Brain-Body Pathways Linking Racism and Health

Keely A. Muscatell[1], Gabriella M. Alvarez[1], Adrienne S. Bonar[1], Megan N. Cardenas[1], Manuel J. Galvan[1], Carrington C. Merritt[1], & Maurryce D. Starks[1]

[1]University of North Carolina at Chapel Hill

Article in press, *American Psychologist*

Author Note:

Keely A. Muscatell https://orcid.org/0000-0002-7893-5565

Gabriella M. Alvarez https://orcid.org/0000-0002-6710-3501

Adrienne S. Bonar https://orcid.org/0000-0002-4887-6867

Megan N. Cardenas https://orcid.org/0000-0001-9406-6606

Manuel J. Galvan https://orcid.org/0000-0003-1879-3275

Carrington C. Merritt https://orcid.org/0000-0003-1450-2178

Maurryce D. Starks https://orcid.org/0000-0002-1573-9997

The authors acknowledge members of the Carolina Social Neuroscience and Health Laboratory for their feedback on the ideas presented in this manuscript. This work was supported by the National Science Foundation via the Graduate Research Fellowship Program fellowships awarded to Gabriella M. Alvarez, Adrienne S. Bonar, and Maurryce D. Starks (DGE-1839302),

and a CAREER grant awarded to Keely A. Muscatell (BCS-2047344). Any opinions, findings, and conclusions or recommendations expressed in this material are those of the author(s) and do not necessarily reflect the views of the National Science Foundation. The work in this publication was also supported by the National Institutes of Health under award number R01HL157422 to Keely A. Muscatell. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. This work was also supported by a Ford Foundation Pre-Doctoral Fellowship (to Gabriella M. Alvarez), and the Robert Wood Johnson Foundation Health Policy Research Scholars Program (to Gabriella M. Alvarez and Manuel J. Galvan).

Correspondence should be addressed to: Keely A. Muscatell, Department of Psychology & Neuroscience, UNC Chapel Hill, 235 E. Cameron Ave. CB 3270, Chapel Hill, NC 27599-3270

Abstract

Racial disparities in health are a major public health problem in the United States, especially when comparing chronic disease morbidity and mortality for Black vs. White Americans. These health disparities are primarily due to insidious anti-Black racism that permeates American history, current culture and institutions, and interpersonal interactions. But how does racism get under the skull and the skin to influence brain and bodily processes that impact the health of Black Americans? In the present paper, we present a model describing the possible neural and inflammatory mechanisms linking racism and health. We hypothesize that racism influences neural activity and connectivity in the salience and default mode networks of the brain, and disrupts interactions between these networks and the executive control network. This pattern of neural functioning in turn leads to greater sympathetic nervous system signaling, hypothalamic-pituitary-adrenal axis activation, and increased expression of genes involved in inflammation, ultimately leading to higher levels of proinflammatory cytokines in the body and brain. Over time, these neural and physiological responses can lead to chronic physical and mental health conditions, disrupt well-being, and cause pre-mature mortality. Given that research in this area is underdeveloped to date, we emphasize opportunities for future research that are needed to build a comprehensive mechanistic understanding of the brain-body pathways linking anti-Black racism and health.

Keywords: racism; health disparities; stress; inflammation; brain function

Public Significance Statement: Health disparities due to racism are a major public health problem in the United States. Here, we present a model outlining the possible neural and

inflammatory pathways linking racism to health for Black Americans. Understanding how racism influences the brain and body is an important next step for research in this area.

Brain-Body Pathways Linking Racism and Health

"But all of our phrasing—race relations, racial chasm, racial justice, racial profiling, white privilege, even white supremacy—serves to obscure that racism is a visceral experience, that it dislodges brains, blocks airways, rips muscle, extracts organs, cracks bones, breaks teeth. You must never look away from this. You must always remember that the sociology, the history, the economics, the graphs, the charts, the regressions all land, with great violence, upon the body."

Ta-Nehisi Coates, *Between the World and Me*

There are long-standing and persistent racial health disparities in the United States. Disparities are particularly pronounced when comparing the health and well-being of Black Americans to that of White Americans. Specifically, Black Americans have significantly higher risk of asthma, diabetes, hypertension, kidney disease, obesity, and pancreatic disease compared to White Americans (Centers for Disease Control and Prevention, 2019). Black Americans also have a shorter life expectancy and more than twice the infant and maternal mortality rate relative to White Americans (Driscoll & Ely, 2020; Hoyert, 2019). These health inequities are a public health crisis that must be addressed to facilitate economic, social, and health justice for all.

The fundamental cause of Black/White racial disparities in health is racism. Despite a long history of racial biological essentialism, race is a social construct and not a coherent biological category (Phelan & Link, 2015; Smedley & Smedley, 2005). It follows that health disparities between Black and White people are not due to inherent biologic or genetic differences by race, but rather, differences in racist treatment encountered by Black individuals (Braveman & Parker Dominguez, 2021). Racism is encountered at nearly every level of society—from institutions to everyday social interactions—and its insidiousness leaves an impact on the brains and bodies of Black Americans. And, like other forms of chronic stress

(Dunkel Schetter et al., 2013), experiencing racism leads to poor health. Below, we briefly outline different subtypes of racism encountered by Black Americans and others from oppressed groups.

The most pervasive form of racism is structural or institutional racism. Structural racism is racism that permeates U.S. laws and institutional policies such that dominant social groups (e.g., White Americans) are advantaged and oppressed groups, including Black Americans, are disadvantaged (Jones, 2000; Williams et al., 2019). Structural racism is, in part, maintained by cultural racism, or the belief that the cultural products (e.g., music, language, preferences) of the dominant group are superior to the cultural products of oppressed groups (Cogburn, 2019; Williams et al., 2019). Such ideas of superiority and inferiority can become a form of internalized racism, where members of oppressed groups may begin to internalize and accept stereotypes about their own group (Sosoo et al., 2020; Speight, 2007; Williams & Mohammed, 2013). As a consequence of these societal conditions, the majority of Americans engage in interpersonal racism (Galvan et al., 2022), whether implicit and unintentional or explicit and intentional, toward members of oppressed racial groups (Dovidio et al., 2002; Jones, 2000). Interpersonal racism can also result in vicarious racism, where members of oppressed groups experience racism indirectly through witnessing the racism encountered by their racial in-group members (e.g., hearing stories, watching footage; Chae et al., 2021; Heard-Garris et al., 2018; Sosoo et al., 2022). Together, each of these subtypes of racism can influence the health of the constituents living within that society, particularly those from oppressed groups such as Black Americans (Nazroo et al., 2020).

Given that racial disparities in health exist and are largely due to these pervasive types of racism in our society, scholars have asked: What are the mechanisms, or pathways, through

which racism leads to poor health? The current paper focuses primarily on the neural and inflammatory processes that contribute to links between racism and health, given the importance of brain-body pathways in linking social processes to disease (McEwen & Gianaros, 2010). However, it is important to acknowledge that the mechanisms linking racism and health are multidetermined and multifaceted (see Table 1 for an overview of multiple mechanisms that play a role in linking racism and health). For example, systemic racism and anti-Black discriminatory behavior limit opportunities for economic mobility of Black Americans, and ultimately result in health disparities at the intersection of race and socioeconomic position, including in education and in the workplace (Braveman et al., 2022). Further, historical and current housing segregation (e.g., redlining) has resulted in disparities in exposure to environmental toxins like lead and cadmium (Masri et al., 2021), which increases risk for heavy metal poisoning and other negative health outcomes. Systemic racism also constrains Black individuals' opportunities for engaging in positive, health-protective behaviors, given a lack of access to recreational green spaces for exercise, inadequate access to affordable, nutritious food, and an absence of quiet conditions conducive for restful sleep (Billings et al., 2019; Li & Yuan, 2022; Nardone et al., 2021). Finally, Black individuals often encounter systemic and interpersonal racism during interactions with the healthcare system and healthcare providers, which prevents them from receiving preventative care and high-quality treatment (Hausmann et al., 2008; Powell et al., 2019). Thus, there are many mechanisms within the historical and current economic, social, and built environments that contribute to racial health inequities. A full mapping of these mechanisms needs interdisciplinary research that acknowledges the multiple levels, from institutions to individuals, through which racism can influence health.

Against the backdrop of this complexity, the present paper seeks to add a relatively new piece to the puzzle by considering the neural and immunological processes that may be affected by racism and lead to racial health inequities for Black Americans. Incorporating brain-body pathways into research on racism and health is important for (at least) three key reasons. First, the brain is the primary organ responsible for initially identifying, appraising, and regulating responses to stressors, including racism (McEwen, 2007). As such, a mechanistic model seeking to map the pathways between racism and health should consider how the brain responds to racism in the moment, as well as how brain functioning is affected by chronic exposure to racism. Second, mounting evidence suggests that inflammation is a key physiological mechanism that plays a role in linking racism and health, given burgeoning literatures showing that differences in inflammation account for at least some Black/White health disparities (Jenny et al., 2019; Kiely et al., 2022; Mukaz et al., 2020; Wang et al., 2015), and that inflammation mediates associations between stress (including discrimination) and health outcomes for Black individuals (McClendon et al., 2020; Simons et al., 2021). Third, as the quote by Ta-Nehisi Coates at the start of this paper so eloquently observes, racism "lands with great violence upon the body," as evidenced in part by the extensive health disparities suffered by Black individuals. We hope that ultimately, research systematically documenting that bodily violence through rigorous scientific evidence will motivate policy makers and the public to understand and work to address the racism that is the fundamental cause of racial health disparities in American society.

In light of the importance of understanding the neural and inflammatory mechanisms linking racism and health, the primary goal of the present paper is to present a model (see Figure 1) that we hope will drive future research in this area. Our model is grounded in rich traditions of

research that have examined the biopsychosocial mechanisms linking racism and health (Brondolo et al., 2009; Clark et al., 1999; Lewis et al., 2019; Neblett, 2019; Williams & Mohammed, 2013), and builds on this work to bring cutting-edge research from neuroimaging and psychoneuroimmunology to the table (for related models incorporating neurophysiological pathways, see also Berger & Sarnyai, 2015; Harrell et al., 2011; Lockwood et al., 2018). We focus on the role of large-scale brain networks in processing and responding to racism, and how activity and connectivity of those networks lead to physiological responses (particularly inflammation) that, over time, can lead to poor health. Our model is grounded in the current literature on the neural and inflammatory impacts of racism, though that literature is underdeveloped. We thus emphasize future research that is needed to test, refine, and improve on the model proposed here. Though we focus primarily on anti-Black racism in the present paper, we note that many other oppressed groups also suffer from discrimination-related health disparities and that more work is needed to establish if similar or different brain-body pathways contribute to health disparities for other groups (Hatzenbuehler, 2014; King et al., 2009; Ruiz et al., 2018; Yip et al., 2021).

Effects of Racism on Brain Function

To understand how racism might influence brain function, we must first consider some basic principles about how the brain is organized and shaped by its environment. One important consideration here is the relationship between brain structure and brain function. Brain structure, which is often studied through the use of magnetic resonance imaging (MRI) and diffusion tensor imaging, examines the size and shape (e.g., volume, thickness) of gray matter structures in the brain, and/or the size, density, and structure of white matter fibers (e.g., fractional anisotropy). A few recent studies have examined associations between racism and brain

structure, with some studies finding that greater exposure to racism is related to smaller volume of some gray matter regions (e.g., hippocampus; Hatzenbuehler et al., 2022) and disruptions to white matter microstructure (Fani et al., 2021). These studies provide important insight into associations between racism and the structural properties of the brain. However, it is important to note that there is not a one-to-one relationship between brain structure and brain function, at least as measured with MRI scans (Batista-García-Ramó & Fernández-Verdecia, 2018; Suárez et al., 2020). As such, we cannot infer that just because someone who has experienced more racism has a smaller hippocampus (a region important for episodic memory), that their hippocampus necessarily functions less efficiently and/or that they will perform worse on a memory test. Thus, it is important to also consider associations between racism and brain *function*, which is a more proximal predictor of physiological activation, as well as social, cognitive, and affective experience, than structural properties of the brain alone (Suárez et al., 2020).

One modern neuroscientific perspective suggests that a fundamental property of a well-functioning brain is the maintenance of allostasis (Katsumi et al., 2022; Sterling, 2012). Allostasis is the process by which the brain makes predictions about future energy demands to efficiently regulate energy in the body. The brain does this in part by preparing to satisfy energy needs before they are necessary. For example, as an individual prepares to start running, the brain preemptively begins to redistribute energy from organs that can spare oxygen (i.e., stomach) to striate muscles that need more resources to facilitate running (Barrett et al., 2016). But how does the brain know that it needs to prepare the body to run, even before the individual begins running? The brain is exceptional at utilizing information from prior experiences to make predictions about the best, most efficient way to engage with the environment in each moment. Thus, the brain is constantly monitoring the external environment for cues to use as predictions

for how to most effectively mobilize physiological processes to meet anticipated energy demands, while also considering the current physiological state of the body.

Given this view that the brain is a predictive organ that uses information from the external and internal environments to efficiently manage metabolic resources, we can consider how repeated exposure to many similar prior experiences might change the predictions made by the brain, which would shape the neurobiological and physiological processes that support those predictions. For example, chronic exposure to negative social contexts, including those characterized by high levels of racism (Payne & Hannay, 2021), may cause the brain and body to regulate energy in ways that are optimized for that specific context (McEwen & Gianaros, 2011). For the brains and bodies of Black individuals, prior experiences of racism might change how the brain manages resources in preparation for encountering potentially threatening or ambiguous social situations. For example, the brain may need to increase cognitive resources and attention to navigate ambiguous or stressful social interactions appropriately (e.g., facilitated by the executive control neural network), while also carefully considering both one's own thoughts, feelings, and behaviors and those of an interaction partner so as to navigate the interaction as smoothly as possible (e.g., facilitated by the default mode neural network), and simultaneously attending to internal physiological changes that might provide cues to if one should prepare to fight or flee a social interaction (e.g., facilitated by the salience and allostatic-interoceptive neural networks; Muscatell et al., 2021). Over time, this frequent preparation in response to racism may shift the brain to maintain increases in certain neural and physiological resources at "default" (Brosschot et al., 2018) to most efficiently prepare to engage in racist social interactions and to cope with their after-effects (Meyer, 2019).

What brain regions or networks are most likely to shift their functioning in response to experiences of racism? In line with other models of the impact of racism on brain functioning (Berger & Sarnyai, 2015), we propose that three intrinsic brain networks, the salience network, the default mode network, and the executive control network, are involved in processing, responding to, and coping with racism, and that chronic exposure to racism likely alters the functioning of these networks. The salience network, composed primarily of anterior cingulate cortex (ACC) and bilateral anterior insula, is thought to guide affective feelings, perceptions, and behavior based on internal shifts in physiological activation or when salient stimuli are detected in the environment (Barrett & Satpute, 2013; Lindquist & Barrett, 2012). The default mode network, comprised of the medial prefrontal cortex (mPFC), medial temporal lobe (i.e., hippocampus, entorhinal cortex), posterior cingulate cortex/precuneus, and bilateral superior temporal sulcus, is primarily responsible for generating representations of the self, others, and past and future experiences (Raichle, 2015). The interactions between the salience and default mode networks, together with subcortical regions such as the amygdala and striatum, have been theorized to make up a broader network called the allostatic interoceptive network (AIN), which may be involved in maintaining allostasis (Kleckner et al., 2017). The executive control network, comprising the bilateral dorsolateral prefrontal cortex (dlPFC), inferior parietal lobe, inferior parietal sulcus, precuneus, and middle cingulate cortex, is thought to be responsible for monitoring the activity of other functional networks as well as supporting working memory and cognitive control (Niendam et al., 2012).

To date, very little research has examined how the brain responds to and is shaped by experiences of racism. This is a major gap in our knowledge that neuroscientists must strive to fill moving forward. The little work that has been done in this area provides preliminary support

for our hypothesis that the salience, default mode, and executive control networks are involved with processing and are affected by racism. For example, one study showed that Black young adults who demonstrated higher levels of distress after being socially excluded by White individuals exhibited greater activity in regions of the salience network (i.e., dorsal ACC, anterior insula), and less activity in executive-control network regions (i.e., dlPFC), compared to those who experienced less distress (Masten et al., 2011). Further, experiencing more racial discrimination has been associated with greater amygdala activity at rest (Clark et al., 2018), as well as greater amygdala activity in response to pictures of White individuals displaying neutral facial expressions (Greer et al., 2012). Given the amygdala's role as a key node of the salience network, these data suggest that experiences of racism may shape the extent to which the salience network is active by default, and in response to potentially threatening or distressing social cues. This is consistent with the generalized unsafety theory of stress (Brosschot et al., 2017, 2018), which argues that, for people from disadvantaged backgrounds, the brain and body operate in a constant state of "unsafety" characterized by vigilance and chronic activation of neural and physiological stress systems. These findings are also consistent with research on other types of social stress (e.g., social rejection, social evaluation), which find greater activity in regions of the salience network (e.g., ACC, insula) in response to socially stressful experiences (for a review, see Berretz et al., 2021; Muscatell et al., 2021).

While very little work has examined associations between racism and neural functioning, an intriguing set of new studies is converging to suggest that racism may also shape functional connections between networks of the brain. This is important, as recent neuroscientific evidence shows that the brain is organized into several intrinsic networks and that emotions, cognitions, behavior and other mental phenomena arise from the functional connections between these

networks, rather than activation of singular regions (Cohen & D'Esposito, 2016; Park & Friston, 2013). As such, examining how racism influences not just brain activity but also connections between brain networks is an important undertaking. Initial research in this area has shown that greater exposure to racism is associated with the functional connectivity between the amygdala and other regions of the salience network, including the anterior insula, dorsal ACC, caudate, putamen, and thalamus, as well as connectivity between the amygdala and regions of the default mode network, including mPFC (Clark et al., 2018; Webb et al., 2022). Similarly, discrimination has been associated with enhanced connectivity between the insula, another key hub of the salience and allostatic-interoceptive networks, and posterior regions of the default mode network, including the precuneus (Webb et al., 2022) and intracalcarine cortex (Han et al., 2021). Finally, while not about racism per say, some prior work on the neural predictors of physiological responses to social evaluative stress shows that greater functional connectivity between the amygdala and the DMPFC, regions of the salience and default mode networks, respectively, is associated with enhanced inflammatory reactivity to social evaluation (Muscatell et al., 2015). Together, these results suggest that exposure to racial discrimination may be related to increased functional connectivity among regions that comprise the salience network, as well as greater coupling of regions of the salience and default mode networks. This shift in brain functioning in the face of racism may help an individual to act adaptively in a socially threatening context.

Finally, we hypothesize that racism also shifts activity in the executive control network, and functional connectivity between the executive control network and the salience and default mode networks. This hypothesis is mostly speculative, as very little neuroimaging research has examined associations between racism and brain activity and connectivity in response to tasks

that require executive control (e.g., working memory, response inhibition, task-switching). Future research should investigate this, as a well-functioning executive control network is important for a variety of health-relevant processes, including emotion regulation, behavior maintenance and/or behavior change, and self-regulation (Lowe et al., 2019; Morawetz et al., 2020). To date, the one known study that investigated associations between racial discrimination and brain functioning during an attentional control task found that greater racial discrimination was associated with more activity in regions within the default mode network (e.g., vmPFC, superior temporal sulcus) and the executive control network (e.g., dlPFC, occipital cortex) when engaging with threatening stimuli in an attentional control task (Fani et al., 2021). Given the dearth of research in this area and yet the importance of activity in and connectivity between the executive control network and other brain networks (Alvarez et al., 2022), future research that documents the associations between racism and functioning of this network is needed.

In sum, we propose (see Figure 1) that the salience and default mode networks, together with the executive control network, are integral to processing, responding to, and coping with the after-effects of racism, and that chronic exposure to racism likely alters the functioning of these networks. To date, these hypotheses are speculative, in part because there is an extremely limited neuroimaging literature that has investigated links between racism and neural functioning. However, given the importance of these networks for responding to other types of social stressors that share features with racism (e.g., socioeconomic deprivation, negative social evaluation, social rejection; Muscatell et al., 2021), it is plausible that similar networks would undergird responses to racism. We also note that all of the limited neuroimaging research on the neural consequences of racism that has been conducted to date has focused on interpersonal racism despite the important role that structural, cultural, internalized, and vicarious racism also

play in health. As such, future research should also examine how exposure to these other types of racism influence brain function. For example, although speculative, we hypothesize that vicarious racism (i.e., second-hand viewing of racist encounters, such as videos of violent interactions with law enforcement) could lead to alterations in executive control network function at rest and/or during challenging cognitive tasks following exposure. We are currently testing this hypothesis in a study in our laboratory. As another example, it is possible that internalized racism could be associated with diminished activity in reward-related brain networks during the viewing of cultural products from the minoritized group (Maxwell et al., 2015). These examples illustrate how different types of racism may influence brain function in networks beyond those focused on in the present model. We note these ideas are purely speculative given the dearth of research in this area, but we hope they spawn future research that investigates how different types of racism may be processed by and influence the functioning of the brain.

Effects of Racism on Physiology

How might the associations between racism and neural activity and connectivity hypothesized here ultimately lead to poor health for Black Americans? The salience, default mode, and executive control networks play a role in initiating and regulating physiological processes that can, if activated repeatedly over time in the face of stress, lead to physiological dysregulation and set the stage for chronic disease (McEwen, 2012; see Figure 1). For example, subcortical regions thought to be involved in the allostatic-interoceptive network (e.g., amygdala, periaqueductal gray, nucleus of the solitary tract) project to brainstem regions (e.g., hypothalamus) that are responsible for mobilizing the sympathetic nervous system (SNS) and the hypothalamic-pituitary-adrenal (HPA) axis, two physiological systems that are consistently activated in the face of stress (Muscatell & Eisenberger, 2012). Specifically, activation of the

SNS leads to the release of the catecholamines epinephrine and norepinephrine, which can bind to beta-adrenergic receptors throughout the body, including on the surface of immune cells (i.e., leukocytes), leading to increased expression of genes involved in inflammation (Irwin & Cole, 2011; MacCormack et al., 2021). Further, activation of the HPA axis ultimately leads to the production of glucocorticoids such as cortisol, a metabolic hormone that can also regulate the expression of genes in immune cells (Miller et al., 2008). While in the short-term cortisol has anti-inflammatory properties, chronic stress has been linked with glucocorticoid resistance, or the tendency for immune cells to no longer be sensitive to the anti-inflammatory effects of cortisol (Miller et al., 2014). Over time, chronic activation of the SNS and HPA can lead to heightened levels of circulating pro-inflammatory cytokines in the body, and elevated levels of inflammation are associated with the development of many chronic physical diseases and psychopathology (Bennett et al., 2018).

Given the major role that that SNS and HPA axis play in responding to stress, much prior work has investigated the acute effects of racism on activity of these physiological systems. Indeed, laboratory studies have demonstrated pronounced cortisol reactivity in response to experimental manipulations of racism, including in response to anticipating interactions with a prejudiced cross-race/ethnicity partner (Sawyer et al., 2012), viewing or overhearing racially discriminatory content (Huynh et al., 2017; Weinstein et al., 2013), and experiencing social rejection by a presumed prejudiced evaluator (Townsend et al., 2014). Prior work has also demonstrated that racism-related stress may evoke a pernicious cardiovascular reactivity pattern characterized by elevated SNS activity and diminished parasympathetic nervous system activity (Sawyer et al., 2012). Laboratory studies in this domain have shown changes in autonomic nervous system activity as a function of reported or manipulated experiences of discrimination

among racial/ethnic minorities, including higher blood pressure (Sawyer et al., 2012), diminished heart rate variability recovery following experiences of racism-related stress (Hoggard et al., 2015; Wagner et al., 2015), and elevated heart rate (Mendes et al., 2008; Sawyer et al., 2012). Thus, a robust literature shows that experiencing racism is associated with increases in SNS and HPA axis activity, which, if prolonged or repeated, could ultimately lead to multisystem physiological dysregulation (i.e., "allostatic load") and chronic disease (McEwen & Seeman, 1999; Ong et al., 2017).

Ultimately, SNS and HPA axis activation likely largely influence health through their effects on inflammatory processes (Miller et al., 2009). However, to date no known research has examined if an acute experience of racism leads to increases in inflammation; current on-going work in our laboratory is investigating this question. Despite this lack of experimental evidence for links between racism and inflammation, cross-sectional studies have shown that greater perceived discrimination is associated with higher levels of markers of systemic inflammation (Cuevas et al., 2020). A few studies have also demonstrated a longitudinal association between racism and inflammation. For example, greater perceived discrimination has been associated with higher levels of C-reactive protein (CRP), a marker of inflammation (Lewis et al., 2010), and a composite score indexed by multiple inflammatory biomarkers (Ong et al., 2017). Furthermore, Boen (2020) found that Black-White disparities in CRP were mediated by participants' reported levels of everyday and major lifetime discrimination, as well as by participants' cumulative stress burden (Boen, 2020). Together, this work suggests that racism may lead to increases in inflammation, though future experimental research in this area is needed to establish causality.

To summarize, we hypothesize based on prior literature that experiencing racism leads to activation of the SNS and the HPA axis, both of which can lead to expression of pro-inflammatory genes and the production of pro-inflammatory cytokines. These racism-induced increases in inflammation can lead to the development of chronic disease and psychopathology (Slavich, 2020), and may also feed back to the brain to cause greater reactivity to social threats and diminished responses to rewards (Eisenberger et al., 2017). There are major opportunities for future work in this area, including integrating neuroimaging and physiological measures (Eisenbarth et al., 2016; Muscatell et al., 2015) to examine the neural predictors of SNS, HPA, and inflammatory responses to racism, as well as work that moves beyond individual experiences of racism toward documenting the impacts of structural, vicarious, and area-level racism on physiological functioning.

Concluding Comments

While most of the present paper focuses on the deleterious effects of racism on neural and inflammatory processes, it is also important to recognize the strengths in Black Americans, including various resilience and protective factors that may break the link between racism and health. Some factors that have been shown to buffer the effects of racism on various health outcomes include: racial socialization, racial identity, spirituality, and sociopolitical activism (Hayward & Krause, 2015; Ingram, 2019; Jones & Neblett, 2016; Neblett et al., 2008, 2013). A few studies have even explored protective factors that may influence physiological responses to racism. For example, individuals who felt more positively about being Black (i.e., the private regard dimension of racial identity) demonstrated reduced autonomic reactivity in response to listening to scenarios describing blatantly racist social interactions (Neblett & Roberts, 2013). Brody and colleagues (2015) found that the association between higher racial discrimination and

elevated levels of inflammation was not significant among adolescents reporting more positive racial identities (i.e., higher racial centrality). Further, the use of spiritual coping in response to recalling racist experiences was associated with decreased diastolic blood pressure reactivity (Cooper et al. 2014). This smattering of findings suggests there are a variety of factors that enable Black Americans to be resilient against the physiological toll of racism. To our knowledge, no known work has examined protective factors that modulate neural responses to racism. More research is needed to document the strengths in Black individuals, families, and communities that may mitigate the neural and inflammatory impacts of racism. However, Black individuals should not be left to defend themselves from racism with individual resiliency alone; it is necessary to address racism at a societal level in order to mitigate long-standing racial inequities in health.

In the present paper, we have outlined a model for understanding the neural and inflammatory mechanisms through which racism may impact health for Black Americans. We hope that having a shared conceptual model to use as a potential roadmap for exploring the relationships between racism and neural and physiological processes will be used to advance rigorous research on the psychoneuroimmunological mechanisms contributing to racial health disparities. Moreover, it is our hope that the advancement of research in this area will not only spur other scholars, but also policy makers and lay people alike, to understand and act against the pervasive racism in our society that perpetually harms Black Americans.

References

Alvarez, G. M., Rudolph, M. D., Cohen, J. R., & Muscatell, K. A. (2022). Lower socioeconomic position is associated with greater activity in and integration within an allostatic-interoceptive brain network in response to affective stimuli. *Journal of Cognitive Neuroscience*, *34(10),* 1906-1927. https://doi.org/10.1162/jocn_a_01830

Auspurg, K., Schneck, A., & Hinz, T. (2018). Closed doors everywhere? A meta-analysis of field experiments on ethnic discrimination in rental housing markets. *Journal of Ethnic and Migration Studies*, *45*(1), 1–20. https://doi.org/10.1080/1369183X.2018.1489223

Barrett, L. F., Quigley, K. S., & Hamilton, P. (2016). An active inference theory of allostasis and interoception in depression. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *371*(1708). https://doi.org/10.1098/rstb.2016.0011

Barrett, L. F., & Satpute, A. B. (2013). Large-scale brain networks in affective and social neuroscience: towards an integrative functional architecture of the brain. *Current Opinion in Neurobiology*, *23*(3), 361–372. https://doi.org/10.1016/j.conb.2012.12.012

Batista-García-Ramó, K., & Fernández-Verdecia, C. I. (2018). What we know about the brain structure-function relationship. *Behavioral Sciences*, *8*(4). https://doi.org/10.3390/bs8040039

Bennett, G. G., Merritt, M. M., Sollers III, J. J., Edwards, C. L., Whitfield, K. E., Brandon, D. T., & Tucker, R. D. (2004). Stress, coping, and health outcomes among African-Americans: a review of the John Henryism hypothesis. *Psychology & Health*, *19*(3), 369–383. https://doi.org/10.1080/0887044042000193505

Bennett, J. M., Reeves, G., Billman, G. E., & Sturmberg, J. P. (2018). Inflammation-nature's way to efficiently respond to all types of challenges: implications for understanding and

managing “the epidemic” of chronic diseases. *Frontiers in Medicine*, *5*, 316. https://doi.org/10.3389/fmed.2018.00316

Berger, M., & Sarnyai, Z. (2015). “More than skin deep”: stress neurobiology and mental health consequences of racial discrimination. *Stress*, *18*(1), 1–10. https://doi.org/10.3109/10253890.2014.989204

Berretz, G., Packheiser, J., Kumsta, R., Wolf, O. T., & Ocklenburg, S. (2021). The brain under stress-A systematic review and activation likelihood estimation meta-analysis of changes in BOLD signal associated with acute stress exposure. *Neuroscience and Biobehavioral Reviews*, *124*, 89–99. https://doi.org/10.1016/j.neubiorev.2021.01.001

Billings, M. E., Gold, D., Szpiro, A., Aaron, C. P., Jorgensen, N., Gassett, A., Leary, P. J., Kaufman, J. D., & Redline, S. R. (2019). The association of ambient air pollution with aleep apnea: The multi-ethnic study of atherosclerosis. *Annals of the American Thoracic Society*, *16*(3), 363–370. https://doi.org/10.1513/AnnalsATS.201804-248OC

Boen, C. (2020). Death by a thousand cuts: stress exposure and black-white disparities in physiological functioning in late life. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences*, *75*(9), 1937–1950. https://doi.org/10.1093/geronb/gbz068

Bowen, S., Elliott, S., & Hardison-Moody, A. (2021). The structural roots of food insecurity: How racism is a fundamental cause of food insecurity. *Sociology Compass*, *15*(7). https://doi.org/10.1111/soc4.12846

Brandt, E. B., Beck, A. F., & Mersha, T. B. (2020). Air pollution, racial disparities, and COVID-19 mortality. *The Journal of Allergy and Clinical Immunology*, *146*(1), 61–63. https://doi.org/10.1016/j.jaci.2020.04.035

Braveman, P. A., Arkin, E., Proctor, D., Kauh, T., & Holm, N. (2022). Systemic and structural racism: definitions, examples, health damages, and approaches to dismantling. *Health Affairs*, *41*(2), 171-178. https://doi.org/10.1377/hlthaff.2021.01394

Braveman, P., & Parker Dominguez, T. (2021). Abandon "race." focus on racism. *Frontiers in Public Health*, *9*, 689462. https://doi.org/10.3389/fpubh.2021.689462

Brondolo, E., Gallo, L. C., & Myers, H. F. (2009). Race, racism and health: disparities, mechanisms, and interventions. *Journal of Behavioral Medicine*, *32*(1), 1–8. https://doi.org/10.1007/s10865-008-9190-3

Brosschot, J. F., Verkuil, B., & Thayer, J. F. (2017). Exposed to events that never happen: Generalized unsafety, the default stress response, and prolonged autonomic activity. *Neuroscience and Biobehavioral Reviews*, *74*(Pt B), 287–296. https://doi.org/10.1016/j.neubiorev.2016.07.019

Brosschot, J. F., Verkuil, B., & Thayer, J. F. (2018). Generalized unsafety theory of stress: unsafe environments and conditions, and the default stress response. *International Journal of Environmental Research and Public Health*, *15*(3). https://doi.org/10.3390/ijerph15030464

Chae, D. H., Yip, T., Martz, C. D., Chung, K., Richeson, J. A., Hajat, A., Curtis, D. S., Rogers, L. O., & LaVeist, T. A. (2021). Vicarious racism and vigilance during the Covid-19 pandemic: mental health implications among Asian and Black Americans. *Public Health Reports*, *136*(4), 508–517. https://doi.org/10.1177/00333549211018675

Clark, R., Anderson, N. B., Clark, V. R., & Williams, D. R. (1999). Racism as a stressor for African Americans. A biopsychosocial model. *The American Psychologist*, *54*(10), 805–816. https://doi.org/10.1037/0003-066X.54.10.805

Clark, U. S., Miller, E. R., & Hegde, R. R. (2018). Experiences of discrimination are associated with greater resting amygdala activity and functional connectivity. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *3*(4), 367–378. https://doi.org/10.1016/j.bpsc.2017.11.011

Cogburn, C. D. (2019). Culture, race, and health: implications for racial inequities and population health. *The Milbank Quarterly*, *97*(3), 736–761. https://doi.org/10.1111/1468-0009.12411

Cohen, J. R., & D'Esposito, M. (2016). The segregation and integration of distinct brain networks and their relationship to cognition. *The Journal of Neuroscience*, *36*(48), 12083–12094. https://doi.org/10.1523/JNEUROSCI.2965-15.2016

Cuevas, A. G., Ong, A. D., Carvalho, K., Ho, T., Chan, S. W. C., Allen, J. D., Chen, R., Rodgers, J., Biba, U., & Williams, D. R. (2020). Discrimination and systemic inflammation: A critical review and synthesis. *Brain, Behavior, and Immunity*, *89*, 465–479. https://doi.org/10.1016/j.bbi.2020.07.017

Dondanville, A. A., Bordewyk, A., & Pössel, P. (2022). Role of rumination in the association between discrimination and adolescents' mental and physical health. *Journal of Child and Family Studies*, 1-12. https://doi.org/10.1007/s10826-022-02401-2

Dovidio, J F, Eggly, S., Albrecht, T. L., & Hagiwara, N. & Penner, L.A. (2016). Racial biases in medicine and healthcare disparities. *TPM: Testing, Psychometrics, Methodology in Applied Psychology, 23(4).*

Dovidio, John F, Kawakami, K., & Gaertner, S. L. (2002). Implicit and explicit prejudice and interracial interaction. *Journal of Personality and Social Psychology*, *82*(1), 62–68. https://doi.org/10.1037//0022-3514.82.1.62

Eisenbarth, H., Chang, L. J., & Wager, T. D. (2016). Multivariate brain prediction of heart rate and skin conductance responses to social threat. *The Journal of Neuroscience*, *36*(47), 11987–11998. https://doi.org/10.1523/JNEUROSCI.3672-15.2016

Eisenberger, N. I., Moieni, M., Inagaki, T. K., Muscatell, K. A., & Irwin, M. R. (2017). In sickness and in health: the co-regulation of inflammation and social behavior. *Neuropsychopharmacology*, *42*(1), 242–253. https://doi.org/10.1038/npp.2016.141

Fani, N., Carter, S. E., Harnett, N. G., Ressler, K. J., & Bradley, B. (2021). Association of racial discrimination with neural response to threat in black women in the US exposed to trauma. *JAMA Psychiatry*, *78*(9), 1005–1012. https://doi.org/10.1001/jamapsychiatry.2021.1480

Fani, N., Harnett, N. G., Bradley, B., Mekawi, Y., Powers, A., Stevens, J. S., Ressler, K. J., & Carter, S. E. (2021). Racial discrimination and white matter microstructure in trauma-exposed black women. *Biological Psychiatry, 91(3),* 254-261. https://doi.org/10.1016/j.biopsych.2021.08.011

Fiscella, K., & Williams, D. R. (2004). Health disparities based on socioeconomic inequities: implications for urban health care. *Academic Medicine*, *79*(12), 1139–1147. https://doi.org/10.1097/00001888-200412000-00004

Fuller-Rowell, T. E., Curtis, D. S., El-Sheikh, M., Chae, D. H., Boylan, J. M., & Ryff, C. D. (2016). Racial disparities in sleep: the role of neighborhood disadvantage. *Sleep Medicine*, *27–28*, 1–8. https://doi.org/10.1016/j.sleep.2016.10.008

Glymour, M. M., & Manly, J. J. (2008). Lifecourse social conditions and racial and ethnic patterns of cognitive aging. *Neuropsychology Review*, *18*(3), 223–254. https://doi.org/10.1007/s11065-008-9064-z

Greer, T. M., Vendemia, J. M. C., & Stancil, M. (2012). Neural correlates of race-related social evaluations for African Americans and white Americans. *Neuropsychology*, *26*(6), 704–712. https://doi.org/10.1037/a0030035

Han, S. D., Lamar, M., Fleischman, D., Kim, N., Bennett, D. A., Lewis, T. T., Arfanakis, K., & Barnes, L. L. (2021). Self-reported experiences of discrimination in older black adults are associated with insula functional connectivity. *Brain Imaging and Behavior*, *15*(4), 1718–1727. https://doi.org/10.1007/s11682-020-00365-9

Harrell, C. J. P., Burford, T. I., Cage, B. N., Nelson, T. M., Shearon, S., Thompson, A., & Green, S. (2011). Multiple pathways linking racism to health outcomes. *Du Bois Review : Social Science Research on Race*, *8*(1), 143–157. https://doi.org/10.1017/S1742058X11000178

Hatzenbuehler, M L. (2014). Structural stigma and the health of lesbian, gay, and bisexual populations. *Current Directions in Psychological Science*, *23*(2), 127–132. https://doi.org/10.1177/0963721414523775

Hatzenbuehler, Mark L, Weissman, D. G., McKetta, S., Lattanner, M. R., Ford, J. V., Barch, D. M., & McLaughlin, K. A. (2022). Smaller hippocampal volume among black and latinx youth living in high-stigma contexts. *Journal of the American Academy of Child and Adolescent Psychiatry*, *61*(6), 809–819. https://doi.org/10.1016/j.jaac.2021.08.017

Hausmann, L. R. M., Jeong, K., Bost, J. E., & Ibrahim, S. A. (2008). Perceived discrimination in health care and health status in a racially diverse sample. *Medical Care*, *46*(9), 905–914. https://doi.org/10.1097/MLR.0b013e3181792562

Hawes, A. M., Smith, G. S., McGinty, E., Bell, C., Bower, K., LaVeist, T. A., Gaskin, D. J., & Thorpe, R. J. (2019). Disentangling race, poverty, and place in disparities in physical activity. *International Journal of Environmental Research and Public Health*, *16*(7).

https://doi.org/10.3390/ijerph16071193

Hayward, R. D., & Krause, N. (2015). Religion and strategies for coping with racial discrimination among African Americans and Caribbean Blacks. *International Journal of Stress Management*, *22*(1), 70–91. https://doi.org/10.1037/a0038637

Heard-Garris, N. J., Cale, M., Camaj, L., Hamati, M. C., & Dominguez, T. P. (2018). Transmitting trauma: A systematic review of vicarious racism and child health. *Social Science & Medicine*, *199*, 230–240. https://doi.org/10.1016/j.socscimed.2017.04.018

Hoggard, L. S., Hill, L. K., Gray, D. L., & Sellers, R. M. (2015). Capturing the cardiac effects of racial discrimination: Do the effects "keep going"? *International Journal of Psychophysiology*, *97*(2), 163–170. https://doi.org/10.1016/j.ijpsycho.2015.04.015

Huynh, V. W., Huynh, Q.-L., & Stein, M.-P. (2017). Not just sticks and stones: Indirect ethnic discrimination leads to greater physiological reactivity. *Cultural Diversity & Ethnic Minority Psychology*, *23*(3), 425–434. https://doi.org/10.1037/cdp0000138

Ingram, L. (2019). Stress from racism, coping responses, and recommendations for colleges. *The Journal of Health Disparities Research and Practice*, *12*(1), 80–112.

Irwin, M. R., & Cole, S. W. (2011). Reciprocal regulation of the neural and innate immune systems. *Nature Reviews. Immunology*, *11*(9), 625–632. https://doi.org/10.1038/nri3042

Jenny, N. S., Callas, P. W., Judd, S. E., McClure, L. A., Kissela, B., Zakai, N. A., & Cushman, M. (2019). Inflammatory cytokines and ischemic stroke risk: The REGARDS cohort. *Neurology*, *92*(20), e2375–e2384. https://doi.org/10.1212/WNL.0000000000007416

Jones, C. P. (2000). Levels of racism: a theoretic framework and a gardener's tale. *American Journal of Public Health*, *90*(8), 1212–1215. https://doi.org/10.2105/ajph.90.8.1212

Jones, S. C. T., & Neblett, E. W. (2016). Racial-ethnic protective factors and mechanisms in

psychosocial prevention and intervention programs for black youth. *Clinical Child and Family Psychology Review*, *19*(2), 134–161. https://doi.org/10.1007/s10567-016-0201-6

Katsumi, Y., Theriault, J. E., Quigley, K. S., & Barrett, L. F. (2022). Allostasis as a core feature of hierarchical gradients in the human brain. *Network Neuroscience*, 1–22. https://doi.org/10.1162/netn_a_00240

Kiely, M., Lord, B., & Ambs, S. (2022). Immune response and inflammation in cancer health disparities. *Trends in Cancer*, *8*(4), 316–327. https://doi.org/10.1016/j.trecan.2021.11.010

Kimmel, P. L., Fwu, C.-W., Abbott, K. C., Ratner, J., & Eggers, P. W. (2016). Racial disparities in poverty account for mortality differences in us medicare beneficiaries. *SSM - Population Health*, *2*, 123–129. https://doi.org/10.1016/j.ssmph.2016.02.003

King, M., Smith, A., & Gracey, M. (2009). Indigenous health part 2: the underlying causes of the health gap. *The Lancet*, *374*(9683), 76–85. https://doi.org/10.1016/S0140-6736(09)60827-8

Kleckner, I. R., Zhang, J., Touroutoglou, A., Chanes, L., Xia, C., Simmons, W. K., Quigley, K. S., Dickerson, B. C., & Barrett, L. F. (2017). Evidence for a large-scale brain system supporting allostasis and interoception in humans. *Nature Human Behaviour*, *1*. https://doi.org/10.1038/s41562-017-0069

Kutateladze, B. L., & Andiloro, N. R. (2014). Prosecution and racial justice in New York County—Technical report. *New York: Vera Institute of Justice*.

Lewis, T. T., Aiello, A. E., Leurgans, S., Kelly, J., & Barnes, L. L. (2010). Self-reported experiences of everyday discrimination are associated with elevated C-reactive protein levels in older African-American adults. *Brain, Behavior, and Immunity*, *24*(3), 438–443. https://doi.org/10.1016/j.bbi.2009.11.011

Lewis, T. T., Lampert, R., Charles, D., & Katz, S. (2019). Expectations of racism and carotid intima-media thickness in African American women. *Psychosomatic Medicine*, *81*(8), 759–768. https://doi.org/10.1097/PSY.0000000000000684

Li, M., & Yuan, F. (2022). Historical redlining and food environments: A study of 102 urban areas in the United States. *Health & Place*, *75*, 102775. https://doi.org/10.1016/j.healthplace.2022.102775

Lindquist, K. A., & Barrett, L. F. (2012). A functional architecture of the human brain: emerging insights from the science of emotion. *Trends in Cognitive Sciences*, *16*(11), 533–540. https://doi.org/10.1016/j.tics.2012.09.005

Lockwood, K. G., Marsland, A. L., Matthews, K. A., & Gianaros, P. J. (2018). Perceived discrimination and cardiovascular health disparities: a multisystem review and health neuroscience perspective. *Annals of the New York Academy of Sciences*, *1428*(1), 170–207. https://doi.org/10.1111/nyas.13939

Lowe, C. J., Reichelt, A. C., & Hall, P. A. (2019). The prefrontal cortex and obesity: A health neuroscience perspective. *Trends in Cognitive Sciences*, *23*(4), 349–361. https://doi.org/10.1016/j.tics.2019.01.005

MacCormack, J. K., Gaudier-Diaz, M. M., Armstrong-Carter, E. L., Arevalo, J. M. G., Meltzer-Brody, S., Sloan, E. K., Cole, S. W., & Muscatell, K. A. (2021). Beta-adrenergic blockade blunts inflammatory and antiviral/antibody gene expression responses to acute psychosocial stress. *Neuropsychopharmacology*, *46*(4), 756–762. https://doi.org/10.1038/s41386-020-00897-0

Masri, S., LeBrón, A. M. W., Logue, M. D., Valencia, E., Ruiz, A., Reyes, A., & Wu, J. (2021). Risk assessment of soil heavy metal contamination at the census tract level in the city of

Santa Ana, CA: implications for health and environmental justice. *Environmental Science. Processes & Impacts*, *23*(6), 812–830. https://doi.org/10.1039/d1em00007a

Masten, C. L., Telzer, E. H., & Eisenberger, N. I. (2011). An FMRI investigation of attributing negative social treatment to racial discrimination. *Journal of Cognitive Neuroscience*, *23*(5), 1042–1051. https://doi.org/10.1162/jocn.2010.21520

Maxwell, M., Brevard, J., Abrams, J., & Belgrave, F. (2015). What's color got to do with it? skin color, skin color satisfaction, racial identity, and internalized racism among African American college students. *Journal of Black Psychology*, *41*(5), 438–461. https://doi.org/10.1177/0095798414542299

McClaran, N., Rhodes, N., & Yao, S. X. (2022). Trust and coping beliefs contribute to racial disparities in covid-19 vaccination intention. *Health Communication*, 1–8. https://doi.org/10.1080/10410236.2022.2035944

McClendon, J., Chang, K., Boudreaux, M. J., Oltmanns, T. F., & Bogdan, R. (2021). Black-White racial health disparities in inflammation and physical health: Cumulative stress, social isolation, and health behaviors. *Psychoneuroendocrinology, 131*, 105251.

McEwen, B S, & Seeman, T. (1999). Protective and damaging effects of mediators of stress. Elaborating and testing the concepts of allostasis and allostatic load. *Annals of the New York Academy of Sciences*, *896*, 30–47. https://doi.org/10.1111/j.1749-6632.1999.tb08103.x

McEwen, Bruce S. (2007). Physiology and neurobiology of stress and adaptation: Central role of the brain. *Physiological Reviews*, *87*(3), 873–904. https://doi.org/10.1152/physrev.00041.2006

McEwen, Bruce S. (2012). Brain on stress: how the social environment gets under the skin.

Proceedings of the National Academy of Sciences of the United States of America, *109 Suppl 2*, 17180–17185. https://doi.org/10.1073/pnas.1121254109

McEwen, Bruce S, & Gianaros, P. J. (2010). Central role of the brain in stress and adaptation: links to socioeconomic status, health, and disease. *Annals of the New York Academy of Sciences*, *1186*, 190–222. https://doi.org/10.1111/j.1749-6632.2009.05331.x

McEwen, Bruce S, & Gianaros, P. J. (2011). Stress- and allostasis-induced brain plasticity. *Annual Review of Medicine*, *62*, 431–445. https://doi.org/10.1146/annurev-med-052209-100430

Mendes, W. B., Major, B., McCoy, S., & Blascovich, J. (2008). How attributional ambiguity shapes physiological and emotional responses to social rejection and acceptance. *Journal of Personality and Social Psychology*, *94*(2), 278–291. https://doi.org/10.1037/0022-3514.94.2.278

Meyer, M. L. (2019). Social by default: characterizing the social functions of the resting brain. *Current Directions in Psychological Science*, *28*(4), 380–386. https://doi.org/10.1177/0963721419857759

Miller, G., Chen, E., & Cole, S. W. (2009). Health psychology: developing biologically plausible models linking the social world and physical health. *Annual Review of Psychology*, *60*, 501–524. https://doi.org/10.1146/annurev.psych.60.110707.163551

Miller, G. E., Chen, E., Sze, J., Marin, T., Arevalo, J. M. G., Doll, R., Ma, R., & Cole, S. W. (2008). A functional genomic fingerprint of chronic stress in humans: blunted glucocorticoid and increased NF-kappaB signaling. *Biological Psychiatry*, *64*(4), 266–272. https://doi.org/10.1016/j.biopsych.2008.03.017

Miller, G. E., Murphy, M. L. M., Cashman, R., Ma, R., Ma, J., Arevalo, J. M. G., Kobor, M. S.,

& Cole, S. W. (2014). Greater inflammatory activity and blunted glucocorticoid signaling in monocytes of chronically stressed caregivers. *Brain, Behavior, and Immunity*, *41*, 191–199. https://doi.org/10.1016/j.bbi.2014.05.016

Miller, H. N., LaFave, S., Marineau, L., Stephens, J., & Thorpe, R. J. (2021). The impact of discrimination on allostatic load in adults: An integrative review of literature. *Journal of Psychosomatic Research*, *146*, 110434. https://doi.org/10.1016/j.jpsychores.2021.110434

Morawetz, C., Riedel, M. C., Salo, T., Berboth, S., Eickhoff, S. B., Laird, A. R., & Kohn, N. (2020). Multiple large-scale neural networks underlying emotion regulation. *Neuroscience and Biobehavioral Reviews*, *116*, 382–395. https://doi.org/10.1016/j.neubiorev.2020.07.001

Kamin Mukaz, D., Zakai, N. A., Cruz-Flores, S., McCullough, L. D., & Cushman, M. (2020). Identifying genetic and biological determinants of race-ethnic disparities in stroke in the United States. *Stroke*, *51*(11), 3417-3424. https://doi.org/10.1161/STROKEAHA.120.030425

Muscatell, K. A., Dedovic, K., Slavich, G. M., Jarcho, M. R., Breen, E. C., Bower, J. E., Irwin, M. R., & Eisenberger, N. I. (2015). Greater amygdala activity and dorsomedial prefrontal-amygdala coupling are associated with enhanced inflammatory responses to stress. *Brain, Behavior, and Immunity*, *43*, 46–53. https://doi.org/10.1016/j.bbi.2014.06.201

Muscatell, K. A., & Eisenberger, N. I. (2012). A social neuroscience perspective on stress and health. *Social and Personality Psychology Compass*, *6*(12), 890–904. https://doi.org/10.1111/j.1751-9004.2012.00467.x

Muscatell, K. A., Merritt, C. C., Cohen, J. R., Chang, L., & Lindquist, K. A. (2021). The stressed

brain: neural underpinnings of social stress processing in humans. *Current Topics in Behavioral Neurosciences*. https://doi.org/10.1007/7854_2021_281

Nardone, A., Rudolph, K. E., Morello-Frosch, R., & Casey, J. A. (2021). Redlines and greenspace: the relationship between historical redlining and 2010 greenspace across the United States. *Environmental Health Perspectives*, *129*(1), 17006. https://doi.org/10.1289/EHP7495

Nazroo, J. Y., Bhui, K. S., & Rhodes, J. (2020). Where next for understanding race/ethnic inequalities in severe mental illness? Structural, interpersonal and institutional racism. *Sociology of Health & Illness*, *42*(2), 262–276. https://doi.org/10.1111/1467-9566.13001

Neblett, E. W. (2019). Racism and health: Challenges and future directions in behavioral and psychological research. *Cultural Diversity & Ethnic Minority Psychology*, *25*(1), 12–20. https://doi.org/10.1037/cdp0000253

Neblett Jr, E. W., Banks, K. H., Cooper, S. M., & Smalls-Glover, C. (2013). Racial identity mediates the association between ethnic-racial socialization and depressive symptoms. *Cultural Diversity and Ethnic Minority Psychology*, *19*(2), 200. https://doi.org/10.1037/a0032205

Neblett, E. W., Terzian, M., & Harriott, V. (2010). From racial discrimination to substance use: the buffering effects of racial socialization. *Child Development Perspectives*, *4*(2), 131–137. https://doi.org/10.1111/j.1750-8606.2010.00131.x

Neblett, E. W., White, R. L., Ford, K. R., Philip, C. L., Nguyên, H. X., & Sellers, R. M. (2008). Patterns of racial socialization and psychological adjustment: can parental communications about race reduce the impact of racial discrimination? *Journal of Research on Adolescence*, *18*(3), 477–515. https://doi.org/10.1111/j.1532-

7795.2008.00568.x

Niendam, T. A., Laird, A. R., Ray, K. L., Dean, Y. M., Glahn, D. C., & Carter, C. S. (2012). Meta-analytic evidence for a superordinate cognitive control network subserving diverse executive functions. *Cognitive, Affective & Behavioral Neuroscience*, *12*(2), 241–268. https://doi.org/10.3758/s13415-011-0083-5

Ong, A. D., Williams, D. R., Nwizu, U., & Gruenewald, T. L. (2017). Everyday unfair treatment and multisystem biological dysregulation in African American adults. *Cultural Diversity & Ethnic Minority Psychology*, *23*(1), 27–35. https://doi.org/10.1037/cdp0000087

Park, H.-J., & Friston, K. (2013). Structural and functional brain networks: from connections to cognition. *Science*, *342*(6158), 1238411. https://doi.org/10.1126/science.1238411

Payne, B. K., & Hannay, J. W. (2021). Implicit bias reflects systemic racism. *Trends in Cognitive Sciences*, *25*(11), 927–936. https://doi.org/10.1016/j.tics.2021.08.001

Perez, A. D., Dufault, S. M., Spears, E. C., Chae, D. H., Woods-Giscombe, C. L., & Allen, A. M. (2022). Superwoman Schema and John Henryism among African American women: An intersectional perspective on coping with racism. *Social Science & Medicine*, 115070. https://doi.org/10.1016/j.socscimed.2022.115070

Phelan, J. C., & Link, B. G. (2015). Is racism a fundamental cause of inequalities in health? *Annual Review of Sociology*, *41*(1), 311–330. https://doi.org/10.1146/annurev-soc-073014-112305

Pollack, C. E., Cubbin, C., Sania, A., Hayward, M., Vallone, D., Flaherty, B., & Braveman, P. A. (2013). Do wealth disparities contribute to health disparities within racial/ethnic groups? *Journal of Epidemiology and Community Health*, *67*(5), 439–445. https://doi.org/10.1136/jech-2012-200999

Powell, W., Richmond, J., Mohottige, D., Yen, I., Joslyn, A., & Corbie-Smith, G. (2019). Medical mistrust, racism, and delays in preventive health screening among African-American men. *Behavioral Medicine*, *45*(2), 102–117. https://doi.org/10.1080/08964289.2019.1585327

Quillian, L., Pager, D., Hexel, O., & Midtbøen, A. H. (2017). Meta-analysis of field experiments shows no change in racial discrimination in hiring over time. *Proceedings of the National Academy of Sciences of the United States of America*, *114*(41), 10870–10875. https://doi.org/10.1073/pnas.1706255114

Raichle, M. E. (2015). The brain's default mode network. *Annual Review of Neuroscience*, *38*, 433–447. https://doi.org/10.1146/annurev-neuro-071013-014030

Ruiz, J. M., Sbarra, D., & Steffen, P. R. (2018). Hispanic ethnicity, stress psychophysiology and paradoxical health outcomes: A review with conceptual considerations and a call for research. *International Journal of Psychophysiology*, *131*, 24–29. https://doi.org/10.1016/j.ijpsycho.2018.04.001

Sawyer, P. J., Major, B., Casad, B. J., Townsend, S. S. M., & Mendes, W. B. (2012). Discrimination and the stress response: psychological and physiological consequences of anticipating prejudice in interethnic interactions. *American Journal of Public Health*, *102*(5), 1020–1026. https://doi.org/10.2105/AJPH.2011.300620

Simoiu, C., Corbett-Davies, S., & Goel, S. (2017). The problem of infra-marginality in outcome tests for discrimination. *The Annals of Applied Statistics*, *11*(3), 1193–1216. https://doi.org/10.1214/17-AOAS1058

Simons, R. L., Lei, M.-K., Klopack, E., Beach, S. R. H., Gibbons, F. X., & Philibert, R. A. (2021). The effects of social adversity, discrimination, and health risk behaviors on the

accelerated aging of African Americans: Further support for the weathering hypothesis. *Social Science & Medicine*, *282*, 113169. https://doi.org/10.1016/j.socscimed.2020.113169

Simons, R. L., Lei, M.-K., Klopack, E., Zhang, Y., Gibbons, F. X., & Beach, S. R. H. (2021). Racial discrimination, inflammation, and chronic illness among african american women at midlife: support for the weathering perspective. *Journal of Racial and Ethnic Health Disparities*, *8*(2), 339–349. https://doi.org/10.1007/s40615-020-00786-8

Slavich, G. M. (2020). Social safety theory: A biologically based evolutionary perspective on life stress, health, and behavior. *Annual Review of Clinical Psychology*, *16*, 265–295. https://doi.org/10.1146/annurev-clinpsy-032816-045159

Smedley, A., & Smedley, B. D. (2005). Race as biology is fiction, racism as a social problem is real: Anthropological and historical perspectives on the social construction of race. *The American Psychologist*, *60*(1), 16–26. https://doi.org/10.1037/0003-066X.60.1.16

Sosoo, E. E., Bernard, D. L., & Neblett, E. W. (2020). The influence of internalized racism on the relationship between discrimination and anxiety. *Cultural Diversity & Ethnic Minority Psychology*, *26*(4), 570–580. https://doi.org/10.1037/cdp0000320

Sosoo, E. E., MacCormack, J. K., & Neblett Jr., E. W. (2022). Psychophysiological and affective reactivity to vicarious police violence. *Psychophysiology*.

Speight, S. L. (2007). Internalized Racism. *The Counseling Psychologist*, *35*(1), 126–134. https://doi.org/10.1177/0011000006295119

Sterling, P. (2012). Allostasis: a model of predictive regulation. *Physiology & Behavior*, *106*(1), 5–15. https://doi.org/10.1016/j.physbeh.2011.06.004

Suárez, L. E., Markello, R. D., Betzel, R. F., & Misic, B. (2020). Linking structure and function

in macroscale brain networks. *Trends in Cognitive Sciences*, *24*(4), 302–315. https://doi.org/10.1016/j.tics.2020.01.008

Townsend, S. S. M., Eliezer, D., Major, B., & Mendes, W. B. (2014). Influencing the world versus adjusting to constraints. *Social Psychological and Personality Science*, *5*(2), 226–234. https://doi.org/10.1177/1948550613490968

Wagner, J., Lampert, R., Tennen, H., & Feinn, R. (2015). Exposure to discrimination and heart rate variability reactivity to acute stress among women with diabetes. *Stress and Health*, *31*(3), 255–262. https://doi.org/10.1002/smi.2542

Wang, N. C., Matthews, K. A., Barinas-Mitchell, E. J., Chang, C. C. H., & El Khoudary, S. R. (2016). Inflammatory/hemostatic biomarkers and coronary artery calcium progression in women at midlife (from the Study of Women's Health Across the Nation, Heart Study). *The American Journal of Cardiology*, *118*(3), 311-318. https://doi.org/10.1016/j.amjcard.2016.05.009

Webb, E. K., Bird, C. M., deRoon-Cassini, T. A., Weis, C. N., Huggins, A. A., Fitzgerald, J. M., Miskovich, T., Bennett, K., Krukowski, J., Torres, L., & Larson, C. L. (2022). Racial discrimination and resting-state functional connectivity of salience network nodes in trauma-exposed black adults in the united states. *JAMA Network Open*, *5*(1), e2144759. https://doi.org/10.1001/jamanetworkopen.2021.44759

Weinstein, A. A., Termini, A., B. Kazman, J., A. Zeno, S., Abraham, P., & Deuster, P. A. (2013). Racial provocation induces cortisol responses in African-Americans. *Open Journal of Medical Psychology*, *02*(04), 151–157. https://doi.org/10.4236/ojmp.2013.24023

Wildeman, C., & Wang, E. A. (2017). Mass incarceration, public health, and widening inequality

in the USA. *The Lancet*, *389*(10077), 1464–1474. https://doi.org/10.1016/S0140-6736(17)30259-3

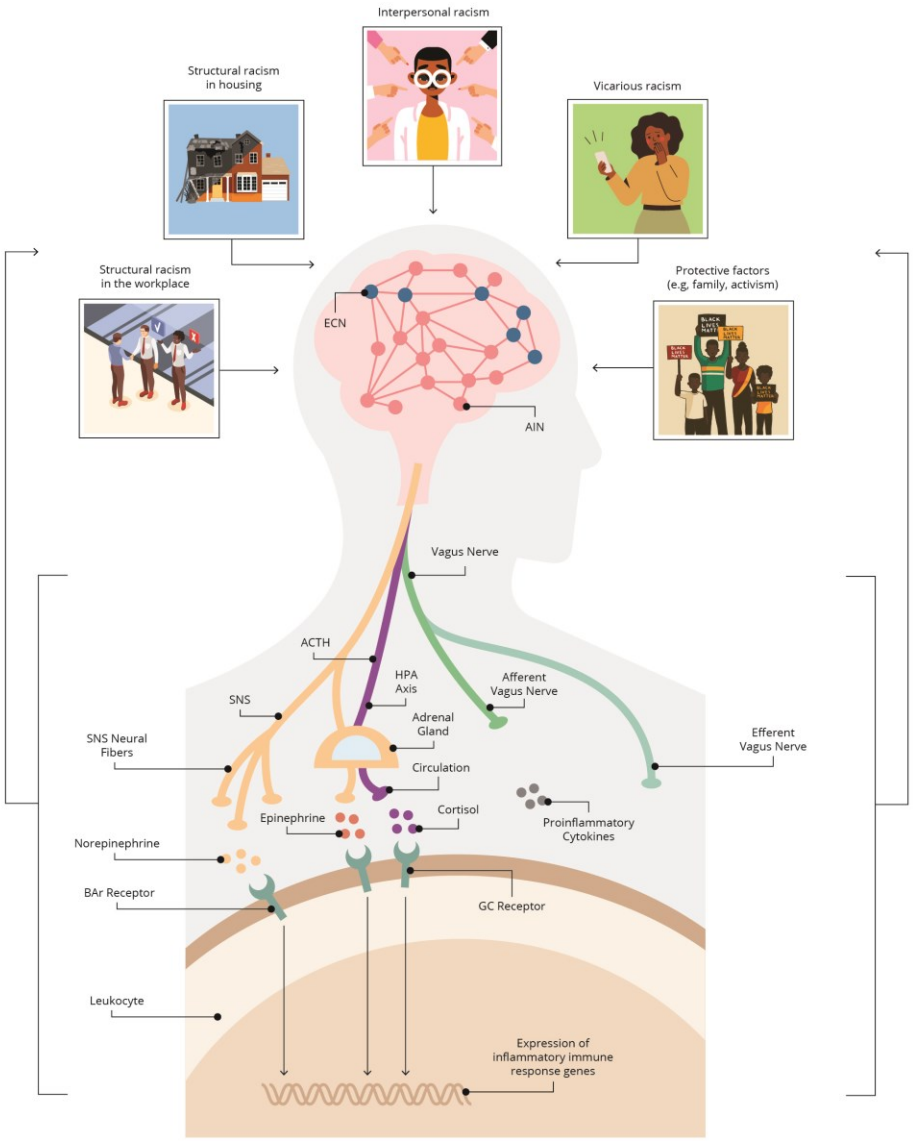
Williams, D. R., Lawrence, J. A., & Davis, B. A. (2019). Racism and health: evidence and needed research. *Annual Review of Public Health*, *40*, 105–125. https://doi.org/10.1146/annurev-publhealth-040218-043750

Williams, D. R., & Mohammed, S. A. (2013). Racism and health I: Pathways and scientific evidence. *The American Behavioral Scientist*, *57*(8). https://doi.org/10.1177/0002764213487340

Yearby, R. (2018). Racial disparities in health status and access to healthcare: the continuation of inequality in the united states due to structural racism. *American Journal of Economics and Sociology*, *77*(3–4), 1113–1152. https://doi.org/10.1111/ajes.12230

Yip, T., Cheah, C. S. L., Kiang, L., & Hall, G. C. N. (2021). Rendered invisible: Are Asian Americans a model or a marginalized minority? *The American Psychologist*, *76*(4), 575–581. https://doi.org/10.1037/amp0000857

Figure 1. Hypothesized Neural and Physiological Mechanisms Linking Racism and Health



Note. We hypothesize that multiple forms of racism (e.g., structural racism in the workplace and in housing; interpersonal racism; vicarious racism), as well as protective factors (e.g., social support from family; activism and civic engagement) shape brain networks and physiological systems to lead to chronic disease and early mortality for Black Americans. Specifically, racism may lead to greater activity in and connectivity within the allostatic-interoceptive network (AIN; red circles on brain graph image), which consists of regions of the

salience network, the default mode network, and subcortical regions. We also speculate that racism leads to differences in functional connectivity between the AIN and executive control network (ECN; blue circles on brain graph image). This pattern of brain activity/connectivity in the face of racism then leads to activation of physiological systems involved in responding to stress, including the sympathetic nervous system (SNS) and hypothalamic-pituitary-adrenal (HPA) axis. Specifically, racism can also lead to activation of the HPA axis, including release of adrenocorticotrophic hormone (ACTH), which can stimulate the adrenal gland to produce cortisol. Cortisol can then bind to glucocorticoid (GC) receptors on the surface of immune cells (i.e., leukocytes), which can also influence gene expression within immune cells. Encountering racism is also hypothesized to lead to activation of SNS neural fibers, which can cause the release of norepinephrine and (via stimulation of the adrenal gland), epinephrine. These catecholamines can then bind to beta-adrenergic (BAr) receptors on the surface of immune cells (i.e., leukocytes), which can lead to increased expression of inflammatory immune response genes and greater production of proinflammatory cytokines. Greater inflammation is then implicated in the etiology and pathophysiology of chronic disease and psychopathology. Further, physiological outputs such as cortisol and pro-inflammatory cytokines can feed back to the brain via afferent vagus nerve signaling to influence neural structure and function, creating a vicious cycle.

Table 1.

Overview of Multiple Mechanisms Linking Racism and Health

Domain	Examples	References
Socioeconomic	Poverty Education Wealth Bias in hiring Bias in housing	Kimmel et al., 2016 Fiscella & Williams, 2004 Pollack et al., 2013 Quillian et al., 2017 Auspurg et al., 2018
Healthcare	Healthcare access Bias in medicine Medical mistrust Delays in preventative care	Yearby, 2018 Dovidio et al., 2016 McClaran et al., 2022 Powell et al., 2019
Criminal Justice	Incarceration Discrimination in police stops Discrimination in sentencing	Wildeman & Wang, 2017 Simoiu et al., 2017 Kutateladze & Andiloro, 2014
Behavior/Environment	Food insecurity/poor diet Limited physical activity Sleep quality Heavy metals poisoning Air pollution exposure Access to greenspaces	Bowen et al., 2021 Hawes et al., 2019 Fuller-Rowell et al., 2016 Masri et al., 2021 Brandt et al., 2020 Nardone et al., 2021
Cognition/Affect	Vigilance Rumination John Henryism Superwoman schema	Lewis et al., 2019 Dondanville et al., 2022 Bennett et al., 2004 Perez et al., 2022
Development	Racial socialization Weathering Allostatic load Cognitive impairment/dementia	Neblett et al., 2010 Simons et al., 2021 Miller et al., 2021 Glymour & Manly, 2008

Note. Although the present paper focuses on the possible neural and inflammatory pathways through which racism may influence health, there are multiple mechanisms that have been shown to contribute to racism-based health disparities. Neurophysiological processes are just one piece of this mechanistic puzzle. This table attempts to highlight some of the additional mechanisms not covered in detail in the current model, and points to additional research that may be of interest to readers. Of note, many of the mechanisms presented here interact with and influence one another and should be thought of as synergistic processes that can come together to set Black individuals on trajectories toward disease and early mortality.