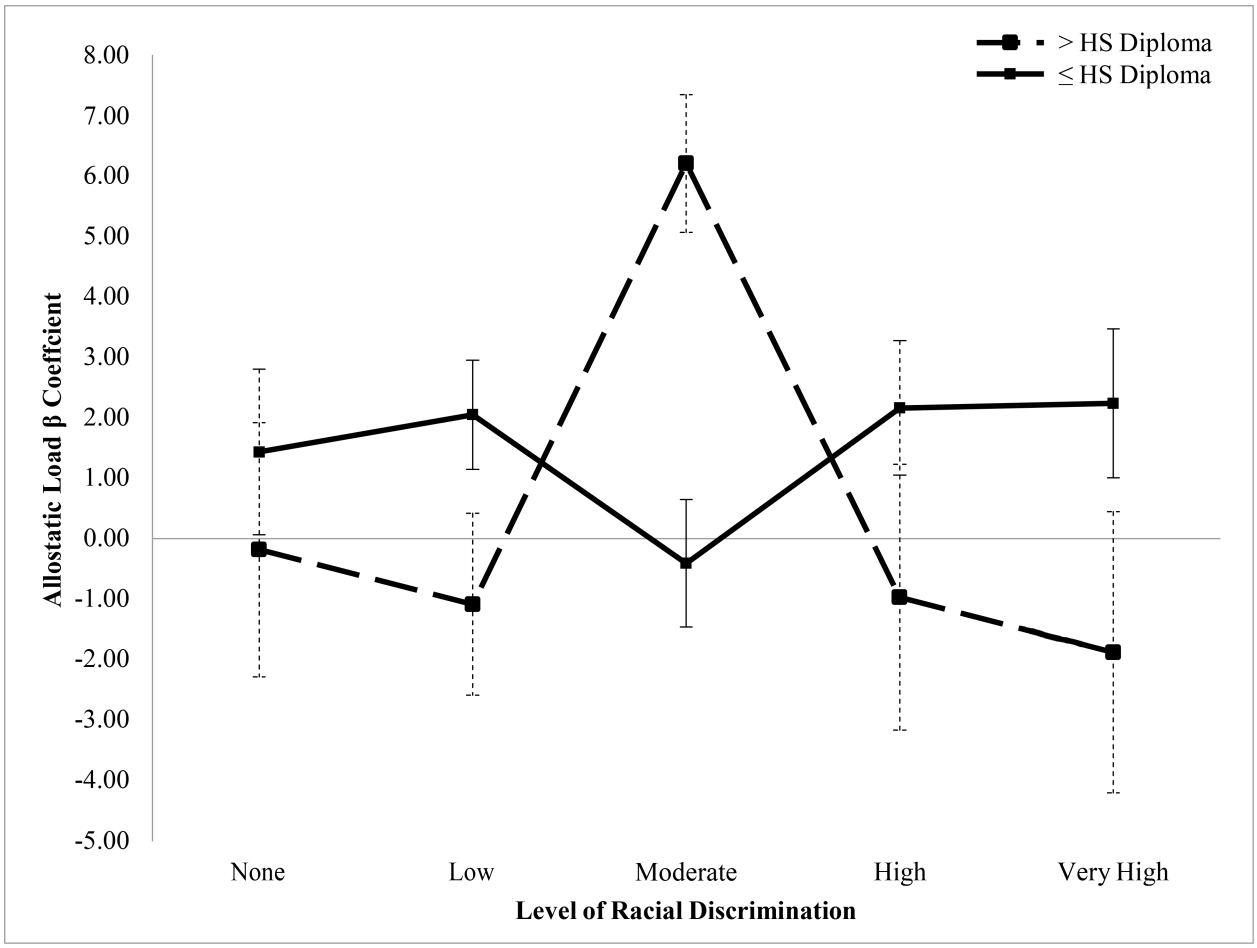

Figure 1:

Allostatic load (AL_{75}) by Racial Discrimination and Educational Attainment (n=206), San Francisco Bay Area

Note: Reference group is moderate. *p<0.10, **p<0.05, ***p<0.01; HS Diploma=High School Diploma

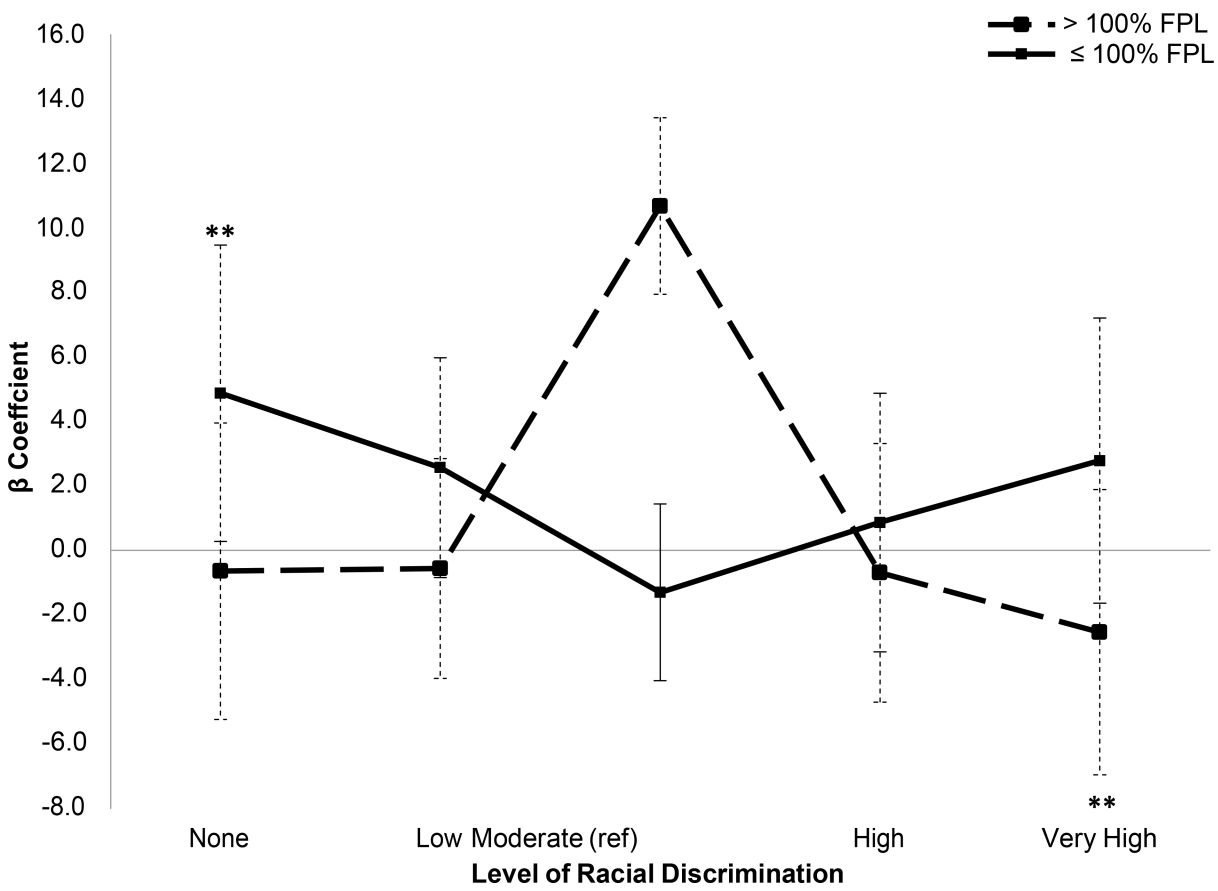

Figure 2:

Linear Regression of Allostatic Load (AL_{IQR}) and Racial Discrimination by Poverty Level (n=206)

Note: Reference group is moderate. FPL is Federal Poverty Line. *p<0.10, **p<0.05, ***p<0.01

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Table 1.

Allostatic Load Biomarker Cutpoints

Biomarker	Used	Cutpoints†	% Above Cutpoint for AL_{75}‡	Cutpoint§	% Above Cutpoint for AL_{90}‡	AL_{IQR} Cutpoints£		
Cardiometabolic System						Low Risk	Moderate Risk	High Risk
HDL (mg/dL)	ATPIII	<50	41.6	<40	12.6	≥50	≥40 & <50	<40
LDL (mg/dL)	ATPIII	≥100	52.2	≥130	16.4	<100	≥100 & <130	≥130
Waist Circumference (in)	ATPIII	>35	72.3	>49	---	<35	≥35 & ≤45	>45
Glucose (mg/dL)	ATPIII	≥100 or <70	17.4	≥126 or <70	8.7	≥70 or <100	≥100 & <126	≥126 or <70
HbA1c (mmol/mol)	ADA	≥5.7	19.3	≥6.5	4.4	<5.7	≥5.7& <6.5	≥6.5
Total Cholesterol (mg/dL)	ATPIII	≥160	66.2	≥200	22.7	<160	≥160 & <200	≥200
Triglycerides (mg/dL)	ATPIII	≥150	7.3	≥200	2.9	<150	≥150 & <200	≥200
BMI (kg/m^2)	ATPIII	≥25 or<18.5	85.5	≥30 or <18.5	63.8	<25	≥25 & <30	≥30 or <18.5
Systolic BP (mm Hg)¥	AHA	≥120	47.3	≥140	15.0	<120	≥120 & <140	≥140
Diastolic BP (mm Hg)¥	AHA	≥80	47.8	≥90	26.6	<80	≥80 & <90	≥90
Neuroendocrine System								
Cortisol (pg/dL)	n/a	>12.7	---	>17.3	---	≤7.4	>7.4 & ≤12.7	>12.7
Epinephrine (pg/mL)	n/a	>77.7	---	>120	---	≤47.4	>47.4 & ≤77.7	>77.7
Norepinephrine (pg/mL)	n/a	>686.3	---	>849	---	≤404.4	>404.4 & ≤686.3	>686.3
Inflammatory System								
il-6 (pg/mL)	n/a	>7.9	---	>17.8	---	≤1	>1 & ≤7.9	>7.9
hsCRP (mg/L)	AHA	>3	49.3	>9.6	---	<1	>1 & <3	>3

Notes:

†75^{th} percentile cutpoints used for biomarkers that don't have established clinical guidelines (Il-6, epinephrine, norepinephrine and cortisol); Established subclinical cutpoints used for rest

‡Cells left empty intentionally because cutpoints are based off distributions, rendering % above cutpoint information redundant.

§90^{th} percentile cutpoints used for biomarkers that don't have established clinical guidelines (Il-6, epinephrine, norepinephrine, cortisol, waist and hs-CRP); Established clinical (high risk) cutpoints used for rest.

£IQR percentile cutpoints used for biomarkers that don't have established clinical guidelines for assessing low, moderate, and high risk (Il-6, epinephrine, norepinephrine, cortisol and waist); Established clinical cutpoints used for the rest, where subclinical cutpoints=moderate risk and clinical cutpoints=high risk.

¥JNC7 used in AL_{75} and AL_{iqr}; JNC8 used in AL_{90}.

Abbreviations:

AL = Allostatic load

ATPIII = Adult Treatment Panel III

ADA = American Diabetes Association AHA = American Heart Association

JNC7 = Seventh Joint National Committee JNC8 = Eighth Joint National Committee

HDL = High-density lipoprotein. LDL = Low-density lipoprotein. BMI = Body mass index

Systolic BP = Systolic blood pressure. Diastolic BP = Diastolic blood pressure. Il-6 = Interlukin 6.

hsCRP = High-sensitivity C-reactive protein.

Table 2.

Study Sample Characteristics (n=207), San Francisco Bay Area

Variable	Mean (SD) or n (%)
COVARIATES (n=207)	
Age, mean (SD)	42 (6)
Educational Attainment *A*	
> High school diploma	138 (66.7)
≤ High school diploma	69 (33.3)
Poverty Status, n (%)	
> 100% Federal poverty level (FPL)	168 (81.2)
≤ 100% Federal poverty level (FPL)	39 (18.8)
Employment Status	
Employed	114 (55.1)
Not employed	93 (44.9)
Health Insurance	
Insured	152 (73.4)
Not insured	55 (26.6)
Marital/Domestic Partnership Status	
Married/domestic partnership	61 (29.5)
Not married	146 (70.5)
Smoking Status	
Non-smoker	118 (57)
Smoker %	89 (43)
Alcohol Use	
< 3 drinks per day	169 (81.6)
≥ 3 drinks per day	38 (18.4)
Exercise	
≥ 5 times per week	74 (35.8)
< 5 times per week	133 (64.3)
Currently Taking Cardiovascular (CV) Medication	
No	164 (79.2)
Yes	43 (20.8)
Currently Taking Diabetes Medication	
No	195 (94.2)
Yes	12 (5.8)
Neuroticism-fleiprSD	3.08 (0.8)
RACIAL DISCRIMINATION	
Experience of discrimination (EOD) Categories	
None (EOD score: 8)	22 (10.6)
Low (EOD score: 9–16)	71 (34.3)
Moderate (EOD score: 17–24)	63 (30.4)
High(EOD score: 25–32)	29 (14.0)

Variable	Mean (SD) or n (%)
Very High (EOD score: 33–40)	22 (10.6)
ALLOSTATIC LOAD MEASURES	
AL_{75}, mean (SD)	6.10 (2.2)
AL^{90}, mean (SD)	2.32 (1.6)
AL_{IQR}, mean (SD)	11.45 (3.8)
SYSTEM-SPECIFIC MEASURES	
Inflammatory System [a]	
Very low risk	33 (15.0)
Low risk	39 (18.8)
Moderate risk	77 (37.2)
High risk	60 (29.0)
Neuroendocrine System [b]	
Low risk	86 (41.6)
Moderate risk	93 (44.9)
High risk	28 (13.5)
Cardiometabolic System, mean (SD) [c]	6.79 (3.10)

Notes:

[a] Interlukin 6 (Il-6 and High-sensitivity C-reactive protein (hsCRP)

[b] Cortisol, epinephrine, and norepinephrine.

[c] Systolic blood pressure, diastolic blood pressure, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides, cholesterol, BMI, waist, glucose, and HbA1c.

Table 3:

Risk of Allostatic Load by Racial Discrimination and Educational Attainment (n=207), San Francisco Bay Area

Variable	b	AL_{75} †‡ 95% CI	*P*
Discrimination X > HS Diploma			
None	−0.18	−1.56, 1.19	0.79
Low	−1.09	−1.99, −0.18	0.02
Moderate (ref)	6.21	5.16, 7.27	<.001
High	−0.97	−2.08, 0.14	0.09
Very high	−1.88	−3.11, −0.65	<.001
Discrimination X ≤ HS Diploma			
None	1.44	−0.67, 3.54	0.18
Low	2.05	0.55, 3.56	0.01
Moderate (ref)	−0.41	−1.55, 0.73	0.50
High	2.16	−0.04, 4.36	0.05
Very high	2.24	−0.08, 4.57	0.06
Covariates∫			
≤ HS diploma∂	---	---	---
Age	0.07	0.02, 0.12	0.01
Not insured	−0.10	−0.78, 0.59	0.78
≤ 100% FPL	0.58	0.16, 1.32	0.12
Taking CV medication	0.99	0.25, 1.73	0.01
Taking diabetes medication	1.59	0.36, 2.81	0.01

Notes:

†‡One outlying observation removed, n = 206.

‡$F_{interaction}$ = 2.21 (p<0.0696), where p<.2 is statistically significant[52]

§$F_{interaction}$ = 0.78 (p<0.5382), where p<.2 is statistically significant[52]

£$F_{interaction}$ = 2.27 (p<0.0637), where p<.2 is statistically significant[52]

¥$F_{interaction}$ = 1.33 (p<0.2588), where p<.2 is statistically significant[52]

¶ Empty cells due to statistically non-significant interaction between discrimination and education level for the model. Main effect of education reported as a covariate.

∫ Referent groups: moderate discrimination, >HS diploma, and the dichotomized low-risk counterpart for all covariates.

∂ Empty cells because among the ≤ HS diploma group, educational attainment is reported as an interaction term.

Abbreviations:

CV medication = cardiovascular medication

HS diploma = high school diploma

FPL = federal poverty level

Table 4:

System-Specific Physiologic Dysregulation by Racial Discrimination and Educational Attainment (n=207), San Francisco Bay Area

Variable		Cardiometabolic †			Neuroendocrine§			Inflammatory£¥	
Discrimination Category	**b**	**95% CI**	***P***	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
Discrimination X > HS Diploma									
None	0.027921	1.88, 1.94	0.977	1.45	0.52, 4.06	0.48	---	---	---
Low	−1.190299	−2.43, 0.05	0.060	1.05	0.51, 2.19	0.89	0.89	0.34, 2.29	0.81
Moderate (ref)	6.261993	4.82, 7.71	0.000				0.75	0.28, 2.04	0.58
High	−1.382565	−2.86, 0.10	0.067	1.87	0.70, 4.96	0.21	0.37	0.12, 1.08	0.07
Very high	−2.636509	−4.32, −0.96	0.002	0.32	0.10, 1.05	0.06	0.71	0.22, 2.32	0.57
Discrimination X ≤ HS Diploma¶									
None	0.4411431	−1.23, 2.11	0.603	---	---	---	---	---	---
Low	1.419099	0.19, 2.64	0.024	---	---	---	---	---	---
Moderate (ref)	−0.5645661	−1.49, 0.36	0.228	---	---	---	---	---	---
High	1.973987	0.23, 3.72	0.027	---	---	---	---	---	---
Very high	2.158017	0.25, 4.06	0.027	---	---	---	---	---	---
Covariates∫									
≤ HS diploma∂	---	---	---	1.5	0.78, 2.88	0.22	1.11	0.55, 2.23	0.77
Age	0.1044384	0.03, 0.18	0.005	1.01	0.96, 1.06	0.78	3.01	1.54, 5.91	<.001
Not insured	0.3999438	−0.53, 1.33	0.398	0.94	0.49, 1.80	0.86	1	0.95, 1.05	0.94
≤ 100% FPL	0.3776245	−0.66, 1.42	0.475	1.46	0.69, 3.09	0.33	1.11	0.61, 2.02	0.73
Taking CV medication€	1.419316	0.38, 2.46	0.008	---	---	---	0.57	0.30, 1.10	0.09
Taking diabetes medication€	2.773564	1.04, 4.51	0.002	---	---	---	1.46	0.76, 2.79	0.25

Notes:

† $F_{interaction}$ = 2.46 (p<0.0469)

§ $F_{interaction}$ = 1.08 (p<0.3626)

£ $F_{intraction}$ = 0.67 (p<0.6128)

¥ Referent group: no discrimination.

¶ Empty cells due to statistically non-significant interaction between discrimination and education level for the model. Main effect of education reported as a covariate.

∫ Referent groups: >HS diploma, and the dichotomized low-risk counterpart for all covariates.

∂ Empty cells because among the ≤ HS diploma group, educational attainment is reported as an interaction term.

€ Empty cells because cardiovascular medication usage not relevant for neuroendocrine dysregulation.

€ Empty cells because diabetes medication usage not relevant for cardiovascular or neuroendocrine dysregulation.

Abbreviations:

OR = Odds Ratio reported for logistic regression

B = Beta reported for ordinary least squares regression

CV medication = cardiovascular medication

HS diploma = high school diploma

FPL = federal poverty level