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The neurophysiological consequences of racism-related stressors in Black Americans

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ABSTRACT

Racism-related stressors, from experiences of both implicit and explicit racial discrimination to systemic socio-economic disadvantage, have a cumulative impact on Black Americans' health. The present narrative review synthesizes peripheral (neuroendocrine and inflammation markers), psychophysiological (heart-rate variability, skin conductance), and neuroimaging (structural and functional) findings that demonstrate unique associations with racism-related stress. Emerging evidence reveals how racism-related stressors contribute to differential physiological and neural responses and may have distinct impacts on regions involved with threat and social processing. Ultimately, the neurophysiological effects of racism-related stress may confer biological susceptibility to stress and trauma-related disorders. We note critical gaps in the literature on the neurophysiological impact of racism-related stress and outline additional research that is needed on the multifactorial interactions between racism and mental health. A clearer understanding of the interactions between racism-related stress, neurophysiology, and stress- and trauma-related disorders is critical for preventative efforts, biomarker discovery, and selection of effective clinical treatments for Black Americans.

1. Introduction

Racism - not race - is a fundamental driver of the disproportionate burden of life stress on Black individuals (Carter et al., 2021, 2022a; Centers for Disease Control and Prevention, 2021). Racism-related stressors exist at both individual and structural levels and are present throughout the lifespan. From economic disadvantage and disproportionately high trauma exposure to experiences of implicit discrimination and explicitly racist behaviors, these stressors have a cumulative impact on mental health. The consequences of racism are observable in stress and trauma-related neuropsychiatric outcomes including a more severe course of posttraumatic stress disorder (PTSD), depression, and anxiety for Black, compared to White, Americans (Williams, 2018; Breslau et al., 2006). Narrowing racism-related mental health inequities requires a thorough understanding of the neurophysiological consequences of racism-related stress to develop generalizable neurobiological models of psychiatric disease.

Racism is a major determinant of the wide racial inequities in trauma- and stress-related disorders with Black Americans experiencing the greatest burden of racism-related stress (Williams, 2018, 1999; Harrell et al., 2011; Williams et al., 2013). Specifically, racism-related stress contributes to complex racial inequities in the onset and course of psychiatric disease. For example, epidemiological data suggests while the prevalence of depression and anxiety is lower in Black individuals compared to White individuals, the prevalence of PTSD is higher (Roberts et al., 2011). A potential complication in evaluating prevalence rates of psychiatric disorders is that Black individuals often face systemic barriers to healthcare utilization (e.g., underdiagnoses or misdiagnoses, negative experiences during treatment) and study recruitment (Snowden, 2003). Alternatively, some work suggests differential engagement of compensatory or coping behaviors partially underlie reduced rates of internalizing disorders in Black individuals (Jackson et al., 2010; Gibbons et al., 2014). Nevertheless, these potential mechanisms highlight both the structural and interpersonal effects of racism that may contribute to the course and severity of psychopathology.

These disparate outcomes and prognoses suggest a potential

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biological embedding of racism-related stress in key neurophysiological circuits related to psychiatric disease (Williams, 1999; Williams et al., 2013). Evidence demonstrates that racism-related stressors uniquely engage physiological responses to stress, including the hypothalamic-pituitary-adrenal (HPA) axis (Berger et al., 2015). However, less attention has been given to the impact of racism-related stress on key neurophysiological circuits that modulate stress responding and affect psychiatric symptom development and expression. In particular, neural circuits involved in threat regulation and social processing may be impacted by racism-related stress (Carter et al., 2021; Berger et al., 2015; Bird et al., 2021; Mekawi et al., 2021a). Threat and social processing circuits are necessary for individuals to appropriately assess, interpret, regulate, and respond to various aversive events in the environment. Together these neural circuits engage behaviors that may serve to protect Black individuals from experiences of racism-related stressors. However, the chronic engagement of these circuits may carry a biological cost that can contribute to negative health outcomes (Colodro-Conde et al., 2018).

A more thorough understanding of the neurophysiological consequences of racism-related stress is necessary to advance effective therapeutics, engage culturally competent treatments, and prevent neuropsychiatric disorders across the entire population. In the present narrative review, we first define personally mediated and structural racism drawing on foundational research from racism scholars. We then describe studies that have examined the effects of personally mediated and structural racism on peripheral biomarkers, psychophysiology, and brain structure and function. Based on recent studies, we suggest that personally mediated and structural racism may have differential impacts on specific brain regions. Although the neuroimaging literature is limited, we highlight how the neurophysiological effects of racism may create susceptibility to stress and trauma-related psychiatric disorders. Finally, we offer recommendations for neuroscience-based investigations of racism-related stress that balance both the critical need for a thorough understanding of how racism impacts the brain with necessary ethical considerations for racism-related neuroscience research.

1.1. Defining race and racism

Race reflects a social categorization system designed to group people based on phenotypic characteristics whereas *racism* encompasses "beliefs, attitudes, institutional arrangements, and acts that tend to denigrate individuals or groups because of phenotypic characteristics or ethnic group affiliations" (Clark et al., 1999). Terminology defining socially constructed racial groups (e.g., Black, White, etc.) therefore represents racialized collective identities based on visible characteristics rather than any fundamental differences. *Racism* is a multi-level system that manifests at both interpersonal and structural levels (Banaji et al., 2021; Carter, 2007). Individuals racialized as Black are disadvantaged by the system of racism whereas individuals racialized as White unjustly benefit. Though often conceptualized around individual thoughts and behaviors, such as prejudice or discrimination (Salter et al., 2018), macrosystem influences (e.g., within institutions, policies, laws, etc.) of racism cannot be discounted (Lewis, 2021). Though the domains of racism vary by conceptual models of racism (reviewed in Neblett, 2019a), we focus here on two major components: personally mediated and structural racism (Fig. 1).

Personally mediated racism refers to interpersonal interactions that encompass discrimination, prejudice, and explicitly racist individual behaviors (Jones, 2000). Personally mediated racism works through various mechanisms such as stereotyping, development of White racialized identity, and in-group/out-group processing (Bodenhausen et al., 2009; Richeson et al., 2004). Outcomes of personally mediated racism include overt (e.g., hate speech) and covert (e.g., insistence on "colorblind" approaches) forms (Hoffman et al., 2016; Jones, 2000; Wong et al., 2014; Yi et al., 2022). Research consistently demonstrates that personally mediated racism is pervasive with over 70% of Black Americans reporting an experience of personally mediated racism across various contexts (e.g., school, work, recreation, medical/legal settings) (Lee et al., 2019). Racial discrimination is also frequent, with Black

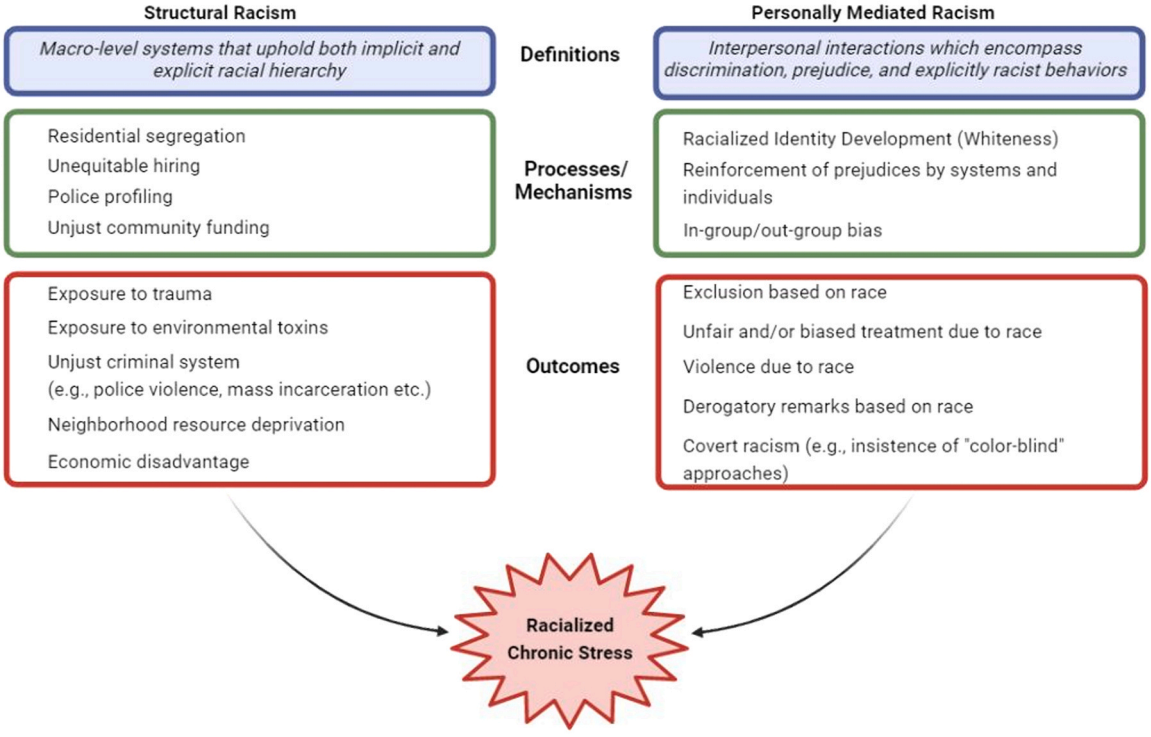

Fig. 1. An overview of the definitions, processes, and outcomes of racism. Both structural racism and personally mediated racism contribute to the magnitude and intensity of racialized chronic stress.

youth reporting more than 5 discriminatory experiences a day (English et al., 2020).

Structural racism refers to macro-level systems that work in unison to uphold an implicit and explicit racial hierarchy (i.e., White supremacy) within the U.S. These systems enforce inequitable access to social and material resources through policies, laws, and practices in societal systems (e.g., labor markets, educational system, criminal justice systems) (Gee et al., 2011; Williams et al., 2019a; Hardeman et al., 2022; Dean et al., 2022). Importantly, it is often difficult to directly measure the *mechanisms* of structural racism in neuroscience investigations due to the conceptual and technical limitations of techniques. Research has therefore largely used *outcomes* of structural racism as proxies for its effects. Quantifiable proxies of structural racism in the U.S. can be indexed from disproportionate exposure to environmental toxins, differences in individual economic disadvantage (i.e., poverty), neighborhood resource disadvantage (e.g., food deserts), and disparate criminal-justice practices (Riley, 2018; Sewell, 2015). However, the use of these variables is not without limitations (Dean et al., 2022; Adkins-Jackson et al., 2021). Selection of one proxy may miss other dimensions of structural racism (Adkins-Jackson et al., 2021) or capture influences from other societal forces that are intertwined with structural racism, such as classism (Cavalhieri et al., 2022). Still, there is considerable evidence that these proxies capture structural racism and their use is preferred over other proxies (e.g., using race) (Adkins-Jackson et al., 2021; Bailey et al., 2021). Employing these indicators provides one method for tying structural racism to neurophysiological mechanisms, however, more nuanced quantitative methods that can directly assess mechanisms are needed.

Recent research has begun to develop harmonized, multilevel assessments across these components (Gee et al., 2011; Adkins-Jackson et al., 2021). Consideration of the multilevel nature of structural racism is critical as separate factors can interact with one another to compound racial inequity. For example, prior work highlights that Black families are less likely to own a home even after controlling for income and education (Choi et al., 2019; Killewald et al., 2018). In fact, Black households with a college degree are less likely to own a home than White households without a high school diploma (Choi et al., 2019; Killewald et al., 2018). Importantly, Black-owned homes are more likely to reside in neighborhoods with higher rates of pollution, less access to greenspace, and higher rates of community violence (Riley, 2018; Sewell, 2015; Bailey et al., 2017). Thus, exposure to one aspect of structural racism can exacerbate exposure to other events that promote racial disparities and inequities. The interrelatedness of these factors highlights the macro-level ways in which structural racism can manifest, and it sheds light on the many ways in which structural racism can influence neurophysiology and neuropsychiatric risk.

2. Biological responses to racism-related stress

Predominant theories of stress, including the allostatic load theory (McEwen, 2000) – propose that a psychosocial stressor activates widespread responses to deal with physiological challenges (McEwen et al., 2010; Richter-Levin et al., 2021; McEwen et al., 2020). Briefly, exposure to acute stress elicits processes that allow an individual to respond to events in the environment. Allostasis is then enacted through feedback responses within biological systems (e.g., hypothalamic-pituitary-adrenal [HPA] axis) to return the body to homoeostasis. However, while acute allostatic processes can be advantageous, prolonged and sustained activity ran result in maladaptive outcomes or toxicity to the body (Richter-Levin et al., 2021; Mcewen, 2004; Schulz et al., 2012). Thus, when a stressor is pervasive, unpredictable, and uncontrollable, allostatic processes are unable to appropriately regulate physiological systems. Cumulative dysregulation of these systems increases the level of "allostatic load" which is associated with vulnerability to neuropsychiatric disorders (Colodro-Conde et al., 2018).

Although traditional models of stress did not specifically consider racism, scholars have connected classical stress theories to models of racism-related stress (Carter et al., 2021; Clark et al., 1999; Mays et al., 2007). Geronimus and colleagues (1992) proposed that prolonged and/or repeated exposure to racism-related stressors contributes to "weathering" in Black individuals which is the result of depleted resources and "wear and tear" on physiological processes (Allen et al., 2019; Carlson et al., 2005; Geronimus et al., 2006). Racism-related stressors can be composed of both discrete incidents (e.g., personally mediated racism), and may also have a sustained presence (e.g., structural racism) and can thus be acute, chronic, or both. Further, the unpredictable – but likely – threat of personally-mediated racism and the ever presence of structural racism create a near inescapable context for racism-related stress to potentially occur. Thus, the "weathering hypothesis" posits that there may be sustained activation of stress response systems in response to racism within the U.S. leading to allostatic overload. We review evidence supporting this hypothesis, indicating the effects of racism-related stressors are apparent across multiple biological systems – from peripheral neuroendocrine and immune responses to psychophysiological arousal and neural reactivity to stress.

2.1. Peripheral responses to racism-related stress

Allostatic load is often operationalized as a composite set of markers assessing neuroendocrine (e.g., cortisol, epinephrine, norepinephrine), immune (e.g., C-reactive protein, pro-inflammatory cytokines), metabolic (e.g., cholesterol), and cardiovascular (e.g., blood pressure) systems. To date, there is no gold-standard for measuring allostatic load, with variation in both the number of indicators used and the biological systems represented (reviewed in Miller et al., 2021; Beese et al., 2022). Despite these measurement differences, a higher allostatic load is significantly associated with racism-related stress (Miller et al., 2021; Duru et al., 2012; Van Dyke et al., 2020). For example, in a cross-sectional study, greater everyday discrimination was associated with higher allostatic load, even after adjusting for other health-related (e.g., medication use, smoking status) and psychosocial (e.g., depression symptoms, lifetime discrimination) factors (Ong et al., 2017). Further, longitudinal work suggests early racial discrimination (at age 16) is predictive of higher future allostatic load (at age 20) (Brody et al., 2006). Black women, in particular, who are impacted by both racism and sexism, show the highest biological burden of allostatic load (Carlson et al., 2005; Geronimus et al., 2006). While the majority of studies have focused on personally-mediated racism (Allen et al., 2019; Miller et al., 2021; Van Dyke et al., 2020; Lucente et al., 2023), structural racism also appears to be related to higher allostatic burden (e.g., Brody et al., 2014; Chen et al., 2015). For example, Black women living in more disadvantaged neighborhoods show significantly higher allostatic load compared to white women in similarly disadvantaged neighborhoods (Wallace et al., 2013). Together, the studies on allostatic load emphasize how the cumulative experience of racism may be associated with enduring consequences across multiple biological systems.

The associations between racism-related stress and biomarkers of specific systems have also received attention. For example, cortisol, a peripheral output of the neuroendocrine system has been consistently associated with racism-related stress (Korous et al., 2017). Exposure to racism is associated with cortisol recordings throughout the day and changes in response to acute stressors (Korous et al., 2017). Studies using racism-related stress tests, in which participants listen to a Black interviewee describe a racist experience (Matheson et al., 2021) or experienced a highly publicized real-life racial stressor (Richman et al., 2008), reveal that acute exposure to racism-related stress is associated with elevated cortisol levels. However, chronic exposure to racial discrimination is also associated with daily cortisol patterns, with results documenting a flatter diurnal cortisol slope (less of a decline from waking to bedtime levels) (Skinner et al., 2011; Zeiders et al., 2014; Zilioli et al., 2023). Notably, this pattern has also emerged in longitudinal work (Adam et al., 2015), mirroring other stress-related changes in

daily cortisol rhythm. Blunted diurnal rhythm is generally associated with biological dysregulation and has been previously associated with neuropsychiatric disorders such as PTSD (Garcia et al., 2020), highlighting yet another possible pathway by which racism may increase biological risk for poorer mental health (Skinner et al., 2011).

The immune system, which increases activity as part of the stress response, can further perpetuate glucocorticoid production and is independently stimulated by adverse effects of chronic stress. Higher levels of pro-inflammatory markers, such as C-reactive protein, interleukins (e.g., IL-6), and tumor necrosis factor, are associated with racial discrimination (Elbasheir et al., 2024; Giurgescu et al., 2016; Ho, 2023; Lewis et al., 2010; Simons et al., 2021). The release of pro-inflammatory cytokines is driven by upstream gene regulation. The gene profile conserved transcriptional response to adversity (CTRA) is a cumulative measure of stress that characterizes alterations to pro-inflammatory and antiviral transcriptional pathways (Cole, 2019). Experiences of racial discrimination are associated with greater CTRA gene expression, with one study finding that approximately half of the race-related differences in CTRA level were explained by racial discrimination (Thames et al., 2019). A separate study found that recent Black trauma survivors who experienced higher levels of racial discrimination showed greater increases in CTRA gene expression across time (Bird et al., 2024). Ultimately, these studies suggest racism is associated with dysregulation of the immune system, as evidenced by alterations in upstream control pathways and peripheral markers, which may affect the body's ability to cope with future and ongoing stressors.

2.2. Psychophysiological responses to racism-related stress

Psychophysiological responsivity and arousal to racism-related stress are typically indexed via changes in heart rate variability (HRV) and skin conductance responses (SCR). HRV is measured by calculating the variability in the duration between consecutive heartbeats and captures the interaction between the parasympathetic and sympathetic nervous systems. SCRs are transient increases in electrical conductance along the dermis caused by sweat activity from eccrine skin glands in response to psychophysiological arousal. Both HRV and SCR are well-validated objective measures of physiological regulation and arousal, respectively, to acute and chronic environmental stressors (Najström et al., 2007; Shaikh al arab et al., 2012; van der Mee et al., 2020; Kudielka et al., 2007). Psychophysiological responsivity is also associated with peripheral markers of neuroendocrine and inflammation systems. For example, inflammatory markers are typically inversely associated with HRV (see meta-analysis Williams et al., 2019b) and limited work suggests waking cortisol levels are associated with heightened SCR during fear conditioning (Pineles et al., 2013). Importantly, research demonstrates psychophysiological indicators are associated with both personally mediated and structural racism.

In general, higher HRV is cardio-protective and associated with better physical and mental health, while lower HRV is linked to stress and trauma-related psychiatric outcomes, including depression and anxiety (see meta-analyses Kemp et al., 2010; Schneider et al., 2020). Despite significant racial inequities in cardiovascular disease, Black Americans tend to show higher HRV compared to White Americans, even after controlling for other factors such as health status, medication use, and age (reviewed in Hill et al., 2015). However, the presence of higher HRV in Black individuals is not always consistent and may depend on moderating factors, including gender (Hill et al., 2015). The finding of higher resting HRV was most consistent in Black women compared to Black men (Hill et al., 2015). This pattern of higher baseline HRV is referred to as the "vagal advantage". Researchers have theorized "vagal advantage" may be related to the anticipation and navigation of discriminatory experiences and ultimately aid in coping with racism-related stress (Hill et al., 2015, 2017).

Paradoxically, there is a consistent pattern of results revealing that exposure to racial discrimination is correlated with lower baseline HRV and related to reduced HRV during both racism and non-racism-related stress tests (Hill et al., 2017; Wagner et al., 2015; Utsey et al., 2007; Hoggard et al., 2015; Neblett et al., 2013). For example, Hoggard and colleagues (2015) demonstrated that Black women discriminated against by a White woman in a laboratory experiment showed significantly lower HRV immediately following the experience and marginally lower HRV a day later (Hoggard et al., 2015). Others have demonstrated similar findings, suggesting that racial discrimination is linked to lower HRV after participants are asked to imagine a discriminatory experience (Neblett et al., 2013) or after experiencing an acute laboratory stressor (public speaking Wagner et al., 2015). The lab-based studies are largely consistent with observational, correlational, studies finding racial discrimination is associated with lower resting HRV (reviewed in Hill et al., 2019); however, more research is needed to connect the epidemiological evidence describing higher HRV at rest to the relationship between racial discrimination and HRV.

It is important to note, however, that the impacts of structural racism on HRV are understudied and therefore it remains unclear if there are differential effects on tonic or stress-induced HRV. Specifically, greater exposure to structural racism or combinatorial exposure with chronic personally mediated racism may alter resting HRV. In general, previous work suggests proxies of structural racism are associated with poorer cardiovascular health (e.g., (Barber et al., 2016; Halonen et al., 2015) and reviewed in Xiao and Graham, 2019); however, further work is needed to explicitly disentangle whether racial differences in HRV are attributable to specific structural racism stressors.

Racism-related stress may contribute to blunting of SCRs, particularly in threat contexts. Previous research observed lower average skin conductance levels and fewer SCRs to threat in Black compared to White Americans (Harnett et al., 2019), and prior studies have documented relatively lower SCR in Black individuals (Lathan et al., 2023; d'Andrea et al., 2013). A study in young adults indicated racialized negative life experiences, such as neighborhood disadvantage, income, and violence exposure, could help explain skin SCRs to threat in Black participants compared to White participants (Harnett et al., 2019). Given that these factors largely reflect structural racism, the findings suggest the persistent/chronic burden of racism-related stress contributes to blunting of peripheral expression of the emotional response in Black individuals. However, Harnett and colleagues (2023) found that while Black trauma survivors showed significantly lower baseline skin conductance levels compared to White trauma survivors, structural inequities did not directly mediate the racial difference. It is also important to note that the salience of the stimulus, context (e.g., acutely following a new trauma), and timing may alter the effect (Lathan et al., 2023). For example, a prior report found that Black Americans who reported experiencing more discriminatory events throughout the day showed *heightened* skin conductance levels (Cheadle et al., 2020). Thus, personally mediated racism may have contrasting effects on the peripheral expression of the emotional response to structural racism.

While preliminary work suggests skin conductance levels and SCRs can be modulated by both personally mediated and structural racism, there are several research challenges to understanding racism-related changes. Historically, psychophysiological guidelines recommended excluding individuals who are "non-responsive", i.e., show blunted reactivity to threat (Boucsein et al., 2012). However, if racism-related stress contributes to blunted SCRs, such criteria may have inadvertently led to the disproportionate exclusion of Black individuals from previous work and therefore the extent of racism-related SCR differences may be underestimated (Webb et al., 2022a). Additionally, most psychophysiological research does not report racial and/or ethnic breakdowns of participants, which precludes any interpretations of the specific effects of racism-related stress in these studies (Webb et al., 2022a; Bradford et al., 2022; Kissel et al., 2023).

2.3. Neural correlates of racism-related stress

The peripheral emotional expression and physiological arousal occur via projections to effectors of the autonomic nervous system. Fig. 2 provides an overview of the roles of these brain regions, their interactions, and influence on SCR and HRV. Briefly, visual stimuli are initially detected by the visual cortex before information is shared with the amygdala, the site for formation of cue-threat contingencies during associative learning. The amygdala is the site for formation of cue-threat contingencies during associative learning and projects downstream to effectors of the autonomic nervous system. In particular, amygdala projections to the dorsal motor nucleus of the vagus nerve through the medulla and the lateral hypothalamus alter HRV (Seligowski et al., 2022) whereas projections from the amygdala to the medial hypothalamus modulate SCR (Wood et al., 2014). The hippocampus supports the encoding and retrieval of contextual information about cue-threat contingencies necessary for appropriate threat responses (Fenster et al., 2018; Harnett et al., 2020). The prefrontal cortex (PFC), which has dense reciprocal neuronal connections with the amygdala and hippocampus, plays a role in selecting the appropriate responses to threats (Fenster et al., 2018; Harnett et al., 2020) including deploying voluntary emotion regulation strategies required to resolve conflicts when/if they arise. The dorsal anterior cingulate cortex (dACC) and rostral ACC (rACC), support integration of relevant internal and external information to rapidly detect social threats (Meyer et al., 2015). Finally, the anterior insula supports interoceptive, visceral sensation, and sensory integration and is linked to the expression of social pain or "unpleasant" feelings in response to social threats (Uddin, 2015; Uddin et al., 2017; Singer et al., 2009).

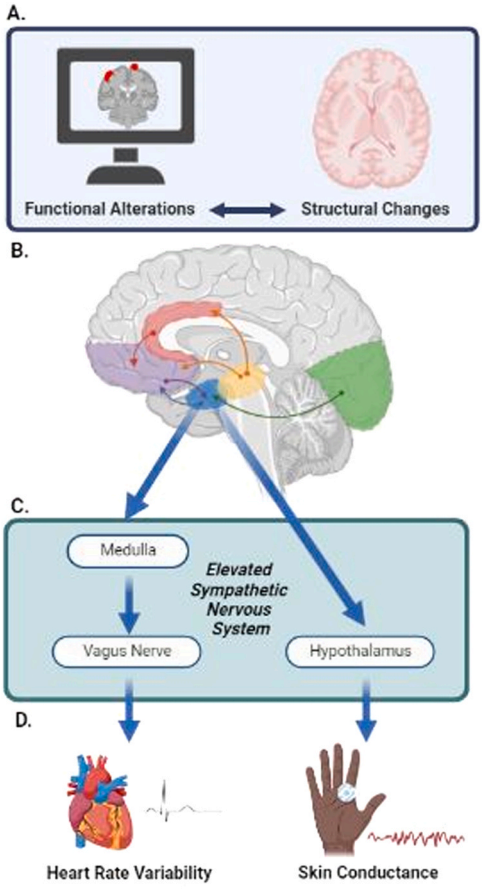

Fig. 2. Neurophysiological Effects of Racism-related Stress and Associated Physiological Expressions of Stress and Emotional Responses. **[A]** Racism-related stress is associated with brain structural and functional alterations in regions involved in threat and social processing. **[B]** The visual cortex (VC; green) shares sensory information with the amygdala (AMYG; blue) where cue-threat contingencies are acquired. The hippocampus (HIPPO; yellow) supports the encoding of fear memories and retrieval of contextual information necessary for selecting threat responses (Harnett et al., 2020; Fenster et al., 2018). The prefrontal cortex (PFC; purple), plays a role in voluntary selection of behavioral responses to threats (Harnett et al., 2020; Fenster et al., 2018). Together, the dorsal anterior cingulate cortex (dACC) and rostral ACC (rACC) (red), supports direction of attention to threat and information integration to select a behavioral response (Meyer et al., 2015). Finally, the anterior insula (INS) supports interoceptive, visceral sensation, and sensory integration (Uddin, 2015; Uddin et al., 2017; Singer et al., 2009). **[C]** Amygdala projections include [neurotransmitter] efferents to the dorsal motor nucleus of the vagus nerve through the medulla and to the lateral hypothalamus to **[D]** induce brady-and-tachycardia. Projections from the amygdala to the medial hypothalamus modulate eccrine sweat gland activity which cause changes in skin conductance.

Interactions between the regions responsible for detecting and processing threats and social conflicts form a neural circuit that responds to racism-related stressors. Both personally mediated and structural racism may contribute to alterations in threat and social processing neurocircuitry such as the including to the amygdala, hippocampus, prefrontal cortex, and insula. Below, we review the growing body of literature (Table 1) identifying associations between racism-related stress and neurobiological features of these regions.

2.3.1. Amygdala

Several studies have found that personally mediated racism is related to amygdala functional dynamics. One study of predominately Black adults demonstrated that discrimination was associated with greater amplitude of amygdala response at rest (Clark et al., 2018) and stronger connectivity between the amygdala and the anterior insula, middle frontal gyrus, and dACC, regions that are involved with salience detection (Clark et al., 2018). Two previous studies, one in recent trauma survivors and another in older adults, observed that greater racial discrimination is also associated with greater functional connectivity between the amygdala and thalamus (Clark et al., 2018; Webb et al., 2021a). The thalamus is a major hub for the integration of sensory, cognitive, and affective information emerging from reciprocal connections with other regions, such as the dACC and anterior insula, and direct thalamus-amygdala connections can rapidly trigger threat-related responses (Garrido et al., 2012; Qi et al., 2020). Together these three studies, which were conducted in varied samples, suggest that exposure to personally mediated racism facilitates communication between regions that process threat-related information to potentially expedite the detection of, and subsequent emotional response to, a discriminatory event.

In contrast, several studies have indicated structural racism is associated with blunted amygdala reactivity to threat. In one study of young adults, Black participants showed reduced amygdala reactivity to threat (and reduced SCRs) compared to White participants during threat conditioning which were largely mediated by differential exposure to outcomes of structural racism including neighborhood disadvantage, violence exposure, and income (Harnett et al., 2019). The literature on amygdala reactivity in youth has been mixed (c.f., Suarez et al., 2022; Huggins et al., 2022), perhaps in part because the majority of work has been conducted in ethnoracially diverse youth and employed different tasks. Still, one study found neighborhood disadvantage was associated with lower amygdala reactivity to negatively-valanced images in children (Huggins et al., 2022). Thus, the effects of structural racism appear to be associated with reduced amygdala reactivity to threat, an effect that parallels the relationship between structural racism and reduced peripheral expression of the emotional response (e.g., lower SCRs).

In adults, structural racism is related to greater amygdala resting-state connectivity with other brain regions involved in threat processing. In a sample of predominately Black adults who recently experienced a traumatic event, participants who lived in areas with greater

Table 1
Overview of Neuroimaging Studies Examining the Effects of Structural and Personally Mediated Racism.

Study	Total N (% gender or sex * and % Black or African American)	Racism measure	Imaging method	Region(s) of Interest	Relevant Finding
Clark, Miller, & Hegde, 2018	N = 74 (43% women; 72% African American)	Racial discrimination (Everyday Discrimination Scale)	Resting-state fMRI.	Amygdala	Greater discrimination associated with greater intrinsic amygdala activity and greater connectivity with salience detection.
Webb et al., (2022)	N = 102 (57% female; 100% Black/African American)	Racial discrimination (Perceived Ethnic Discrimination Questionnaire)	Resting-state fMRI.	Amygdala and Insula	Greater discrimination associated with greater amygdala -thalamus and insula – precuneus connectivity.
Harnett et al., (2019)	N = 198 (50% female; 72% Black American)	Violence exposure, neighborhood disadvantage, family income	Task-based fMRI; electrodermal activity.	Amygdala	Lower SCL and fewer SCRs to threat in Black compared to White participants. Reduced amygdala reactivity during threat conditioning task in Black compared to White participants.
Webb et al., (2021)	N = 165 (55% female; 58% Black/African American)	Neighborhood disadvantage (Area Deprivation Index)	T1w structural MRI; resting-state fMRI.	Amygdala, Hippocampus, PFC, and Insula	Greater neighborhood disadvantage related to reduced hippocampal and vmPFC volume. Greater disadvantage associated with greater amygdala – inferior parietal and insula-ventrolateral PFC connectivity.
Harnett et al., (2023)	N = 283; 64% female; 47% Black American)	Neighborhood disadvantage (Area Deprivation Index)	Task-based and resting-state fMRI; electrodermal activity; startle responses.	Amygdala	Black trauma survivors showed lower skin conductance levels and startle responses compared to White trauma survivors. Black and Hispanic trauma survivors displayed greater amygdala connectivity with salience regions and cerebellum compared to White trauma survivors. There were no significant ethnoracial differences in amygdala reactivity to threat.
Zahodne et al., (2022)	N = 221 (66% female; 100% Black individuals; 92% US-born)	Racial discrimination (Everyday Discrimination Scale and Major Experiences of Lifetime Discrimination Scale)	T1w structural MRI; T2w FLAIR.	Hippocampus and whole brain	Lifetime racial discrimination, but not non-specific discrimination, associated with reduced hippocampal volume. Everyday racial discrimination related to greater white matter hyperintensity over time.
Fani et al., (2022)	N = 81 (100% women; 100% Black American)	Racial discrimination (Experiences of Discrimination Scale)	T1w structural MRI	Whole brain	Greater exposure to racial discrimination associated with lower caudal ACC, left rostral ACC, and posterior cingulate cortex. Racial discrimination was positively associated with right hippocampus and negatively associated with posterior cingulate volume before correction for multiple comparisons.
Fani et al., (2022)	N = 116 (100% women; 100% Black American)	Racial discrimination (Experiences of Discrimination Scale)	Diffusion tensor imaging	Whole brain	Greater exposure to racial discrimination associated with lower fractional anisotropy in the corpus callosum, cingulum, and superior longitudinal fasciculus.
Bell et al., (2021)	N = 303 (50% female; 68% Black American)	Neighborhood disadvantage and violence exposure	Diffusion tensor imaging	Whole brain	Greater neighborhood disadvantage, but not violence exposure, was associated with lower quantitative anisotropy of the cingulum bundle, uncinate fasciculus, stria terminalis, and fornix.
Saxbe et al., (2018)	N = 22 (57% male; 9% African-American; 14% multi-racial; 36% Hispanic/Latino)	Community Violence (Modified Survey of Children's Exposure to Community Violence)	T1w structural MRI; resting-state fMRI	Hippocampus and Amygdala	Community violence exposure was associated with smaller hippocampal and amygdala volume. Greater right hippocampal connectivity with the super temporal gyrus and insula was associated with greater violence exposure.
Hunt et al. (2020)	N = 951 (67% female; 8.2% Black or African American)	Neighborhood disadvantage (Area Deprivation Index)	T1w structural MRI	Whole brain	Living in the top 20% of disadvantaged neighborhoods was associated reduced hippocampal volume and lower total brain tissue volume.
Weissman et al., 2023	N = 11,533 (48% female; 15.0% Black American)	State-level macro-economic factors (cost of living, cash assistance, Medicaid expansion)	T1w structural MRI	Hippocampus	Cash benefits helped attenuate the relationship between lower income and hippocampal volume.
Hatzenbuehler et al., 2021	N = 11,534; 47% girls; 20% Black American)	Structural stigma (derived through factor analysis with various publicly available data) and non-specific discrimination	T1w structural MRI; Task-based fMRI	Hippocampus and Amygdala	Black youth living in states with higher structural stigma displayed smaller hippocampal volumes compared to White youth; however, no significant

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Table 1 (*continued*)

Study	Total N (% gender or sex * and % Black or African American)	Racism measure	Imaging method	Region(s) of Interest	Relevant Finding
					effect of non-specific discrimination was observed. There was no effect of structural stigma or non-specific discrimination on amygdala reactivity to threat.
Reda et al., (2021)	N = 52 (100% Black American)	Community violence (Violence Exposure Scale for Children-Revised)	T1w structural MRI; resting-state fMRI	Hippocampus	Greater violence exposure was associated with reduced hippocamps-insula connectivity and age-related decreases in connectivity were only president in youth with low exposure.
Marusak et al., (2017)	N = 86 (65% female; 45% African American)	Threat exposure (violence or abuse as defined by Children's Trauma Assessment Center Screen Checklist)	Resting-state fMRI	Ventral tegmental area	Greater exposure to early life threat was associated with lower connectivity between the ventral tegmental area and hippocampus.
Fani et al., (2021)	N = 55 (100% women; 100% Black American)	Racial discrimination (Experiences of Discrimination Scale)	Task-based fMRI	Whole brain	Racial discrimination was associated with greater responses in the ventromedial prefrontal cortex and middle occipital cortex in response to trauma-relevant versus neutral images. More exposure to racial discrimination was associated with significantly fewer errors on the task.
Elbasheir et al., (2024)	N = 40 (100% women; 100% Black American)	Racial discrimination (Experiences of Discrimination Scale)	Task-based fMRI	vmPFC and middle occipital cortex (based on Fani et al., 2021)	C-reactive protein significantly moderated the relationship between racial discrimination and neural activity in the vmPFC, but not the middle occipital cortex. Individuals with higher levels of C-reactive protein (but not low or moderate) showed significant associations between racial discrimination and vmPFC activity during attention to threat.
Masten et al., (2011)	N = 18 Black Americans (50% women)	Self-reported discriminatory attributions following the cyberball task	Task-based fMRI	Whole brain	Participants showed greater activity during exclusion in the insula and prefrontal cortex compared to inclusion. Individuals who attributed to the exclusion to racial discrimination displayed greater activity in the rostral anterior cingulate and less activity in the dorsal anterior cingulate cortex.
Han et al., (2020)	N = 124 (100% Black American; 86% female)	Racial discrimination (Everyday Discrimination Scale)	Resting-state fMRI	Insula and Amygdala	Greater insula connectivity with the intracalcarine cortex and reduced connectivity with the left dorsolateral PFC and left supplementary motor area was associated with greater racial discrimination. There was no significant effect of racial discrimination of amygdala connectivity.
Okeke et al., 2023	N = 79 (100% Black American; 100% women)	Racial discrimination (Experiences of Discrimination Scale)	T1w structural MRI	Cingulum and corpus callosum	Greater exposure to racial discrimination was significantly linked to a higher number of medical disorders via the association with cingulum bundle and corpus callosum-genu fractional anisotropy.
Dumornay et al., (2023)	N = 9382 (47% girls; 20% Black American)	Neighborhood disadvantage (Area Deprivation Index), family conflict, material hardship, trauma history, family income, employment status, parental educational attainment	T1w structural MRI	Whole brain	Black children displayed reduced amygdala, hippocampus, and PFC volumes compared to White children. Race-related structural differences were largely attenuated after accounting for structural inequities
Gard et al., 2020	n = 167 (41.4% Black American; 100% boys); n = 77 (76% Black American; 100% boys)	Neighborhood disadvantage; family-level adversities (e.g., family income; maternal education)	Task-based fMRI	Amygdala	Greater neighborhood disadvantage during early childhood was associated with greater amygdala activity to ambiguous neutral faces.
Fani et al., 2023	N = 48 (100% Black American; 52% female)	Community violence (Violence Exposure Scale for Children-Revised)	Diffusion tensor imaging	Whole brain	Greater violence exposure was associated with greater mean diffusivity in the corpus callosum, cingulum bundle – hippocampal segment, and uncinate fasciculus. Significant interactions of pubertal stage and community violence exposure were

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Table 1 (*continued*)

Study	Total N (% gender or sex * and % Black or African American)	Racism measure	Imaging method	Region(s) of Interest	Relevant Finding
					found in all three tracts. Females, but not males, showed a significant relationship between violence exposure and right uncinate fasciculus integrity.
Huggins et al., (2022)	N = 254 (48% female; Black American 30%)	Neighborhood disadvantage (Area Deprivation Index)	Task-based fMRI	Whole Brain	Greater neighborhood disadvantage was associated with greater activity in the left anterior cingulate cortex and reduced activity in the right parahippocampal gyrus, hippocampus, and amygdala to negative versus neutral pictures.
Ramphal et al., (2020)	N = 127 (48% female; 20% Black American)	Neighborhood disadvantage (Area Deprivation Index)	resting-state fMRI	Amygdala; ventromedial PFC	Greater neighborhood disadvantage was associated with decreased amygdala-ventromedial PFC connectivity in youth.
Tomas et al., 2022	N = 90 (57% female; 53% Black American)	Neighborhood disadvantage (Area Deprivation Index)	Task-based fMRI	Whole brain	Neighborhood disadvantage was related to less activation in the anterior cingulate cortex during anticipation of unpredictable neutral stimuli compared to predictable neutral stimuli.
Jorgensen et al., 2022	N = 165 (53% female; 22% Black American)	Neighborhood disadvantage (Area Deprivation Index); Economic hardship; parental education and family income.	Task-based fMRI	Whole brain	In Black youth, neighborhood disadvantage was associated to greater ACC, insula, amygdala, putamen, and inferior frontal gyrus, reactivity to threat compared to White youth. Neighborhood disadvantage was associated with greater neural reactivity to reward in Black youth compared to White youth in the insula, putamen, inferior frontal gyrus, temporoparietal junction, PFC, amygdala, and ventral striatum.

Note: * Author's reported sex (e.g., "female") and/or gender (e.g., "women") is provided. **Abbreviations: ACC:** anterior cingulate cortex; **PFC**: prefrontal cortex; **SCL:** skin conductance level; **SCR:** skin conductance response.

neighborhood disadvantage displayed greater amygdala connectivity with the inferior parietal lobule (Webb et al., 2021b). Another study, also in trauma-exposed adults, found Black participants showed greater connectivity between the amygdala and insula, dorsolateral PFC, and cerebellum acutely post-trauma compared to White participants (Harnett et al., 2023). Notably, connectivity between the amygdala and these regions was predictive of greater PTSD symptoms three-months later but only in Black individuals (Harnett et al., 2023). As the majority of this work has been conducted in recent trauma survivors, additional studies should examine amygdala connectivity and reactivity in trauma-naïve individuals. However, the emergent pattern reveals structural racism may contribute to blunted amygdala reactivity to threatening stimuli but stronger amygdala connectivity to regions that modulate expression of the emotional response.

2.3.2. *Hippocampus*

Personally mediated racism is associated with alterations to hippocampal structural features. In a longitudinal study, lifetime discrimination was associated with reduced hippocampal volume among Black older adults (Zahodne et al., 2022). Racism-related stress further appears to contribute to deterioration of hippocampal white matter pathways. In a sample of trauma exposed Black women, racial discrimination was associated with lower integrity in the cingulum, a primary white matter connection between the hippocampus and prefrontal cortex, as well as the corpus callosum and superior longitudinal fasciculus (Fani et al., 2022a). Together, these findings suggest that racial discrimination impacts hippocampal structure as well as structural connectivity between the hippocampus and other regions involved in threat processing (e.g., amygdala, PFC) which may result in perturbations in emotion regulation and responses to threatening stimuli.

Similar to personally mediated racism, structural racism appears to impact hippocampal microarchitecture and structure. In an ethnoracially diverse sample, greater neighborhood disadvantage during adolescence was linked to lower white matter tract integrity in adulthood of the dorsal cingulum and the fornix, which connects the hippocampus to subcortical regions including the ventral striatum and hypothalamus (Bell et al., 2021). Racism-related stressors in the form of socioeconomic-based adversity and trauma exposure are also related to lower integrity in these two tracts (Averill et al., 2018; Rakesh et al., 2021). Neighborhood poverty and community violence – which are more often experienced by Black individuals compared to White individuals – are also consistently associated with hippocampal structural reductions across the lifespan (Webb et al., 2021b; Saxbe et al., 2018; Hunt et al., 2020).

A recent study found that Black youth living in states with higher structural stigma showed smaller hippocampal volumes compared to White youth (Hatzenbuehler et al., 2022). Structural stigma was quantified using a factor analytic approach with publicly available indicators (e.g., project implicit) and captured stigma related to race, ethnicity, and sex/gender (Hatzenbuehler et al., 2022). However, in this study, discrimination was not associated with hippocampal volume for Black youth in highly stigmatized environments (Hatzenbuehler et al., 2022). Notably, the measure of discrimination collected as part of the parent study (the Adolescent Brain Cognitive Development Study) was non-specific and did not differentiate between racial, gender, or other forms of discrimination, possibly masking important differences. Beyond the effects of stigma, environmental toxins, such as lead, have a great affinity for hippocampal tissue and induce neurotoxic affects which influence the molecular underpinnings of memory (e.g., neurotransmitter receptor levels) (Zhao et al., 2021). Disparate exposure to environmental toxins is a documented component of systemic environmental racism, which perpetuates health inequities (Washington, 2019). For example, Black families are more often exposed to lead through a number of sources, and lead is known to cause hippocampal atrophy

(Sharifi et al., 2002; Marshall et al., 2020). Thus, various mechanisms of structural racism can simultaneously target the hippocampus and link racism to alterations in a region underlying threat processing.

Two recent studies suggest that structural racism may also alter how the hippocampus functionally interacts with other threat-related regions. In Black youth, greater exposure to community violence was associated with greater hippocampus connectivity with the posterior cingulate cortex (PCC) and reduced connectivity with the insula (Reda et al., 2021). The PCC is involved in directing internal attention toward emotionally-charged stimuli and self-reflection (Reda et al., 2021). These findings underscore that structural racism is associated with disruptions in hippocampal connections with threat-related regions, but recent work suggests connections with reward-related regions are also altered. In a separate study of racially diverse youth found that participants exposed to early life threat (violence and abuse) displayed reduced connectivity between the hippocampus and ventral tegmental area compared to trauma naïve youth (Marusak et al., 2017).

2.3.3. Prefrontal cortex

Recent work demonstrates personally mediated racism has discernable effects on the function of prefrontal cortex (PFC) subregions (Fani et al., 2021a). For example, racial discrimination was associated with greater reactivity in the vmPFC and visual regions to threat-relevant images in a sample of trauma-exposed Black women and this effect persisted when accounting for PTSD symptoms (Fani et al., 2021a). Notably, a follow-up, multi-modal analysis found that levels of C-reactive protein moderated the associations between racial discrimination and the vmPFC activity (Elbasheir et al., 2024). Only individuals with higher levels of the inflammatory marker showed a relationship between racial discrimination and greater vmPFC activity. In a separate study, Black participants who faced exclusion during a cyberball task showed greater activity in the vmPFC when the exclusion was attributed to racial discrimination (Masten et al., 2011). Individuals who attributed the exclusion as racially discriminatory displayed less activity in dACC and greater activity in the rostral ACC (rACC) (Masten et al., 2011). Whereas the dACC is thought to detect social threat, the rACC is thought to help control the emotion response during social situations (Whalen et al., 1998). Together, these findings may suggest that personally mediated racism leads to greater recruitment of regions which aide emotion regulation and threat response suppression strategies.

In addition to differential functional activity of the PFC (Fani et al., 2021a), Black women with more experiences of racial discrimination also show lower gray matter volume of the PFC and lower white matter integrity of the dorsal cingulum bundle and superior longitudinal fasciculus which connect the PFC and posterior cingulate and parietal areas (Fani et al., 2022a, 2022b). Importantly, the effects of racial discrimination were persisted when accounting for other types of trauma and PTSD symptoms in the sample. Furthermore, lesser integrity of these tracts explained the link between racial discrimination and physical health outcomes (Okeke et al., 2023). Taken together, this collection of results from similar samples suggest personally mediated racism can alter the structure of the PFC which may contribute to differential health outcomes.

Structural racism also has demonstrable effects on the structure of subregions within the prefrontal cortex (PFC). Components of structural racism including neighborhood disadvantage, various environmental toxins, and lower socioeconomic position, are all significantly associated with reduced PFC volume and thickness (Webb et al., 2021b; Rakesh et al., 2021; Gale et al., 2020; Cecil et al., 2008). While the majority of this work has been conducted in ethnoracially diverse samples, a recent study (Dumornay et al., 2023) suggests these variables help explain racism-related differences in neurobiology. Dumornay and colleagues (2023) found structural inequities contribute to lower PFC volume (as well as reduced amygdala volume) in Black compared to White youth. In studies on fear learning, PFC reductions are related to differences in reactivity to threat and the expression of the peripheral threat response (Milad et al., 2005), suggesting a potential mechanism underlying differences in SCR and HRV.

In Black youth, neighborhood disadvantage was associated with greater reactivity to social threat in the ACC (as well as insula, amygdala, putamen, and inferior frontal gyrus) compared to White youth (Jorgensen et al., 2023). In adult trauma survivors, neighborhood disadvantage was associated with reduced activity in the ACC during anticipation of unpredictable neutral stimuli compared to predictable neutral stimuli, suggesting that predictability of threat may modulate threat reactivity. Neurodevelopmental timing may also help explain differential effects of structural racism. Among ethnoracially diverse youth, greater neighborhood disadvantage was associated with accelerated maturation of vmPFC - amygdala connectivity (Ramphal et al., 2020). Youth whose neurodevelopment diverged from this pattern showed more severe anxiety, suggesting this neurobiological adaptation may confer an initial benefit to youth (Ramphal et al., 2020). However, more longitudinal work is needed, as this pattern is related to anxiety in adulthood (Ramphal et al., 2020). Together, these studies suggest structural racism has an important impact on threat reactivity that varies with the type of threat (e.g., social, predictable) and developmental period.

2.3.4. Anterior insula

Personally mediated racism is also associated with the activity and connectivity of the insula. During the aforementioned study employing the cyber-ball task, Black participants also showed greater activity in the anterior insula (Masten et al., 2011). In contrast to previous work which has linked the anterior insula to affective responses (Uddin, 2015; Uddin et al., 2017; Singer et al., 2009), insula activity was not correlated to the participant's self-reported distress following the event (Masten et al., 2011). In Black trauma survivors, exposure to racial discrimination is also associated with greater connectivity between the anterior insula and other regions such as the precuneus and intracalcarine cortex which support self-referential processing and evaluation of threatening situations (Webb et al., 2022b). Both the precuneus and intracalcarine cortex support mental imagery in social situations and processing of visual stimuli, respectively (Cabanis et al., 2013; Cavanna et al., 2006). For example, prior work on non-specific discrimination in general has demonstrated that the precuneus responds to social conflict and shows greater activity when a participant attempts to take the perspective of another individual (Petrini et al., 2014). Therefore, the pattern of results from these two studies imply that racism potentiates neural systems implicated in identifying social violations.

The anterior insula is also implicated in non-social threat learning and has reciprocal connections with established threat network nodes, including the PFC (Olson et al., 2019). In older adults, greater exposure to racial discrimination is associated with reduced connectivity between the insula and dorsolateral PFC (Han et al., 2020). As described above, the PFC helps down-regulate subcortical threat responses (e.g., insula activity) and may mediate the cognitive processes required to assess and respond to social threats. However, additional work is needed to determine whether persistent exposure to racial discrimination reliably affects connectivity between the two regions typically characterized as underlying both threat and social processing.

2.4. Summary

As reviewed above, both personally mediated and structural racism are associated with changes in threat-related neurophysiology. The established threat network (i.e., amygdala, hippocampus, prefrontal cortex) appears to undergo significant alterations, from smaller structural volumes to changes in neural reactivity to threat (Fig. 3). Despite the recent growth of research in the neurobiological effects of racism-related stress, there are several noteworthy gaps in our understanding of the effect of racism-related stress on the discussed circuitry. For example, the impact of racism-related stress on neurobiology may vary

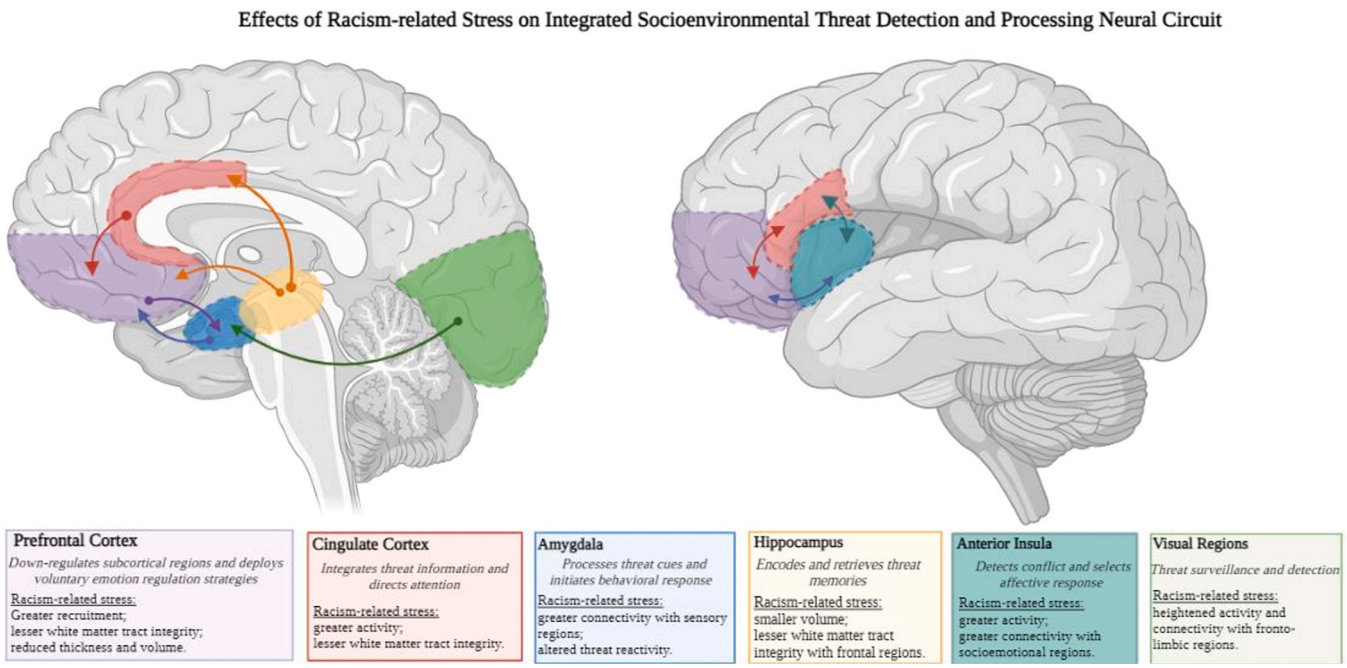

Fig. 3. Racism-related stressors are associated with alterations to neural circuits underlying threat and social processing. For each color-coded region, the related functions are italicized, and the effects of racism-related stress are listed in the color-corresponding box below.

based on sample characteristics (e.g., community sample, undergraduate students, location, ethnoracially diverse) and current research may not have high representation of the breadth of socioeconomic backgrounds of people within different ethnoracial groups. Further, developmental timing of racism-related stress exposure may influence chronicity, duration (i.e., acute vs chronic exposure), or specific types of stressors (e.g., discrimination at school), which may be tied to differing neurobiological effects. Still, although the research on racism-related stress and neurophysiology is limited, the most consistent theme is that racism is a unique form of stress, affecting brain structure and function above and beyond other forms of stress (e.g. traditional trauma exposure) (Fani et al., 2022a, 2022b).

The reviewed work illustrates that both social and threat regulation processes are required to confront racism-related stress. We suggest that the literature currently reveals mixed patterns of engagement in threat and social processing neurophysiology that appear to depend, in part, on whether the stressor reflects personally mediated racism or structural racism. For example, structural racism appears to blunt peripheral expression of the emotional response and reactivity in threat-related neural circuitry. While structural racism may initially facilitate amygdala preparedness to rapidly receive threat-relevant sensory information, such constant recruitment may in fact lead to attenuation of the resultant threat response. In contrast, personally mediated racism may invoke greater engagement of threat-related regions. Increased activity of regions involved in threat and social processing may represent an adaptation driven by chronic and frequent – but unpredictable – racism-related adversity.

Neural adaptions may support resiliency in the face of a discriminatory experience by priming circuitry to identify early signs of racism and prepare the brain to respond in the safest manner. However, prolonged recruitment of threat circuitry at unpredictable times may result in a significant biological cost as evidenced by reduced gray and white matter structure (wear and tear). The emerging empirical findings (particularly the studies on racial discrimination and PFC activity and structure) align well with theoretical frameworks outlining the potential consequences of neural adaptations. Geronomius and colleagues (Geronimus, 1992) noted that adaptive, compensatory mechanisms may mitigate immediate effects of racism but have negative downstream health outcomes. Prior work suggests Black individuals may engage in "high-effort coping" strategies in response to racism such as cognitive reappraisal (Geronimus et al., 2006). However, cognitive and affective resources needed to engage in coping strategies are finite, and perpetual deployment of these strategies may lead to increased stress on neurophysiological systems underlying threat and social processes (Geronimus et al., 2006). The increased demand may accelerate decline or dysfunction of biological systems and contribute to overall declines in both physical and mental health. Ultimately understanding erosive consequences of racism-related stress on neurophysiological processes may reveal possible pathways to the development of stress- and trauma-related disorders.

3. Racism-related stress and neural bases of stress- and trauma-related disorders

A more thorough characterization of the neurophysiological effects of racism-related stress may facilitate greater understanding of racially inequitable risk for neuropsychiatric disorders. The research reviewed above indicates racism-related stress contributes to variation in neural circuits and processes known to play critical roles in depression, anxiety, and posttraumatic stress disorder. Further, many of the patterns associated with racism-related stress (e.g., reduced insula-dlPFC connectivity, greater amygdala reactivity to threat, lower cingulum white matter tract integrity, etc.) are present in individuals with anxiety, depression, and PTSD. Although not all of the patterns may be indicative of causal links between racism-related stress and neuropsychiatric conditions, some of the neurophysiological changes associated with racism-related stress may contribute to race-related differences observed across these disorders. In this section, we briefly present possible neurophysiological mechanisms linking racism to these disorders.

The different types of racism-related stress may differentially exacerbate structural and functional alterations in the amygdala relevant to psychiatric conditions. The effects of personally mediated racism mirror many of the typical neural signatures of trauma and related neuropsychiatric disorders. For example, greater amygdala reactivity to threat cues is linked to stress and trauma-related disorders including PTSD and general anxiety (Cisler and Koster, 2010; Fani et al., 2012; Powers et al.,

2019). In contrast, structural racism is associated with less reactivity to threat (Harnett et al., 2019). Amygdala hypoactivity to threat is linked to feelings of emotional numbing and disconnection from self (e.g., dissociation) (Fenster et al., 2018). Although the effects of personally mediated racism and structural racism on amygdala activity may differ, both components share similarities with neural features of stress- and trauma-related disorders symptom profiles.

Racism-related stress and stress- and trauma-related neuropsychiatric conditions are often both associated with smaller hippocampal volume. Racial discrimination is associated with smaller hippocampal volume across time (Zahodne et al., 2022) and reductions in hippocampal volume may be both a risk factor and/or a consequence of various neuropsychiatric conditions across the lifespan (Morey et al., 2016; Bonne et al., 2001; Hayes et al., 2017; Neumeister et al., 2005; Mondelli et al., 2011). Hippocampal structural differences are frequently linked to experiences of psychological trauma and may have predictive utility for PTSD and depression (Morey et al., 2016; Neumeister et al., 2005). In relation to threat processing, smaller hippocampal volume is associated with greater reactivity to threat (Fani et al., 2013). Together, in addition to amygdala changes, hippocampal changes may help explain the relationship between personally mediated racism and stress- and trauma-related disorders (Mekawi et al., 2021b; Lu et al., 2017; Cisler et al., 2010).

Anterior insula alterations may facilitate the development of stress- and trauma-related symptoms. For example, differences in insula resting-state connectivity, including with regions associated with outcomes of structural racism such as the precuneus, can help explain depressive and anxiety symptoms (He et al., 2022). Moreover, PTSD is associated with reduced resting-state connectivity between the dorsolateral PFC and anterior insula (Rangaprakash et al., 2017) and current work reveals PTSD and racial discrimination evoke the same patterns of functional dynamics between these regions (Olson et al., 2019). However, additional work is needed to clarify the anterior insula's contribution to processing racially discriminatory events.

The literature offers a persuasive link between racism-related stressors, the structure and function of the PFC, and PTSD symptom development (Harnett et al., 2023; Fani et al., 2021a). The reviewed studies suggest that repeated exposure to racial discrimination recruits critical cognitive resources to cope with threat, evidenced by greater engagement of PFC regions in response to threat-relevant images (Fani et al., 2021a). However, depletion of resources may diminish the neural ability of the PFC to respond in future stressful or traumatic events and more broadly weather neural circuitry (e.g., as evidenced by lesser white matter tract integrity and decreased cortical thickness (Fani et al., 2022a, 2022b). In tandem with alterations to other regions, we propose these neurophysiological effects that may uniquely contribute to susceptibility for stress and trauma-related disorder development.

4. Considerations and future research directions

Future work is needed to fully capture the neurobiological consequences of racism and begin to translate research into effective interventions at both systemic and individual levels. Major limitations of the current body of work include that studies are predominantly cross-sectional and correlational, employ a single measure of racism (e.g., neighborhood disadvantage), and are unimodal (e.g., examine just neural activity). We highlight four relevant lines of inquiry which, if addressed, will offer valuable information on how racism-related stress impacts the health and wellbeing of Black individuals. The first recommendation is to disentangle the effects of personally mediated and structural racism. The second recommendation is to consider intersectionality in study designs which requires actively welcoming marginalized individuals in research. The third recommendation, which calls for more research on racism-related stress across the life course, is emphasized by the dearth of work on racism and neurodevelopment. The fourth recommendation proposes that multi-modal work may reveal additional mechanisms through which racism may contribute to biological susceptibility to neuropsychiatric disorders. Finally, we end by outlining future directions in the characterization of resilience/resistance factors which may provide a stress-buffering role.

4.1. Disentangling and measuring domains of racism-related stress

Although personally mediated and structural racism may have differential effects on neurophysiology, there are limited studies that have adequately assessed either domain. Neurobiological studies of racism-related stress have further not addressed interactions among the domains and have relied on relatively weak proxy measures (Hardeman et al., 2022; Dean et al., 2022; Adkins-Jackson et al., 2021). Considering both individual and combinatorial effects of personally mediated and structural racism may aide in characterizing the full neurophysiological impacts of racism-related stress.

Although the quantification of racism has progressed, there is also a need for more refined and comprehensive assessments (Adkins-Jackson et al., 2021). A complete review of methodological challenges is outside the scope of this article (for more in-depth reviews see (Adkins-Jackson et al., 2021; Neblett, 2022), however we note that, across the studies reviewed in this article, indicators of racism-related stress are inconsistent which creates challenges with interpreting collective findings. Part of this inconsistency, particularly when quantifying structural racism, reflects the multidimensional nature of the oppressive system. The complexities of measuring racism across individuals, place, and time, further emphasizes the need and opportunity for interdisciplinary approaches (as emphasized by Neblett, 2022).

In addition, close attention should also be directed to how personally mediated racism is experimentally studied. Currently, studying neurophysiological changes in response to acute personally mediated racism often involves an experimental manipulation. Prior work has designed different manipulations that subject the participant to a laboratory-based racially discriminatory event. The study of personally mediated racism does not necessitate subjecting participants to racial discrimination. Self-report measures of personally mediated racism offer high validity and reliability (Krieger et al., 2005; Motley et al., 2023), with similar potential issues (e.g., recall bias) associated with other self-report measures (e.g., assessments of trauma exposure). Alternative approaches, such as ecological momentary assessment, may help address these potential issues and be better suited to study real-time responses to real-world racial discrimination which may already be frequently occurring in Black participants' everyday lives.

4.2. Intersectionality and inclusion of marginalized groups

An individual's experience of racism varies based on their other identities. For example, Black women, who are impacted by both racism and sexism, show the highest biological burden of exposure to racism-related stress (Allen et al., 2019; Carlson et al., 2005; Geronimus et al., 2006). Nearly all the reviewed work was constricted to one axis of oppression (racism) with few considering other systems of power (e.g., classism, sexism). This one-dimensional approach constricts individuals to a single identity and impedes the characterization of how cumulative oppressive stress may be impacting neurophysiology and mental health (Carter et al., 2022b). Additional work, which leverages both the theoretical and statistical utility of intersectionality, will help elucidate whether the associations reviewed are specific to racism or related to the effect of interconnected societal forces.

In order to actually employ an intersectional approach, recruitment of representative research participants must be purposeful. Participants of neuroimaging studies are predominately White, college-educated, and from Western countries (Ricard et al., 2023) which can yield erroneous insights into neurophysiological processes. Biased recruitment practices along with under-reporting of demographic information impedes assessment of the quality of the evidence, particularly the

generalizability of neural biomarkers. For example, a recent study attempted to evaluate whether the relationship between hippocampal volume and depression was moderated by structural inequities, however, too few studies reported race and ethnicity to reliably conduct the metanalysis (Keyes et al., 2023).

4.3. Considering differential effects of racialized stress across the life course

Critical to understanding the neurobiological consequences of racism is a better characterization of its effects across development. Nearly 90% of Black youth in the United States report experiencing discrimination in the past year (Seaton et al., 2008). Psychological research reveals that associations between racism and mental health vary with developmental timing (Neblett, 2019b; Jones et al., 2017) and likely have intergenerational effects (Kirkinis et al., 2018). For example, a longitudinal study demonstrated that Black youth experiencing higher levels of racial discrimination were more likely to develop future depression symptoms than youth reporting less discrimination (Lavner et al., 2021). In addition, Black youth who experienced higher exposure to discrimination compared to earlier timepoints also showed increases in depression symptoms (Lavner et al., 2021), suggesting the effects of racial discrimination were amplified across over the one year study. Future work is needed to evaluate how racism-related stress differentially impacts neurodevelopment across life stages and how exposure may have compounded effects across the lifespan in individuals as well as their offspring.

Limited work to date has directly investigated developmental impacts of racism-related stress on threat neurocircuitry. Emergent work in children further suggests structural racism impacts gray and white matter volume of the circuit (Hatzenbuehler et al., 2022; Dumornay et al., 2023; Fani et al., 2021b; Dufford et al., 2019), albeit the direction of findings have been mixed depending on exposure. Still, the majority of studies are consistent with general research that has investigated socioenvironmental impacts on brain development in general and have shown that early chronic stress (e.g., childhood maltreatment) is associated with accelerated maturation of brain volume and cortical thickness that contribute to altered neurobiology in adulthood (Teicher et al., 2003). In addition, studies on socioeconomic disadvantage have shown that this chronic stress is initially associated with earlier maturation of fronto-limbic circuitry and greater sensory network integration (Rakesh et al., 2021; Noble et al., 2012; Hardi et al., 2022), even in neonates (Lean et al., 2022; Brady et al., 2022).

However, additional work is needed to fully disentangle how the effects of racism-related stress on neural networks may unfold over time. Increased attention should be given to the neural effects of racism-related stress in early developmental periods. Given chronicity of racism-related stress is associated with differential neural patterns, examining impact of these stressors across sensitive windows in development (e.g., puberty) is critical. Further work should also consider potential intergenerational transmission of stress and resilience between parents and children. Parental behaviors and coping strategies for racism-related stress may be passed to children and affect neurocircuitry. In addition, longitudinal studies designed to elucidate how racism becomes biologically embedded throughout the life course are needed. Longitudinal studies often show a clearer impact of racism on psychological functioning than cross-sectional studies (Kwate et al., 2015). Therefore, resources should be directed towards nuanced investigations of how racism-related stress affects neurodevelopment.

4.4. Leveraging multimodal approaches to examine biological mechanisms

The majority of reviewed studies have examined the effects of racism-related stress on a single modality, examining either peripheral indices or neural activity. However, additional multimodal work is needed to establish the mechanistic roles and relationships of these indicators. One promising pathway to explore is between inflammation and neural activity. Pro-inflammatory proteins and cytokines influence changes in neurotrophin expression, including reductions in brain-derived neurotrophic factor (BDNF) (Calabrese et al., 2014). BDNF plays a critical role in neural development and function and significantly predicts symptoms of neuropsychiatric disorders, particularly depression and PTSD (Zhang et al., 2016; Porter et al., 2022). While no work to date has investigated inflammatory markers, BDNF, and neural activity, emerging studies suggest inflammation may influence observed neural changes associated with racism-related stress. As previously mentioned, Elbasheir and colleagues (2024) demonstrated levels of C-reactive protein modified associations between racial discrimination and reactivity to threat. However, this work was cross-sectional and future directions should include exploring longitudinal relationships between various inflammatory markers, neurotropic factors, and neurophysiology, specifically testing whether inflammation may be the primary mediator.

4.5. Characterizing and promoting resilience / resistance factors

An important future direction for the field is to understand how to increase resilience to racism-related stress. Although part of that research involves understanding the neurophysiological mechanisms, focus should include what factors foster Black individuals' functioning, adapting, and thriving even when in the context of ongoing racism. Psychological resilience / resistance factors may buffer against effects of racism-related stress or facilitate the development of protective physiological adaptations. Emerging work has evaluated moderators that may help buffer against racism-related neuronal atrophy. For example, in older Black men, greater social support was associated with greater hippocampal volume (Bygrave et al., 2021). Future directions include extending the substantial work on resilience / resistance factors and psychological functioning suggesting racial-ethnic identity, community support, and societal engagement can protect against stress- and trauma-related disorder development.

Addressing racism requires structural societal changes. Research focused on neurophysiological mechanisms can elucidate how racism-related stressors become biologically embedded. However, this work in isolation will not overhaul racism's roots (i.e., laws, policies, and practices) or give rise to lasting change. More specifically, mitigating the effects of structural racism through individual intervention is misguided as it shifts societal responsibility to Black individuals. Neuroscience research should assist ongoing work examining the effectiveness of structural changes. Future neuroscience work could examine whether population-level interventions also confer protective effects against racism-related changes in threat and social processing neural circuitry. Thus, neuroscience may help guide changes in institutions and monitor the effectiveness of structural change (Jay et al., 2022).

5. Conclusion

Racism-related stressors contribute to differential neurophysiological responses. The shared and distinct effects of personally mediated and structural racism become more apparent when considering evidence from both physiological and neuroimaging studies. While structural racism is associated with diminished threat-responses, personally mediated racism seems to elicit heightened reactivity to threat. Further, the evidence demonstrates that beyond threat-related circuitry, regions involved in social processing are also engaged by experiences of racism. Neural changes in these circuits may serve to protect individuals from experiences of racism-related stress. However, the persistent activation of these circuits carries a significant biological cost. This biological cost becomes tangible when comparing how similar the neural underpinnings of stress- and trauma-related disorders are to the neural effects of racism-related stress. Thus, the study of neurophysiological responses to racism is essential to addressing the racial inequities in

neuropsychiatric disorders.

Ignoring the effects of racism-related stress, applying a colorblind neuroscience or psychological framework (in which individuals are treated without consideration to race, culture, or ethnicity), or generalizing findings from samples comprised entirely of White individuals, will not yield more insight into risk for stress- and trauma-related disorders in Black individuals (Carter et al., 2022a; Webb et al., 2022a). Context matters when interpreting the neurobiological basis and development of these and other disorders. From behavior and neurophysiology to clinical symptoms, the effects of racism become encapsulated in results. Without this consideration, findings of studies can be interpreted inaccurately, and in ways that further stigmatize and harm Black individuals. This conceptualization is also necessary for developing preventative efforts, discovering biomarkers, selecting effective clinical treatments for Black individuals, and informing structural changes.

Disclosures

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