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Perceived discrimination is associated with the inflammatory response to acute laboratory stress in women at risk for cardiovascular disease

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ABSTRACT

Cardiovascular disease (CVD) is the leading cause of death in the United States and exacts a disproportionate toll on minorities. Growing evidence demonstrates that perceived discrimination is a significant contributing factor to psychological distress, chronic low-grade inflammation, and cardiovascular health. However, little is known regarding the extent to which perceived discrimination contributes to the inflammatory response to acute stress. Therefore, the purpose of this study was to examine the influence of perceived discrimination on the inflammatory response to a laboratory acute stress paradigm in women at risk for CVD. A cross-sectional sample of 99 postmenopausal women (50 African American and 49 non-Hispanic White) (mean age 60.2 years) with at least two risk factors for CVD underwent the Trier Social Stress Test (TSST). Subjects completed the Detroit Area Study Discrimination Scale (DAS-DS) Everyday Discrimination subscale and provided blood and saliva samples prior to the TSST and every 15 min up to 90 min post-TSST to measure a pro-inflammatory cytokine, interleukin-6 (IL-6). Perceived discrimination was significantly associated with the salivary IL-6 response to the TSST ($b = 0.49$, SE = 0.13, $p = < 0.001$) controlling for age, race, marital status, household income, BMI, statin use, childhood maltreatment, depressive symptoms, and subjective social status. Women who reported higher levels of perceived discrimination had higher levels of salivary IL-6 at baseline and following the TSST as compared to women who reported lower levels of perceived discrimination. Results suggest that higher levels of perceived discrimination, regardless of race and socioeconomic status, may heighten levels of inflammation, prior to and following an acute stress exposure. The circulating Il-6 response was associated with BMI only and did not correlate with salivary IL-6. These data suggest that perceived discrimination may contribute to the salivary-IL-6 acute stress response. However, more research is needed to help clarify the complex relationships among stress and salivary proinflammatory cytokines.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of death in the United States (Heart, 2015) and exacts a disproportionate toll on minorities (Benjamin et al., 2017). For example, the CV death rate for African Americans (AA) is 37% higher than for Whites and the risk for having a first-time stroke is almost two times greater for AAs than for Whites (Benjamin et al., 2017). Cardiovascular health disparities emerge by middle age and exist across all socioeconomic levels. Traditional risk factors such as obesity, hypertension, and diabetes do not fully explain these disparities (Wong et al., 2002; Jolly et al., 2010; Kuzawa and Sweet, 2009). Growing evidence demonstrates that perceived discrimination is a significant contributing factor to psychological distress, chronic low-grade inflammation, and cardiovascular disease (Wagner and Abbott, 2007; Barber et al., 2016; Belgrave and Abrams, 2016; Kershaw et al., 2016; Mouton et al., 2017; Wagner et al., 2015; Mwendwa et al., 2011). A recent epidemiological study found that frequent perceived discrimination was associated with nearly twice the odds of having a chronic illness (Siddiqi et al., 2017).

Racism and discrimination are pervasive, insidious, and distressing realities of everyday life for many individuals (Utsey and Ponterotto, 1996) regardless of color (colorism), socioeconomic status, or residence

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(Williams and Jackson, 2005). Furthermore, AA women experience greater perceived discrimination than AA men (Jackson et al., 2017). Despite progress in reducing racism in the U.S., there is strong evidence for its persistence (Williams and Mohammed, 2013). A 2012 national U.S survey revealed that 67% of non-Hispanic Whites (NHW) and 90% of AAs agreed that AAs and Hispanics currently experience discrimination and 74% of AAs and 31% of Whites report that they had personally experienced racial discrimination (Schoen, 2012).

1.1. Discrimination

Discrimination refers to unfair treatment based upon personal characteristics such as age, race, sex, religion, or sexual orientation (Pascoe and Smart, 2009) and is considered to be a chronic stressor. Strong evidence demonstrates that perceived discrimination is associated with negative mental and physical health consequences (Pascoe and Smart, 2009), such as depression (Walker et al., 2017), sleep disturbance (Grandner et al., 2012), poor self-rated health (Cuevas et al., 2013), cardiovascular disease (Mwendwa et al., 2011; Goosby et al., 2015), and morality (Williams and Mohammed, 2009). African American women who reported race-related chronic stress had significantly greater carotid artery plaque than those who did not report racial discrimination (Troxel et al., 2003). In addition, a significant association has been demonstrated between perceived discrimination and hypertension, particularly among AAs (Dolezsar et al., 2014). It has been posited that perceived discrimination may be an important underlying factor explaining health disparities among AAs that cannot be accounted for by sociodemographic variables (Goosby et al., 2015; Race, 1999).

1.2. Discrimination, stress, and inflammation

Despite abundant evidence linking perceived discrimination to poor health, the mechanism whereby perceived discrimination results in negative health outcomes, such as CVD, is unknown. It is established, however, that acute and chronic stress exposure is associated with increased proinflammatory cytokines, such as interleukin-6 (IL-6) (Izawa et al., 2013; Gouin et al., 2012). This has been demonstrated in situations of naturalistic stress, including stress associated with providing informal care to chronically ill family members (Sherwood et al., 2016), job burnout (Gajewski et al., 2017), and low socioeconomic status (de Britto Rosa et al., 2011). As well, laboratory paradigms simulating acute stress also lead to elevations in proinflammatory cytokines, particularly IL-6 (Carpenter et al., 2010). For example, individuals subjected to social evaluative stress [(i.e., Trier Social Stress Test (TSST)] exhibit elevations in both circulating IL-6 (Carpenter et al., 2010; Derry et al., 2013) as well as salivary IL-6 (Izawa et al., 2013; Janusek et al., 2017) Sex differences in the inflammatory response to stress have also been demonstrated (Endrighi et al., 2016). Compared to men, postmenopausal women exhibit greater IL-6 reactivity in response to acute laboratory stress, which may intensify their risk for CVD as they age (Endrighi et al., 2016). Stress-induced inflammation may also result from perceived discrimination. Using a stress and coping framework, evidence supports the idea that discrimination-related stress appraisal triggers emotion dysregulation that leads to chronic inflammation, increasing risk for CVD (Doyle and Molix, 2014). Uncontrolled and sustained generation of proinflammatory cytokines, like IL-6, can promote pathophysiologic processes that drive the development of CVD. In particular, IL-6 promotes the development of CVD by regulating fibrinogen synthesis (Carty et al., 2010) and was found to predict acute stroke survival (Shenhar-Tsarfaty et al., 2010), as well as CVD (Patterson et al., 2010).

Although less is known regarding the influence of perceived discrimination, a chronic stressor, on inflammation, there is some evidence that perceived discrimination is associated with inflammatory biomarkers (Kershaw et al., 2016; Goosby et al., 2015; Lewis et al., 2010; Stepanikova et al., 2017). For example, an evaluation of men and women participating in the Survey of Midlife in the U.S study, revealed that lifetime perceived discrimination was related to higher levels of not only IL-6, but also fibrinogen and E-selectin independent of socioeconomic status and demographic variables (Stepanikova et al., 2017). In women, the perception of everyday discrimination has been linked with elevated circulating levels C-reactive protein (CRP) (Lewis et al., 2010). In a large population study[41] of racially diverse midlife women, investigators found that non-obese women who perceived higher levels of everyday discrimination exhibited higher CRP levels over the 7-year observation period. It is notable that these findings persisted after controlling for demographic, negative affect, biomedical, and behavioral confounds. An evaluation of a large multiethnic sample of men and women revealed associations among discrimination and inflammatory markers, using three measures of discrimination: everyday discrimination, lifetime discrimination due to any attribution, and lifetime discrimination attributed to race/ethnicity (Kershaw et al., 2016). For women, all three measures of discrimination were related to higher IL-6 (Kershaw et al., 2016), which is linked to a greater risk for CVD (Kumari et al., 2011; Volpato et al., 2001). In men, only everyday discrimination was associated with higher IL-6. Of note among women, following adjustment for body mass index (BMI), there was no significant association between IL and 6 and measure of discrimination suggesting that BMI accounted for the relationships between IL and 6 and discrimination. Discrimination and CRP were not associated in either men or women.

Although the association between perceived discrimination and inflammation is fairly well established, only a few studies have evaluated linkages among perceived discrimination and the inflammatory response to acute stress. In a study (Lucas et al., 2017) of AA men and women (N = 85), salivary CRP, salivary cortisol, dehydroepiandrosterone-sulfate, and salivary alpha-amylase were measured before and after the TSST, a laboratory social-evaluative acute stressor (Kirschbaum et al., 1993).

Findings demonstrated that in subjects who reported strong racial identity, higher levels of perceived discrimination predicted higher levels of inflammation following the TSST. In another study (Christian et al., 2013), comparing the effects of race and pregnancy on the inflammatory response following the TSST, AA women, both pregnant and non-pregnant, demonstrated a greater inflammatory response as measured by circulating IL-6 to the acute stressor as compared to NHW women. Although AA women reported higher levels of discrimination than NHW women did, the racial difference in inflammatory response did not change when controlling for discrimination. However, these studies did not consider subjective social status, depressive symptoms, or early life adversity in relationship to the inflammatory response. In addition, IL-6 response to the acute stressor was not evaluated in terms of perceived discrimination in either study. Evidence demonstrates chronic stressors over the lifespan, such as early life adversity (Carpenter et al., 2010; Janusek et al., 2017; Witek Janusek et al., 2013), depressive symptoms (Fan et al., 2017), and lower social subjective status (Derry et al., 2013) intensify the proinflammatory response to an acute laboratory stressor.

In summary, although evidence demonstrates that perceived discrimination is linked to inflammation and inflammatory disease, little is known regarding the extent to which perceived discrimination contributes to the inflammatory response to acute stress. Therefore, the purpose of this study was to examine the influence of perceived discrimination on the inflammatory response (IL-6) in blood and saliva to a laboratory acute stressor in women at risk for CVD.

2. Methods

2.1. Study design and participants

Participants included 99 postmenopausal women (50 AA and 49