# RACISM'S IRREFUTABLE HARMS

## How Racial Trauma Has Been Shown to Impact the Brain for Generations

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# INTRODUCTION

Racism, a deeply entrenched social construct, has impacted minoritized populations globally for generations. This has led to discrimination, lost economic opportunities, incarceration, and premature death.[1] In 2021, the United States Centers for Disease Control and Prevention (CDC) declared racism a "serious public health threat."[2] According to the CDC, racism impacts physical and mental health outcomes disparately across minoritized communities.[2,3] Now, research suggests that the insidious nature of discrimination, racism, and perpetual racial trauma endured by minoritized individuals acts as a chronic stressor.[4] This stressor is associated with structural and functional changes in brain regions involved in threat detection and emotional processing.[4–9] The impact of racism on the brain appears to mirror neural activity patterns observed in trauma-related neuropsychiatric disorders, such as post-traumatic stress disorder (PTSD), depression, anxiety disorders, bipolar disorder, and borderline personality disorder, potentially linking racism to disparate rates of mental health.[1,4,10,11]

The pernicious effects of historical, structural, and personally mediated racism extend beyond individuals who directly experience racial trauma and into subsequent generations. The chronic stress of racism can heighten awareness and sensitization, embedding itself into neurobiological systems through mechanisms such as epigenetic modifications, altered gene expression, and dysregulated stress responses. This toxic effect of racism may begin as prenatal stress, disrupting maternal neuroendocrine functions and fetal neurodevelopment, thereby furthering disparate mental health outcomes.[12–19]

This evidence points to the profound and far-reaching implications of racism across generations. This report analyzes how racial trauma affects brain structure and function and how these effects manifest in neuropsychiatric conditions such as depression, PTSD, and anxiety. It also examines the genetically and epigenetically embedded impact that begins in prenatal stages and extends to subsequent generations. Thus, this narrative beckons a bridging of neuroscience, social justice, and public health, urging an integrated approach to mitigating the perpetuating cycle of racial trauma and mental health inequities in minoritized communities.



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# PURPOSE OF THE REPORT

Racism, as a social determinant of health, is consistently linked to psychological distress and neuropsychiatric disorders, including mood disorders, psychotic disorders, PTSD, neurodegenerative diseases, and substance use disorder (SUD).[4,6,20–23] Recent research has examined the link between racial trauma and neurobiological changes among minoritized populations, with current evidence suggesting racial discrimination can trigger changes in brain structure and function.[5-9,24,25] While the recent research is a promising indicator of growing interest in determining the role racism plays in mental health inequities, research on the effects of racial discrimination on mental health, neurobiology, and across generations, more needs to be done. This report provides an in-depth analysis of the literature, offering a comprehensive assessment of the pathophysiological and intergenerational impact of racial trauma on historically minoritized populations.

**RACISM IS CONSISTENTLY TIED TO MOOD DISORDERS, PSYCHOTIC DISORDERS, PTSD, NEURODEGENERATIVE DISEASES AND MORE.[4,6,20-23]**

This report also reviews the current epidemiology, which is the study of how often diseases occur in different groups of people and why, specifically focusing on mental health conditions among minoritized populations while acknowledging that there are persistent limitations in the breadth and depth of currently available studies. The lack of research on mental health inequities, which are the unfair differences in mental health care and outcomes among different groups, significantly hampers studies examining the impact of racism on mental health. Without robust data on existing inequities in mental health access, treatment, and outcomes, researchers have an incomplete picture of the systemic barriers—widespread obstacles within society and institutions—that exacerbate these mental health concerns. This knowledge gap makes it difficult to accurately identify the extent to which racism influences mental health, as disentangling its effects from broader health care inequities is challenging. Consequently, the conclusions may be less precise, and the development of targeted interventions may be less effective, perpetuating inadequate mental health care for many minoritized communities.[4,26-28] Additional limitations are briefly discussed on page 8 and have been extensively reviewed.

The objectives of this report are to:

- Elevate awareness of the association between racial trauma and the impact on brain structure and function in historically minoritized communities.
- Identify strategies to address multifaceted barriers at the individual, societal, and systems levels to advance neuropsychiatric care and mitigate the generational impact of racial trauma.
- Review the current landscape of mental and cognitive health inequities among historically minoritized communities.

By showing up as a beacon for research and innovative solutions, Otsuka, in close collaboration and partnership with critical stakeholders, continues a generational conversation built on 30 years of experience in neuroscience and mental health. These collective insights seek to identify solutions and create tools and resources that may help mitigate the adverse effects of racial trauma and support the advancement of neuropsychiatric care in historically underserved communities and future generations.

# THE LINKS BETWEEN RACISM, RACIAL DISCRIMINATION, AND RACIAL TRAUMA

Discussing the impacts of racial trauma on the brain requires a clear understanding of key terms related to race and racism. The terms and definitions listed below are used throughout the report regardless of how they are discussed in this narrative review.

- *Racism* is a belief that race is a determinant of human traits and capacities and that racial differences produce an inherent superiority of a particular race.[29] Racism results in conditions that unfairly advantage some and disadvantage others.[2]
- *Racial discrimination* is inclusive of unjust treatment, marginalization, and unequal experiences. The lived experience of racism is inclusive of racial discrimination. This may include physical violence, daily insults, frequent acts, and verbal expressions of contempt and disrespect.[30]
- *Racial trauma* is a psychological and emotional response resulting from repeated exposure to racism.[31] Racial trauma focuses on how repeated racism can cause psychological and emotional responses similar to those caused by other traumatic events. Racial trauma can be the result of a specific incident or the cumulative experiences of racism, including as a byproduct of more expansive systems (e.g., systemic or institutional racism).[31]

# DIRECT AND INDIRECT IMPACTS OF RACISM ON HEALTH

An emerging body of research indicates that the stress of racial trauma negatively impacts the body, manifesting in diverse and complex ways. Experiencing racial discrimination is associated with a higher risk of chronic metabolic diseases (e.g., cardiovascular disease, coronary artery calcification, diabetes), mental health conditions (e.g., depression, anxiety disorders, post-traumatic stress disorder), and nonspecific pathology (e.g., inflammation, oxidative stress, cortisol dysregulation).[21]

The relationship between racism and health is nuanced, and assessing the direct impact of racial trauma on health is complex and difficult. Racism acts as both a direct stressor and an indirect determinant of health. Social determinants of health (SDOH) refer to the conditions in which people "live, learn, work, play, worship, and age that affect a wide range of health, functioning, and quality-of-life outcomes and risks."[22] Due to structural racism, minoritized populations often live and work in places that reduce access to a broad range of resources that enhance health.[1] Racism exacerbates health inequities in historically minoritized communities by directly impacting physical well-being through physiological stress and indirectly through the inequitable opportunities for achieving good health in their environments.[1]



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Research on health inequities has highlighted differences in health outcomes across minoritized populations in recent years. For example, a recent report (2023 data) by KFF (formerly Kaiser Family Foundation) found:[3]

- Diabetes rates for Black, Hispanic, and Indigenous adults were all higher than the rate for white adults.
- Black, Hawaiian, Pacific Islander, Indigenous, and Hispanic adults all had higher obesity rates than white adults.
- Black and Indigenous women also had the highest rates of pregnancy-related mortality, with Black women 3-4 times more likely to die from a pregnancy-related cause than white women.

While numerous studies have observed overarching inequities in health outcomes, others have examined the direct association between perceived or lived experiences of racism and adverse health conditions.[1]

- Self-reported discrimination among Asian Americans was a significant predictor of chronic health conditions, including cardiovascular, respiratory, and pain outcomes.[27]
- Prospective cohort data from the Black Women's Health Study found positive associations between racism and asthma and breast cancer incidence.[32,33]
- Studies have correlated racism to a variety of nonspecific pathologies, such as increased nighttime blood pressure and shortened telomeres.[20,24]

**RECOGNIZING THE LINK BETWEEN RACIAL TRAUMA AND HEALTH CONDITIONS IS VITAL FOR UNDERSTANDING THE LASTING IMPACTS ON MINORITIZED COMMUNITIES.**[1,3,12,20-22,24,27,29,32-36]

In health care, historically marginalized populations continue to face racism and discrimination. They may experience inequities in treatments, implicit bias by providers, cultural insensitivity, and blatant stereotyping.[35] According to the results from the KFF 2023 Racism, Discrimination, and Health Survey, about one in five (18%) Black and one in 10 Hispanic (11%), Asian (10%), and Indigenous (12%) adults reported they were personally maltreated or disrespected by a health care provider in the past three years because of their race or ethnic background compared to 3% of white adults.[36] Such encounters can foster persistent mistrust in the health care system and may dissuade patients from seeking medical care, leading to adverse health outcomes.[35]

Studies have also linked racism to "diminished participation in healthy behaviors (e.g., sleep and exercise) and increased engagement in unhealthy behaviors (e.g., alcohol consumption) either directly as stress coping, or indirectly, via reduced self-regulation."[37] While engaging in high-risk behaviors can contribute to the risk of developing mental and somatic disease, research indicates that the risk of developing such conditions is outsized in minoritized populations and is likely not caused by behavioral or lifestyle factors alone.[12]

Understanding the link between racial trauma and the development of mental and physical health conditions is essential for comprehending the enduring health impacts faced by minoritized communities subjected to racial discrimination.[1,3,12,20-22,24,27,29,32-36] To further understand this linkage, it is paramount that research seeks to identify and understand the physiological mechanisms by which the experience of racial discrimination impacts the body.





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# THE PHYSIOLOGICAL STRESS RESPONSE TO RACISM

Research suggests that worse morbidity and mortality in minoritized populations may be, in part, due to both the acute and chronic stress of racism.[12] Physiological stress responses (i.e., "fight or flight" states) lead to the release of stress hormones such as cortisol. These hormones can potentially elevate blood pressure, heart rate, and blood sugar levels and, with prolonged exposure, may escalate inflammation and harm the organs and systems of the body.[12,37]

Frequent activation of the body's physiological stress response disrupts the equilibrium of bodily systems (allostasis), as these response mechanisms require regulation and deactivation following a stressful event.[12] When a chronic stressor regularly disrupts allostasis, it results in wear and tear on the body, referred to as allostatic load.[12] Research has shown that allostatic load leaves individuals more vulnerable to disease, resulting in worse health in historically marginalized and ethnic minority populations.[38]

The impact of allostatic load is encapsulated by the concept of "weathering." The original weathering hypothesis states that the cumulative impact of adversity and marginalization experienced by Black women resulted in adverse health outcomes at earlier ages as compared to their white counterparts. This hypothesis may be applied to any population that regularly experiences racial trauma and marginalization: the accumulation of adaptive responses to stress advances health deterioration, or "weathering," of the body.[39]

The weathering effects of racism are additive, with the health deterioration associated with allostatic load accumulating across the lifespan. Children as young as seven years old understand feelings of racial discrimination and their negative impacts. With chronic stress from anticipated or experienced racism beginning in childhood, the harmful effects accumulate throughout an individual's lifespan. They may contribute to the overall shorter life expectancy of minoritized populations.[40,41]

# DEFINING TRANSGENERATIONAL TRAUMA

Historical and ongoing racial discrimination impacts not only individuals who directly experience racial trauma but also affects subsequent generations, a phenomenon termed "transgenerational trauma."[12] Studies indicate a correlation between intergenerational trauma (trauma transmitted from parent to offspring) and psychopathology, suggesting that such trauma can be transmitted between generations through various mechanisms.[12-17]

For example, epigenetic changes (alterations in gene expression rather than genetic makeup) may result from the accrued stress linked to racial discrimination.[14,18,19] Consequently, the ramifications of racism are effectively transmitted to the unborn child, and the effects of racial trauma are perpetuated across generations, further adding to the gravity of the issue.[12,16]



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# RACISM & MENTAL HEALTH

While significant institutions are beginning to recognize and vocalize the impact of racism and racial discrimination on population health, additional research is vital to understanding the mechanisms by which racial trauma affects mental and physical health. One critical gap lies in the scarcity of studies that adequately capture the complex interplay between racial trauma and mental health outcomes across diverse racial and ethnic groups. Existing research often fails to account for the unique sociocultural contexts and historical legacies that shape experiences of racial trauma among different communities. Moreover, there is a shortage of longitudinal studies examining the long-term effects of racial trauma on mental health, hindering our understanding of its enduring impact. Additionally, there is limited research exploring effective interventions to address the mental health needs of individuals coping with racial trauma. As a result, there is an urgent need for more comprehensive and culturally humble research initiatives to bridge these gaps and inform the development of targeted interventions to support those affected by racial trauma.[4,26-28]

# REPORT LIMITATIONS

This narrative review has several limitations. One limitation arises from the heterogeneity of the human brain. Research suggests brain structure can vary across demographics (for example, across age groups and biological sex), which may represent normal variations influenced by a blend of genetic and environmental factors, which may also introduce potential bias in understanding how racial discrimination affects the human brain across diverse minoritized groups.[42]

Second, this report is structured as a narrative review, a form of non-systematic, non-peer-reviewed synthesis of the current literature which encompasses a broader array of studies than traditional systematic reviews. A broadened review of the literature allows for flexible analysis and interpretation of presented studies. While beneficial for generating a comprehensive understanding of a topic, the broad and interpretative nature of narrative reviews may potentially lead to a sample selection that does not comprehensively reflect all available evidence or perspectives on a topic.[43]

For example, the predominant body of peer-reviewed evidence presented in this report is designed cross-sectionally, limiting the generalizability of these findings and precluding the ability to draw causality. The literature reviewed may contain small sample sizes, homogenous samples, and/or may not be designed to prospectively match samples to potential confounders.[4-6,8,9,17,24,25] Additionally, this narrative review pre-defines the terms "racism," "discrimination," and "racial trauma" and uses these terms consistently throughout the report regardless of how these terms are presented in the peer-reviewed literature. To be inclusive of the caustic effects that minoritized individuals suffer because of their minority status throughout the globe and across epochs, this report incorporates studies on variable minoritized groups, including Black, Latino, and Jewish populations.

Lastly, this analysis also focuses strictly on the associations between self-reported instances of racial discrimination. Several publications discussed in this narrative use the Everyday Discrimination Scale (EDS) to assess self-reported experiences of discrimination, a validated instrument extensively used in psychosocial research to quantitatively measure the frequency and severity of daily, "every day" social experiences of discrimination. Developed to capture the subtle and overt forms of interpersonal discrimination that individuals encounter, the EDS assesses the impact of these experiences based on perceptual reports of unfair treatment. Other forms of racism and their impact have not been discussed in this narrative report.[5,9]

Furthermore, this report does not address the role of intersectionality in the study of discrimination and health. While the report focuses on a single characteristic as the source of discriminatory experiences, it is important to recognize that factors such as gender, socioeconomic status, and other social disadvantages can interact and contribute to combined effects. Each individual experiences discrimination through multiple overlapping identities.[20,44] Finally, while this report focuses only on the pre-defined topics and their ties to mental health in minorities communities, a dearth of data supports the effects of racism, discrimination, and racial trauma on somatic health outcomes as well.[1,3,21]



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# BRAIN REGIONS AND CIRCUITS ASSOCIATED WITH RACIAL DISCRIMINATION

# BRAIN REGIONS AND CIRCUITS ASSOCIATED WITH RACIAL DISCRIMINATION AND MENTAL HEALTH DISORDERS

Racist encounters trigger complex physiological, affective, and cognitive responses involved in threat detection and emotional regulation in the brains of victims.[4,23] Influenced by prior encounters with racism, the brain may initiate a response to racist events before conscious awareness sets in by redistributing cognitive resources to manage complex social interactions. Simultaneously, the brain balances self-awareness and the perception of others' behaviors while regulating internal physiological signals to decide whether to confront or avoid threatening situations.[45] This complex neural processing is overseen by neural networks such as the salience network (SN), default mode network (DMN), and central executive network (CEN), which include brain structures like the amygdala, insula, and prefrontal cortex. These networks serve distinct but interconnected functions related to emotional regulation, managing complex cognitive tasks, and orchestrating responses to internal and external environments.[45] Over time, the chronic stress of enduring discrimination may modify these neural networks by draining the mental and physical resources required for vigilance against racial threats. This can lead to a constant state of hyperarousal, sensitization to perceived threats, heightened awareness, and increased wear on the body, known as "allostatic load."[4,39]

Racism, as a persistent traumatic stressor, increases the risk of neuropsychiatric disorders.[4,20,21] These disorders are characterized by abnormal cognitive and emotional regulation processes reliant on the proper functioning of the SN, DMN, and CEN.[46] The impact of racism on the brain mirrors neural patterns also seen in trauma-related neuropsychiatric conditions.[4] For instance, the SN, which includes the amygdala, anterior cingulate cortex (ACC), and anterior insula, plays a critical role in detecting emotionally salient stimuli, integrating sensory data, and facilitating interactions with other networks that oversee cognition and emotional regulation (figure 1).[10]

The SN is also crucial for modulating the switch between the DMN, which governs self-referential thoughts, and the CEN, associated with higher-order cognitive processes and decision-making.[10,42] Altered SN circuitry has been linked to symptoms of post-traumatic stress disorder (PTSD), including hyperarousal and generalized anxiety disorder (GAD).[7] The amygdala, an essential component of the SN, plays a crucial role in evaluating emotionally salient stimuli and mediating stress responses, particularly those related to fear and threat detection.[5] Individuals with PTSD and depression have been shown to exhibit greater connectivity between the amygdala and SN.[5]

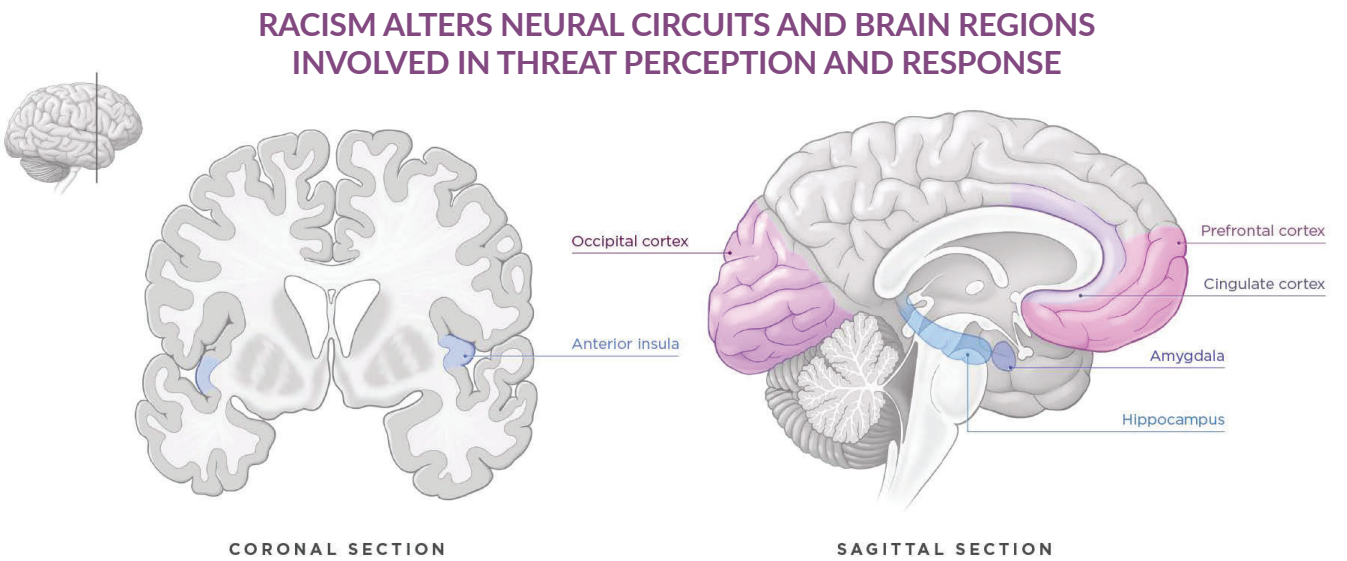


**Figure 1.** Coronal (vertical, left to right) section and sagittal (vertical, front to back) section of the brain. Racism alters neural circuits and brain regions involved in threat perception and response. Neural circuits are critical for threat detection. They also activate emotions during racial discrimination. The occipital cortex processes visual information, while the anterior insula detects conflict. The prefrontal cortex is responsible for emotional regulation, while the cingulate cortex integrates threat cues. The amygdala initiates a behavioral response and the hippocampus draws on threatening memories. Adapted from Webb EK, et al. *Neurosci Biobehav Rev.* 2024.[4]



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The insula, a component of the SN, is involved in recognizing emotional states and physiological effects and may mediate how racial bias is internally experienced. Alterations in the anterior insula have been linked to the development of stress and trauma symptoms, and aberrant insula resting-state connectivity has been associated with depression and anxiety. Recent studies suggest that experiences of discrimination and PTSD share similar patterns of functional interaction across the insula and prefrontal cortex (PFC), which governs executive functioning, social interaction, and complex cognitive behaviors. Additionally, research links racism as a stressor to functional and structural changes in the PFC, contributing to PTSD symptoms.[4]

The ACC, part of the SN, is involved in integrating social cues and knowledge of complex social experiences.[10,45] Structural and functional changes in the perigenual ACC (pACC) have been associated with schizophrenia onset.[24] Conversely, the posterior cingulate cortex (PCC) of the DMN manages attentional focus and rumination.[8,42] Changes in PCC structure have been observed across various neuropsychiatric conditions.[8] The ACC and PCC together form the cingulate cortex (CC), which is involved in emotional regulation and cognitive functioning. Studies suggest that accelerated CC atrophy may be linked to Alzheimer's disease. Cingulate cortex thinning may predict attention and memory problems, indicating a heightened risk for neuropathology.[8] Older Black individuals are at greater risk for Alzheimer's disease compared to their white counterparts.[8,47] Other minoritized groups are also at increased risk; factors such as lower socioeconomic status, restricted access to health care, and higher rates of chronic conditions contribute to a higher risk of Alzheimer's disease in these minoritized communities.[47]

In addition to altered neural circuitry, racism-related stress has significant effects on brain structure.[8,9] Stress-related disorders, trauma-related disorders, and racism-related stress have all been linked to reduced hippocampal volumes.[4] The hippocampus, part of the DMN, is involved in memory recall and formation; thus, structural alterations in the hippocampus can be both a risk factor and a consequence of neuropsychiatric disorders throughout the lifespan.[4] Furthermore, decreased gray matter and white matter integrity have been associated with a higher frequency of reported racial discrimination.[8,9,11] The integrity of white matter tracts, such as the corpus callosum (CoC), superior longitudinal fasciculus (SLF), and cingulum bundle (CB), which are primarily composed of myelinated axons to facilitate communication across the brain, has also been implicated in various neuropsychiatric disorders. Reduced integrity of white matter microstructure has been identified as a biomarker for neurodegenerative diseases like Alzheimer's disease.[9] Specifically, the CoC, the largest white matter structure in the brain, which facilitates interhemispheric communication, has shown morphological changes due to early life adversity and PTSD.[9] Disruptions to the CoC genu, which connects the frontal lobes of the left and right brain hemispheres, have been associated with cognitive and emotional dysregulation and impulse control.[11] The SLF is involved in functions like attention and executive function and has been implicated in trauma responses.[9] The SLF is involved in functions like attention and executive function and has been implicated in trauma responses.[9] The compromised structural integrity of the CB is widely considered to be an indicator of trauma and PTSD.[9,11]

In sum, evolving research reveals the pernicious effects of racism on the brain both immediately and over the long term. Over time, a heightened state of vigilance strains global neural circuits, promoting pathological changes in brain areas involved in threat processing, emotional regulation, and cognitive processing. These pathological changes have also been observed across several neuropsychiatric disorders, which may indicate an increased risk for mental health conditions. These associations highlight the importance of addressing racial trauma not only as a societal issue but as a critical public health concern.



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# RACIAL DISCRIMINATION IS LINKED TO CHANGES IN BRAIN NETWORK CONNECTIONS

# RACIAL DISCRIMINATION IS LINKED TO CHANGES IN BRAIN NETWORK CONNECTIONS ASSOCIATED WITH SOCIAL STRESS AND THREAT DETECTION

Racial trauma continues to permeate current society and manifests in various forms, including frequent discriminatory encounters, microaggressions, disproportionate incidents of police brutality, racial profiling, and unequal access to health care.[1,2,28,48-52] A growing body of evidence shows associations between self-reported experiences of racial discrimination and altered neural circuitry in regions involved in social stress and threat detection, both acutely and longitudinally.[5-7,24,25] Altered functional connectivity in regions involved in emotional regulation, social pain processing, and stress response may reflect a broader neurobiological response to perceived racial discrimination.[5-7,24,25] These insights serve as a window into the experiences of individuals facing racial discrimination and highlight the importance of considering both immediate neural reactions and long-term psychological ramifications.[5-7,24,25] In this section, we present an analysis of the complex association between racial discrimination, neural responses, and social stress processing to deepen an understanding of how racial discrimination impacts neural circuitry related to social stress both in the moment and over the lifespan.[5-7,24,25]

## *IN VIVO* STUDIES OF SELF-REPORTED RACIAL DISCRIMINATION REVEAL CHANGES IN NEURAL ACTIVITY WITHIN BRAIN REGIONS INVOLVED IN SOCIAL PAIN AND EMOTIONAL REGULATION[25]

Research into neural activity during racially discriminatory experiences from victims' perspectives finds that negative social experiences attributed to race elicit higher activity in regions involved in emotional regulation and decreased activity in areas involved in social pain processing. This research aims to identify specific brain regions activated by experiences of social exclusion and to understand how these neural mechanisms are influenced by the interpretation of such exclusion as racially motivated. This contributes to a deeper understanding of the psychological and neural dimensions of racially discriminatory experiences. Thus, minoritized communities, who regularly face negative social interactions, may process and manage these experiences as they occur.

**NEGATIVE RACIAL EXPERIENCES INCREASE EMOTIONAL STRESS AND MAY REDUCE THE BRAIN'S ABILITY TO PROCESS SOCIAL PAIN[25]**





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In one experiment, researchers recruited 18 Black participants (9 female, 9 male) aged 19–28 to participate in a game of "Cyberball," a virtual ball-tossing game designed to evoke feelings of exclusion and simulate social exclusion attributable to racial discrimination. Participants underwent functional magnetic resonance imaging (fMRI) tasks to analyze neural activity during one round of inclusionary Cyberball and one round of exclusionary gaming. White interviewers and imaging technologists were selected to study the implications of racial discrimination. Participants were introduced to and excluded by two digital characters named "White confederates" prior to the neuroimaging session to subtly prime awareness of race without directly mentioning minoritized status.

Following the neuroimaging task session, participants' self-reported experiences of distress and discrimination were collected, along with observer-rated assessments of distress from videotaped interviews providing behavioral feedback immediately after the scans. This mix of self-reported measures and observer assessments aimed to balance self-reports of discrimination with more objective evaluations of distress. Cyberball rounds were modeled separately to compare neural activity between exclusion and inclusion segments for each participant. Individual images were used in group-level, whole-brain analyses to evaluate associations between neural activity and self-reported distress, observer-rated distress, and perceived racial discrimination.

Neuroimaging results from the study showed an association between simulated discrimination and neural activity during social exclusion rounds (figure 2). Greater activity was observed in neurocircuitry involved with emotional regulation of threat responses, such as the rostral anterior cingulate cortex (rACC), while lower activity was observed in areas involved in distress and social threat perception, such as the dorsal ACC (dACC). Thus, findings suggest the perception of social exclusion motivated by race may modify neural responses: attributing negative social interactions to discrimination is linked to decreased neural activity associated with social pain and increased activity related to regulation. These changes may reduce the impact of social exclusion on brain areas associated with distress while activating regulatory mechanisms to better manage negative emotional responses during discriminatory experiences. Furthermore, changes in the connectivity of brain areas involved in emotional regulation, social stress processing, and stress response during incidences of discrimination suggest a mechanism by which individuals respond to racially discriminatory acts as they occur. Over time, continual activation of brain regions responsible for social threat detection and emotional control may impair the capacity to manage new stressors, potentially leading to increased long-term psychological and physical stress.

## NEGATIVE RACIAL EXPERIENCES TRIGGERED QUICK CHANGES IN BRAIN ACTIVITY[25]



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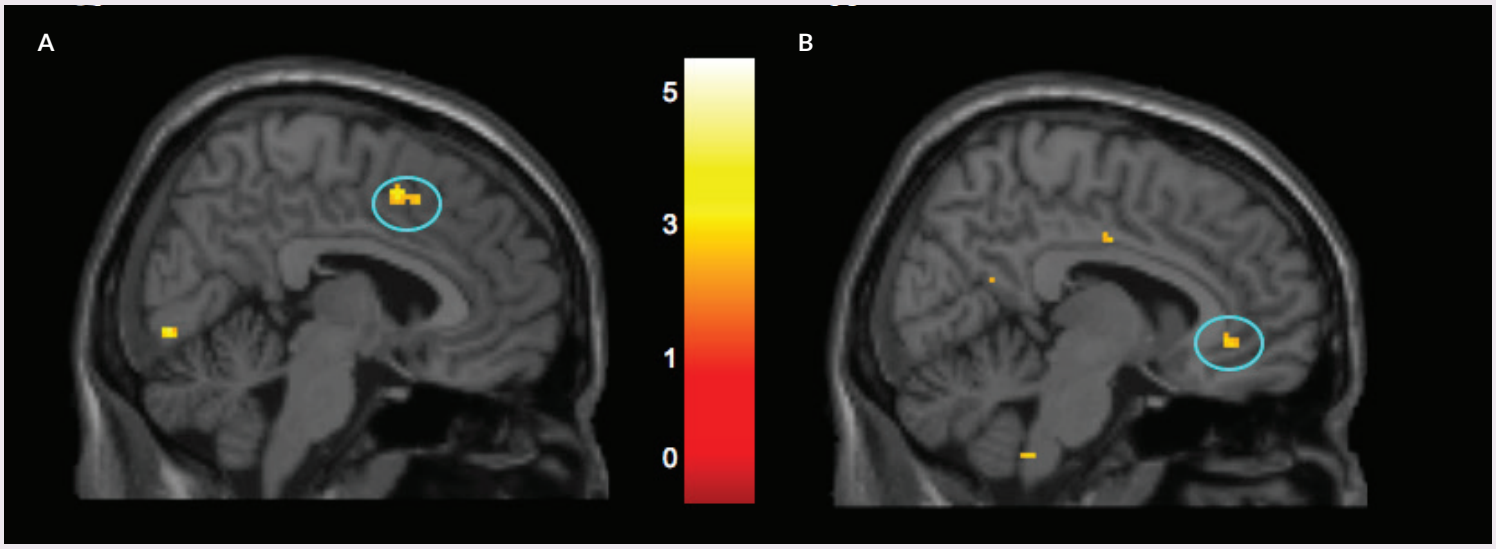
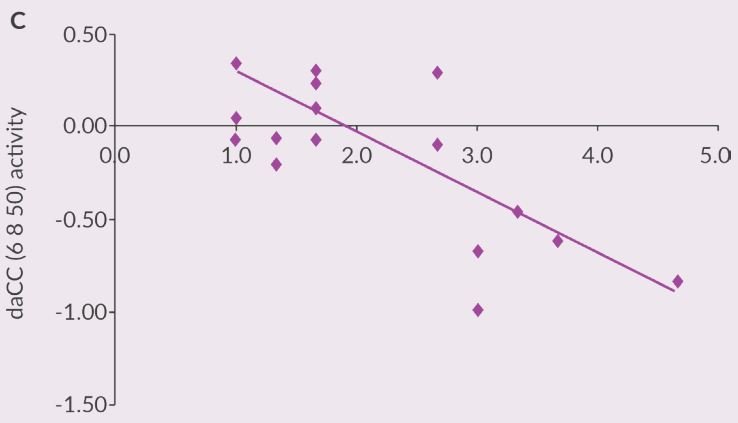
## CHANGES IN BRAIN ACTIVITY ARE ASSOCIATED WITH SELF-REPORTED DISCRIMINATION



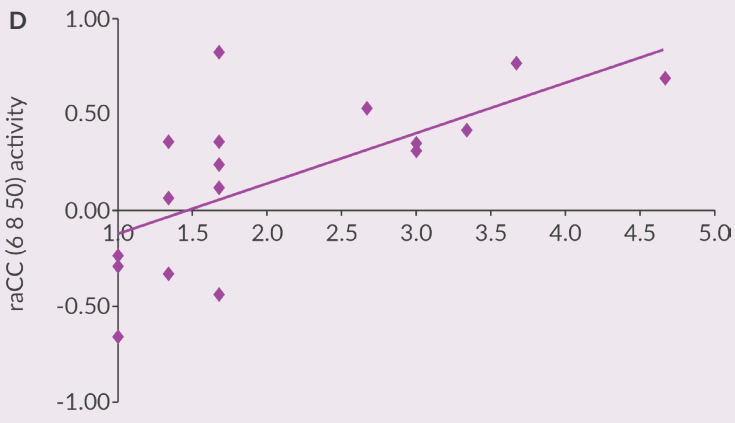




**Figure 2.** Functional MRI brain scans and statistical scatter plots of individuals reporting exclusion due to race. Exclusion based on race showed a negative correlation with activity in the dACC (A, C) and a positive correlation with activity in the rACC (B, D). Adapted from Masten CL, Telzer EH, Eisenberger NI. *J Cogn Neurosci.* 2011.[25]



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# CHRONIC STRESS FROM INCIDENCES OF DISCRIMINATION MAY AFFECT HOW MINORITIZED INDIVIDUALS PROCESS STRESS[24]

A separate study found that social stress processing is altered and influenced by incidences of discrimination in minoritized individuals. This study recruited participants born in Germany and divided them into groups based on familial background: those of German descent (n=40), or ethnic minorities whose parents migrated from Turkey, Italy, or Poland (n=40). Groups underwent fMRI tasks designed to elicit responses to social stress and to assess emotional and cognitive processing, aiming to highlight any differences in neural activity that could be attributed to experiences of racial discrimination. Blood-oxygen-level-dependent (BOLD) responses, functional connectivity, and psychological and physiological measures of stress were analyzed throughout these tasks.[24]

Results showed greater chronic stress ($p=0.02$) and higher levels of perceived group discrimination in minoritized individuals. Stress induction led to the activation of broad neurocircuitry across all participants, including the perigenual ACC (pACC) ($p<0.001$), ventral striatum ($p<0.001$), frontoinsular cortex ($p<0.001$), hippocampus ($p<0.001$), and amygdala ($p<0.04$). However, ethnic minority participants exhibited greater activation of the pACC ($p=0.005$, $r2=0.2$) and increased functional connectivity between the pACC and the dACC ($p=0.01$, $r2=0.16$). The increased activation and connectivity were not attributable to acute stress induction or social distancing effects (e.g., conducting group comparisons where the ethnic background of investigators matches that of the participants to control for potentially confounding variables which may influence results.)[24]

Subsequent analyses showed that chronic stress significantly mediated the relationship between acts of discrimination and functional connectivity of the pACC to dACC ($p<0.05$), providing insight into the neurobiological pathways through which discrimination might exert its long-term effects on the brain. Additionally, there may be a distinct neural pattern of social stress processing among minoritized individuals that correlates with ongoing experiences of discrimination and social stress in society. Altogether, this study suggests that minoritized individuals process social stress differently, and this altered social stress processing may be significantly influenced by simulated discrimination.[24]

**CHRONIC STRESS FROM DISCRIMINATION LED TO SIGNIFICANT CHANGES IN THE BRAIN'S CONNECTIVITY IN REGIONS ESSENTIAL FOR EMOTIONAL REGULATION AND STRESS MANAGEMENT.[24]**



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# LONG-TERM EFFECTS OF RACIAL DISCRIMINATION ON NEURAL NETWORKS

# LONG-TERM EFFECTS OF RACIAL DISCRIMINATION ON NEURAL NETWORKS

Sustained exposure to racial discrimination over time may continue to activate neural circuits, potentially leading to structural and functional changes within these networks. Initially, these adaptations may serve as coping or defense mechanisms. However, they may eventually contribute to alterations in the brain's circuitry and structure. Therefore, racism can be seen as a pervasive source of stress for minoritized communities, independent of other forms of stressors.[5-7]

# GREATER REPORTS OF RACIAL DISCRIMINATION ARE ASSOCIATED WITH SPONTANEOUS AMYGDALA ACTIVITY AT REST AND FUNCTIONAL CONNECTIVITY WITHIN THE SALIENCE NETWORK (SN)[5]

A study on the relationship between self-reported exposure to discrimination and activity of the amygdala was conducted in a diverse population of 74 native English-speaking adults aged 21–70 in New York City. Participants were selected based on diverse demographic and social factors historically linked to a heightened risk of experiencing discrimination, including human immunodeficiency virus (HIV) status, age, sex, race, ethnicity, and sexual orientation (57% male; 72% African American; 20% non-White Hispanic; 32% homosexual/bisexual). They underwent functional magnetic resonance imaging (fMRI) to evaluate the activity and functional connectivity of the amygdala at rest prior to completing self-reported ratings of daily discrimination exposure and psychological well-being, including levels of current stress, depression, anxiety, and post-traumatic stress disorder (PTSD)-related symptoms.

## ASSOCIATION BETWEEN SELF-REPORTED DISCRIMINATORY EXPERIENCES AND LEFT AMYGDALA FUNCTIONAL CONNECTIVITY

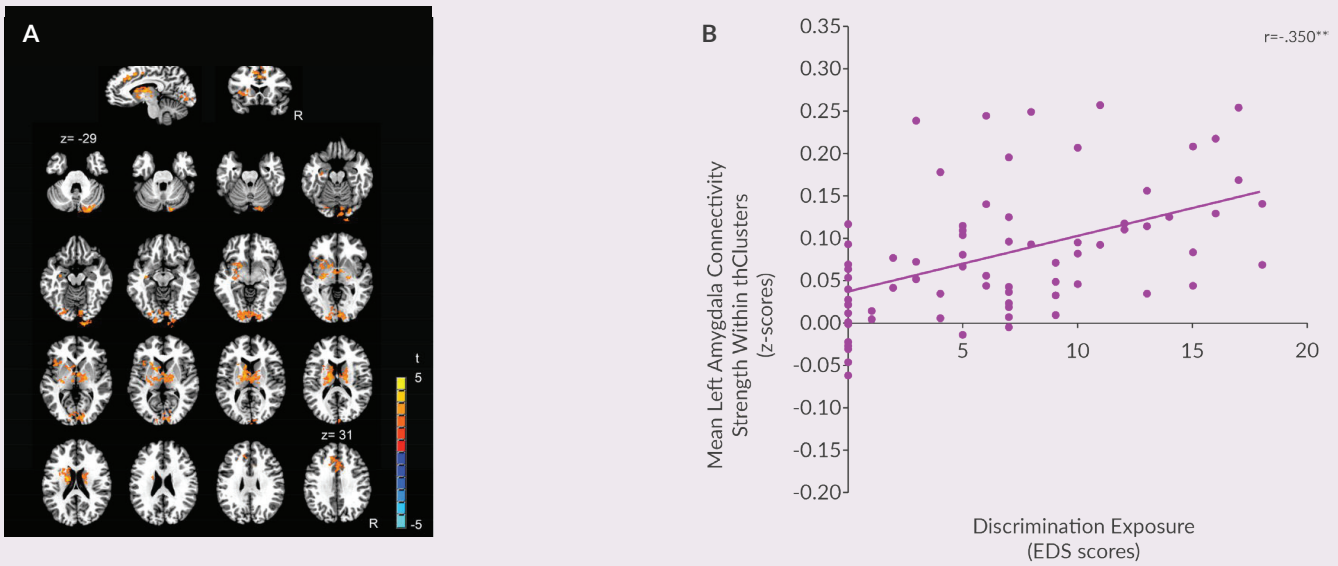


**Figure 3.** (A) Functional MRI brain scans featuring Sagittal (upper left), coronal (upper right), and axial images. (B) Scatter plot showing Mean left amygdala connectivity strength within the clusters shown in (A). Amygdala connectivity strength is associated with self-reported discrimination scores. Adapted from Clark US, Miller ER, Hegde RR. *Biol Psychiatry Cogn Neurosci Neuroimaging*. 2018.[5]



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## PARTICIPANT DEMOGRAPHICS

| | |
|---|---|
| Age, Years, Mean ± SD | 47.46 ± 10.95 |
| Education, Years, Mean ± SD | 14.39 ± 2.53 |
| Mini-Mental State Exam (of 30), Mean ± SD | 29.03 ± 1.20 |
| Male % | 56.8 |
| Racial Composition | |
| Caucasian/white, % | 9.5 |
| African American/black, % | 71.6 |
| Asian American, % | 1.4 |
| Biracial/Multiracial, % | 9.5 |
| Other, % | 8.1 |
| Ethnic Composition | |
| White, Hispanic, % | 2.7 |
| Nonwhite, Hispanic, % | 20.3 |
| White, Non-hispanic, % | 6.8 |
| Nonwhite, Non-hispanic, % | 70.3 |
| HIV Positive, % | 35.1 |
| Homosexual/Bisexual, % | 32.4 |
| Positive Marijuana Toxicology, % | 16.2 |
| Discrimination – EDS (of 27), Mean ± SD | 6.80 ± 5.36 |
| Current Stress – PSS (of 56), Mean ± SD | 31.04 ± 8.20 |
| Depression – CES-D (of 60), Mean ± SD | 10.41 ± 9.08 |
| Anxiety – BAI (of 63), Mean ± SD | 5.04 ± 7.22 |
| PTSD Symptoms – PCLC (of 85), Mean ± SD | 28.46 ± 11.55 |

**Table 1:** Adapted from Clark US, Miller ER, Hegde RR. *Biol Psychiatry Cogn Neurosci Neuroimaging*. 2018.[5]

The study found significant associations between higher exposure to discrimination and increased levels of stress ($p<0.001$), depression ($p<0.001$), anxiety ($p<0.001$), and PTSD-related symptoms ($p<0.001$). A statistically significant association was observed between greater reported discrimination and spontaneous amygdala activity in the left hemisphere ($p<0.041$) (figure 3). This association persisted after accounting for race and other demographic covariates and was independent of psychosocial functions. Additionally, greater reports of discrimination were associated with stronger functional connectivity between the left amygdala (figure 4) and regions within the SN at rest, including the anterior insula, putamen, caudate, anterior cingulate cortex (ACC), medial frontal gyrus, and thalamus, independent of demographic covariates and psychosocial function ($p=0.003$).

Thus, frequent experiences of discrimination not only affect psychological well-being but also have a measurable impact on brain function and connectivity. In this study, these findings remained consistent across participants and independent of psychosocial function, suggesting that the connection between discrimination exposure and amygdala activity may be distinct from other forms of stress. Such insights into the neural basis of racial discrimination underscore the need for further exploration into the long-term health effects of discrimination exposure within minoritized communities.

## RESTING STATE ACTIVITY OF THE LEFT AMYGDALA AND DISCRIMINATION EXPOSURE

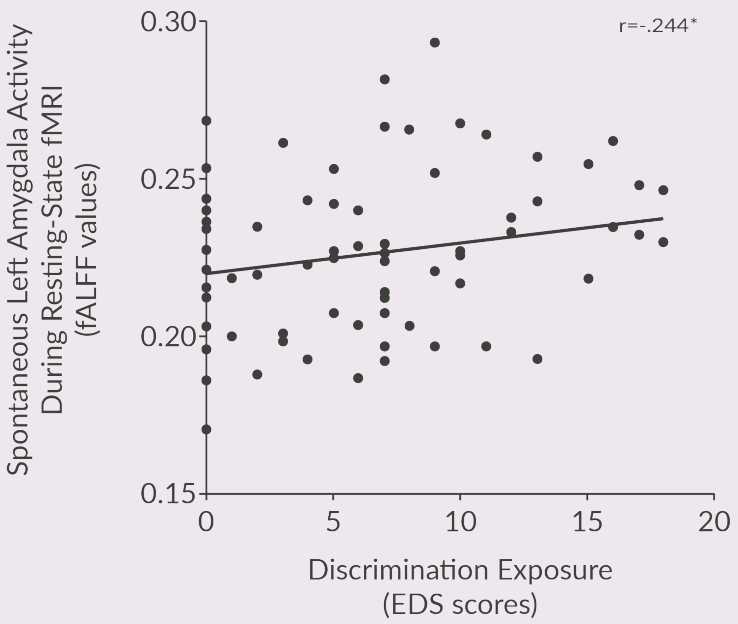


**Figure 4.** Scatter plot of the relationship between the resting state activity of the left amygdala (measured during fMRI) and self-reported discrimination. Spontaneous left amygdala activity is associated with self-reported discrimination ($p<0.05$). Adapted from Clark US, Miller ER, Hegde RR. *Biol Psychiatry Cogn Neurosci Neuroimaging*. 2018.[5]





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# GREATER REPORTS OF RACIAL DISCRIMINATION ARE ASSOCIATED WITH HEIGHTENED ACTIVITY IN NEURAL NETWORKS RESPONSIBLE FOR THREAT DETECTION AND REGULATION[6,7]

Building on previous work, task-based functional magnetic resonance imaging (fMRI) data have demonstrated increased activity in regions associated with vigilance and hyperarousal, specifically the middle occipital cortex and ventral prefrontal cortex (vPFC). These areas are involved in visual attention, emotional regulation, and fear inhibition and are linked to greater experiences of racial discrimination.[6] Similarly, greater reports of racial discrimination were independently associated with resting-state fMRI (rsfMRI) data showing greater functional connectivity in areas of the salience node (SN) such as the amygdala–thalamus and the anterior insula–precuneus following acute trauma.[7] This evidence reinforces previous research and suggests that racial discrimination is associated with altered functional connectivity in regions involved in vigilance among minoritized individuals, providing a potential pathway that can help explain mental health inequities among minoritized populations.

In one study, Black women aged 22–61 years (n=55) with prior trauma exposure were recruited to assess the impact of racial discrimination on neural responses to threat cues. Participants underwent clinical assessments evaluating their lifetime trauma exposure and frequency, current post-traumatic stress disorder (PTSD) symptoms, and self-reported experiences of racial discrimination. The fMRI investigation involved participants completing an affective Stroop task against trauma-relevant and neutral distractor images. The affective Stroop task is an adaptation of the classic Stroop task used to measure attention control. Unlike the traditional task where participants name the ink color of words that could semantically conflict with the color (like "red" in blue ink), the affective Stroop task involves participants quickly quantifying numbers shown while ignoring distracting images of various emotional content (trauma-relevant, positive, and neutral). This method measures how emotional content impacts attention and cognitive control by analyzing response times and error rates.[6,55]

Participants reported moderate levels of current PTSD symptoms, and exposure to discrimination correlated with current PTSD symptoms (p=0.009). Moreover, experiences of racial discrimination were significantly associated with increased blood-oxygen-level- dependent (BOLD) responses in areas responsible for emotional regulation and fear inhibition (ventromedial prefrontal cortex [vmPFC]; figure 5), as well as visual attention (middle occipital cortex) during trauma-relevant distractor tasks versus neutral tasks, independent of reported trauma exposure and PTSD symptoms. Lastly, greater reports of racial discrimination were associated with fewer errors on trauma-relevant distractor tasks after accounting for current PTSD symptoms and trauma exposure, but no significant correlation was found between experiences of discrimination and response time.[6]

## CORRELATION BETWEEN RACIAL DISCRIMINATION AND RESPONSE TO THREAT-SPECIFIC STROOP TASKS

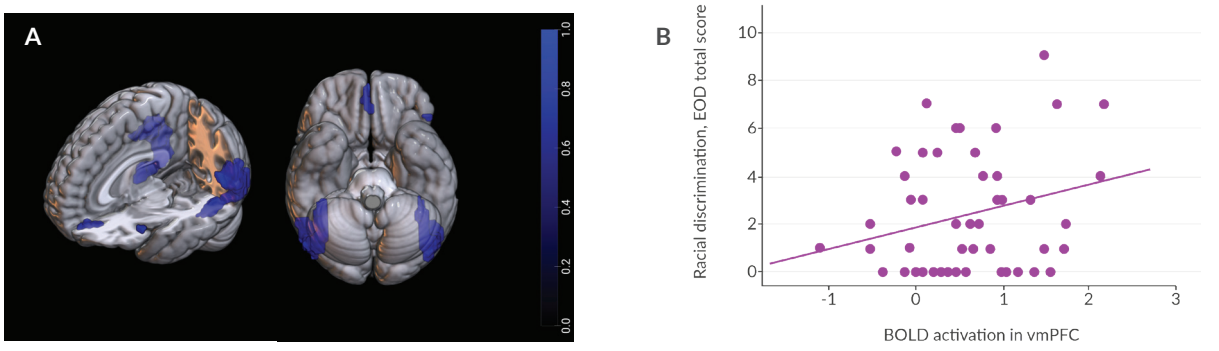


**Figure 5.** (A) Brain image demonstrating brainwide association between racial discrimination scores and response to threat-relevant versus threat-neutral Stroop trials. (B) Scatter plot showing heightened activity in the vmPFC during threat-related versus threat-neutral tasks is associated with greater experiences of racial discrimination. Adapted from Fani N, et al. *JAMA Psychiatry*. 2021.[6]



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Expanding upon this work, a separate study sought to demonstrate an association between self-reported experiences of racial discrimination and altered resting-state connectivity of SN nodes, particularly the amygdala and anterior insula, in the aftermath of an inciting traumatic event.[7] Black adults aged 18–65 (n=102) with recent exposure to trauma (within two weeks between the inciting event and initial study visit) were recruited to undergo structural and rsfMRI following self-reported assessments of lifetime exposure to racial discrimination, lifetime trauma exposure, acute PTSD symptoms, and income levels.[7]

Higher reports of acute PTSD symptoms in the aftermath of recent trauma were associated with greater reports of discrimination ($p<0.001$) and lifetime trauma ($p<0.001$). Notably, the study revealed significant associations between levels of reported racial discrimination and altered connectivity in regions of the SN. Greater reports of discrimination were independently associated with heightened connectivity between the amygdala and the thalamus ($p=0.03$; figure 6) and greater connectivity between the insula and precuneus ($p=0.02$; figure 7) after accounting for acute PTSD, lifetime trauma, and income. Therefore, greater exposure to racial discrimination may be associated with altered resting state functional connectivity of SN nodes involved in vigilance, threat appraisal, and emotional regulation.[7]

## INCREASED AMYGDALA-THALAMUS CONNECTIVITY ASSOCIATED WITH HIGHER LEVELS OF RACIAL DISCRIMINATION EXPOSURE

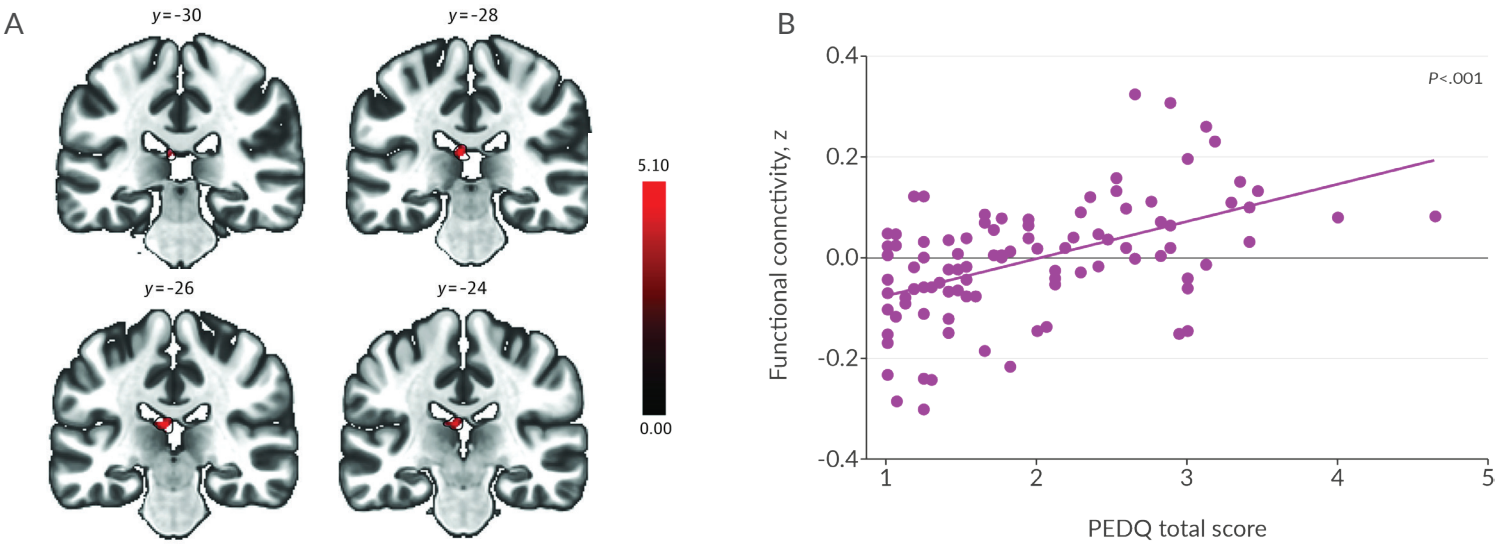


**Figure 6.** (A) Resting-state fMRI scans recorded after a traumatic episode. (B) A scatter plot showing increased exposure to racial discrimination is associated with increased connectivity of the bilateral amygdala and the thalamus after adjusting for PTSD symptoms, lifetime trauma, and income. Adapted from Webb EK, et al. *JAMA Netw Open*. 2022.[7]



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## RACIAL DISCRIMINATION LINKED TO ENHANCED CONNECTIVITY IN ANTERIOR INSULA AND PRECUNEUS REGIONS

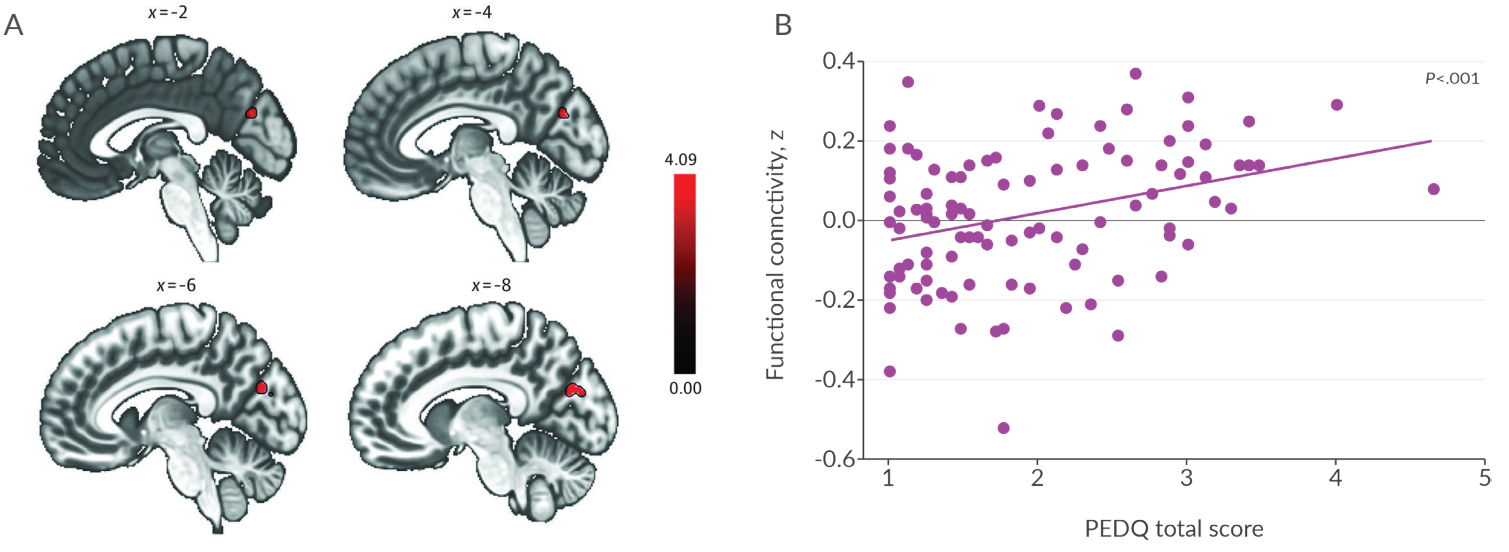


**Figure 7.** (A) Resting-state fMRI scans following a traumatic episode. (B) A scatter plot demonstrating greater exposure to racial discrimination was associated with increased connectivity between the bilateral anterior insula and precuneus and the thalamus after adjusting for acute PTSD, lifetime trauma, and income. Adapted from Webb EK, et al. *JAMA Netw Open*. 2022.[7]

Given the involvement of these structures in vigilance, threat appraisal, and hyperarousal, the findings across these two studies collectively uncover a complex relationship between racial discrimination experiences and the neural mechanisms underlying states of vigilance and regulation responses. In the first study, greater reports of racial discrimination were associated with greater activity in neurocircuitry involved in visual attention (middle occipital cortex), emotional regulation, and fear inhibition (vmPFC) when trauma-exposed participants were exposed to trauma-relevant images, even after controlling for participants' current PTSD symptoms and trauma exposure.[6] Researchers also observed an association between experiences of racial discrimination and better performance (i.e., fewer errors) in an attentionally demanding affective Stroop task during exposure to threat-relevant stimuli after accounting for current PTSD symptoms and trauma exposure. There were no significant correlations between racial discrimination experiences and response time, indicating that discriminatory encounters were not associated with attentional control but with emotional regulation and threat inhibition. In the second study, racial discrimination was independently associated with altered functional connectivity of the amygdala and anterior insula at rest after accounting for acute PTSD symptoms, reported lifetime trauma exposure, and income. The authors suggest increased connectivity between the amygdala and thalamus cat rest may reflect a heightened sensitivity to potential threats, and enhanced connectivity between the resting-state insula and precuneus might indicate improved situational and self-awareness, preparing an individual for a readiness response.[7] Together, this evidence links racial discrimination to changes in the connectivity of brain regions associated with vigilance and threat responses. The pervasive nature of racism and frequent exposure of minoritized individuals to discriminatory behaviors may be driving an adaptive response to racial discrimination. This response may lead minoritized individuals to become more vigilant and responsive to potential threats in their environments. Consequently, attentional and regulatory responses to trauma stressors and regulatory resources are more robustly modulated in anticipation of discriminatory or exclusionary situations. This evidence underscores a neural link between racial discrimination and heightened attentional/emotional regulatory responses, shedding light on a potential mechanism by which racial discrimination contributes to disparate mental health outcomes in minoritized individuals.



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# EXAMINING THE EFFECTS OF RACIAL DISCRIMINATION ON BRAIN STRUCTURE





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# EXAMINING THE EFFECTS OF RACIAL DISCRIMINATION ON BRAIN STRUCTURE

The functional neurocircuitry of the human brain, which ranges from basic sensory processing to complex cognitive operations, is fundamentally determined by structural attributes that encode the "hardware" necessary for neural circuits to function effectively. Therefore, brain structure and function are intricately linked and profoundly influence one another.[45] These changes provide critical insight into the neuroplastic alterations associated with exposure to discrimination.[8,9] By integrating prior research on functional connectivity with morphological modifications discussed in this section, we can assess the overarching effects of societal and psychological stressors enabled by racial discrimination.[45] This approach provides holistic evidence for the neurobiological sequelae of racial discrimination at multiple levels.

**BRAIN STRUCTURE CAN BE INFLUENCED AND RESHAPED OVER TIME[8,9,45]**

# HEIGHTENED REGULATORY FUNCTIONS ASSOCIATED WITH GREATER REPORTS OF RACIAL DISCRIMINATION MAY BE LINKED TO DECREMENTS IN CINGULATE GREY MATTER[8]

Research shows that the cingulate cortex (CC) may undergo neuroplastic changes in response to the chronic stress and vigilance demanded by repeated experiences of racial discrimination. In one study, 81 Black American women aged 19–62 years with no history of neurological or select psychiatric disorders (including bipolar disorder or current substance use/alcohol dependence) were recruited to investigate the relationship between racial discrimination and gray matter morphology in the CC, hippocampus, and amygdala. Participants underwent assessments for lifetime trauma, post-traumatic stress disorder (PTSD) symptoms, and experiences of discrimination attributed to their race. Magnetic resonance imaging (MRI) was used to assess CC cortical volume, which is a function of cortical thickness and surface area—two other outcomes individually analyzed in this study. Subregions of interest within the CC included the rostral anterior cingulate cortex (rACC), caudal anterior CC (caCC), and posterior CC (PCC). Gray matter volume of the amygdala and hippocampus were also analyzed.



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Results revealed nuanced insights into self-reported experiences of racial discrimination and neuroanatomical changes, particularly in regions of the brain involved in emotional processing and stress response. After adjusting for lifetime trauma exposure, PTSD symptoms, income, and individuals' intracranial volume, findings suggest racial discrimination has a striking effect on cingulate structures. Notably, greater experiences of racial discrimination were associated with lower cortical thickness of the left rACC ($p=0.007$), left caCC ($p=0.014$), and left PCC ($p=0.007$), while no statistically significant associations were found with cingulate surface area and volume. However, the robustness of associations diminished with age as an additional covariate, highlighting the potential modulating impact of age on the relationship between racial discrimination and brain structure.

Interestingly, the study did not detect significant associations of racial discrimination with the right side of the cingulate cortex, suggesting a lateralized effect of discrimination on the brain. Measures of CC surface area did not show a statistically significant association with racial discrimination. In contrast, a nominally significant association was detected in left PCC volume, suggesting that cortical thickness may be a more sensitive metric to the impact of discrimination than overall surface area or volume. Similarly, a nominally positive association with right hippocampal volume was detected, although this did not withstand statistical correction. This may suggest that while racial discrimination may be associated with alterations in subcortical structures, this may not be as pronounced as those observed with cortical thickness.

Altogether, these results suggest racial discrimination is associated with tangible morphologic changes in regions involved in emotional, cognitive, and behavioral responses to complex social contexts. Specifically, greater experiences of racial discrimination were associated with thinning of the left cingulate cortex, even after accounting for socioeconomic variables. The specificity of these findings to the CC (particularly the left hemisphere) in addition to the non-significant results of the amygdala, hippocampus, or control regions, suggests a targeted influence of racial discrimination on the left CC. Therefore, the thinning of the left CC may reflect a chronic, heightened state of vigilance or regulatory effort in response to the stress of enduring persistent racism.  Together with previous research, these observations suggest a potential brain mechanism by which racial discrimination burdens cognitive and affective regulation.

**RACIAL DISCRIMINATION IS LINKED TO NOTICEABLE CHANGES IN BRAIN REGIONS RESPONSIBLE FOR EMOTIONAL, COGNITIVE, AND BEHAVIORAL RESPONSES IN SOCIAL SITUATIONS[8]**



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# RACIAL DISCRIMINATION IS ASSOCIATED WITH DISRUPTIONS IN WHITE MATTER INTEGRITY[9]

In addition to structural alterations in gray matter morphology, researchers have found links between racial discrimination and alterations in white matter structural integrity (figure 8). To explore the impact of racial discrimination on brain health, investigators recruited 116 trauma-exposed Black American women aged 18–62 with no history of neurologic or select psychiatric disorders (including bipolar disorder or current substance use/alcohol dependence) to evaluate the structural integrity of selected white matter tracts in association with racial discrimination. Participants underwent assessments for lifetime trauma assessments, post-traumatic stress disorder (PTSD) symptoms, and experiences of discrimination attributed to race prior to magnetic resonance imaging (MRI) scanning. Statistical analyses examined the impact of racial discrimination on fractional anisotropy (FA) and mean diffusivity (MD) values of selected white matter tracts, controlling for PTSD symptoms, trauma exposure, monthly income, and scanner location.

White matter tracts of interest included the uncinate fasciculus (UF), cingulum bundle (CB), superior and inferior longitudinal fasciculus (SLF and ILF, respectively), fornix, and corpus callosum (CoC), which have been linked to poverty, trauma exposure, and PTSD in separate studies. Given the span of the CoC, investigators also analyzed segments of the CoC, including the genu, body, and splenium, in separate statistical models to pinpoint specific associations within its subdivisions.

## BRAIN WHITE MATTER TRACTS MAY BE VULNERABLE TO RACISM-RELATED STRESS

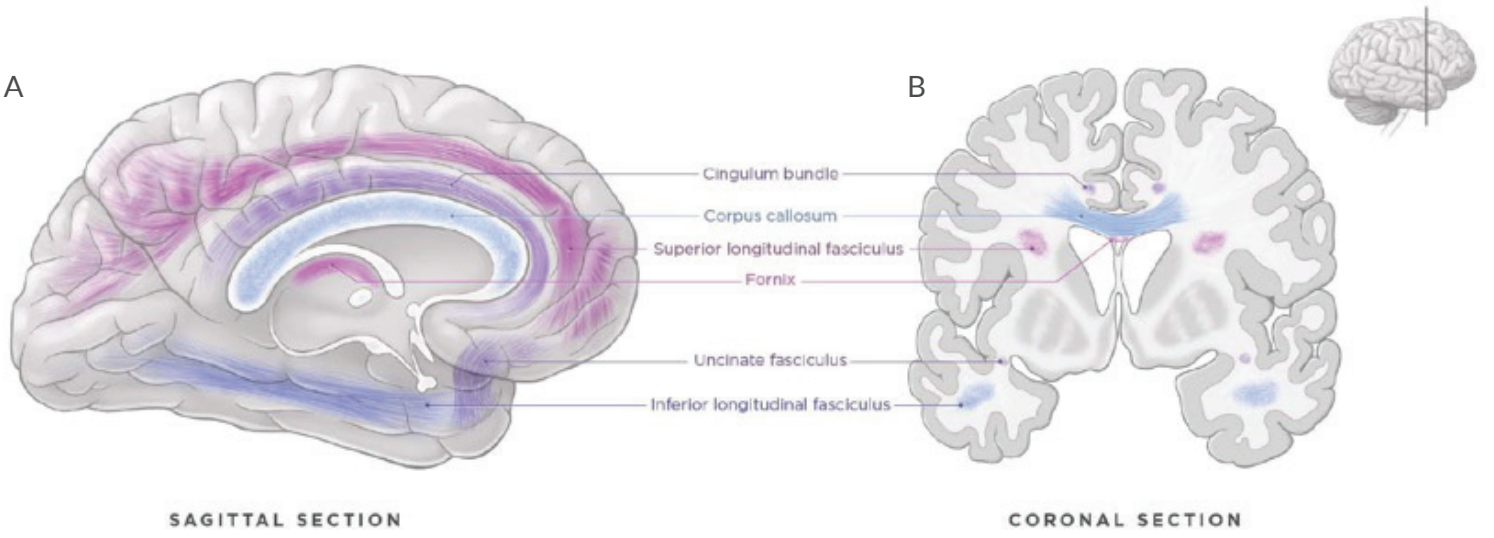


**Figure 8.** The key white matter tracts in the brain that are potentially vulnerable to degradation from stress related to experiences of racism. Highlighted are major tracts in both sagittal (A) and coronal sections (B): uncinate fasciculus (UF), cingulum bundle (CB), superior longitudinal fasciculus (SLF); inferior longitudinal fasciculus (ILF), and fornix.[56,57]



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Racial discrimination emerged as a significant predictor of lower FA values for the CoC, SLF, and left anterior CB after accounting for the socioenvironmental factors mentioned above. The most significant correlation between racial discrimination and FA was seen in the left anterior CB (p=0.0004), where statistical models accounted for 20% of the variance in FA. Additional analyses showed that racial discrimination explained 10% of the observed variance (ΔR2=0.11), suggesting that discrimination may contribute to changes in the integrity of white matter pathways involved in emotional regulation, attention, and cognitive processing. In the CoC, the model accounted for 18% of the variance in FA (p=0.002), with racial discrimination helping to explain 10% of this variance (ΔR2=0.10). Researchers then examined associations between racial discrimination and the genu, body, and splenium of the CoC and found significant associations within the genu and body (ΔR2=0.14 and 0.10, respectively). Lastly, right SLF analyses showed that the model accounted for 15% of the variance in FA, with racial discrimination accounting for 9.5% variance (ΔR2=0.095). Analyses of the left SLF showed that the model accounted for 19% variance in FA, with racism discrimination accounting for 8% variance (ΔR2=0.78).

Additional analyses were conducted to assess the potential confounding effects of age and racial discrimination on FA of the CoC, SLF, and left anterior CB. These analyses showed that both age and racial discrimination significantly contributed to variance in FA values across the examined pathways without any significant interaction between the two factors, suggesting that the impact of racial discrimination on white matter integrity is significant regardless of age. In contrast, the association between racial discrimination and FA values did not reach the corrected statistical threshold for other tracts (right ILF, right UF, fornix, and various segments of the CB), suggesting that the effects of racial discrimination might be more pronounced in certain brain regions than others.

In sum, this study observed a statistically significant association between racial discrimination and alterations in white matter microstructure within a sample of trauma-exposed Black Americans, emphasizing the robust associations between racial discrimination and white matter microstructure in major brain commissural and associational tracts (notably the CoC, anterior cingulum, and SLF). Racial discrimination independently accounted for approximately 10% of the variance in FA across major white matter pathways such as the CoC, particularly its anterior segments, as well as the SLF and the anterior CB. Even when factors such as age were controlled, racial discrimination continued to significantly influence FA values, underlining its potent and unique contribution to brain microstructural changes. The findings identify specific neural pathways that may be particularly sensitive to the stress of racial discrimination, such as the CoC, SLF, and anterior CB—tracts critical for cognitive and emotional functioning and frequently implicated in trauma and PTSD—and suggest that prolonged exposure to racial discrimination-related stressors may erode the integrity of these pathways over time.

## LONG-TERM EXPOSURE TO RACIAL DISCRIMINATION-RELATED STRESSORS CAN DAMAGE NEURAL PATHWAYS OVER TIME[9]





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# BIOLOGICAL IMPRINTING OF CHRONIC STRESS FROM RACIAL TRAUMA





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# BIOLOGICAL IMPRINTING OF CHRONIC STRESS FROM RACIAL TRAUMA

Racial discrimination creates persistent chronic stress on the neurobiology of minoritized individuals, altering brain structure and function and potentially predisposing them to disparate neuropsychiatric health outcomes.[5-9,20-22,24,25] Therefore, racially discriminatory experiences are not merely individual afflictions but a barrage of traumatic experiences that may leave an imprint of chronic stress—not just on individuals but across generations as well. The intergenerational transmission of trauma describes how the effects of past traumas among a collective minoritized group extend beyond immediate pathology in individuals to permeate subsequent generations. This "biological memory" of distressing experiences has been described through the mechanisms by which racial trauma embeds into and transmits itself throughout the fabric of minoritized individuals and communities.[12,16]

**RACIALLY DISCRIMINATORY EXPERIENCES MAY LEAVE A LEGACY OF CHRONIC STRESS, AFFECTING INDIVIDUALS AND SPANNING GENERATIONS** [5-9,12,16,20,21,24,25]

# SELF-REPORTED EXPERIENCES OF RACIAL DISCRIMINATION ARE ASSOCIATED WITH DNA METHYLATION ALTERATIONS IN PROTEIN-CODING GENES[18]

Epigenetic modifications may serve as a plausible vehicle for intergenerational transmission of racial trauma. Epigenetic modifications are essential regulatory changes to DNA structure that modulate gene expression without altering primary DNA sequences. DNA methylation, for instance, involves the addition of a methyl group to DNA, typically resulting in the suppression of gene activity.[18] Epigenetic modifications can be induced via environmental exposures, including nutrition, psychosocial stress, and environmental exposure to toxins, and have profound implications for mental health outcomes in minoritized communities.[13]

A study investigated the association between self-reported racial discrimination and DNA methylation in African American women aged 20–49 years who had no prior history of neuropsychiatric disorders. Clinical assessments and salivary samples were collected for DNA analysis during the initial visit ("T1"). Clinical data and psychological measures (parenting, depression, and reported experiences of discrimination measured by two separate clinical tools) were also collected at T1 using computer-assisted self-interview software designed to enhance the accuracy of self-reported data by minimizing social desirability bias. An epigenome-wide association study (EWAS) assessed DNA methylation profiles from salivary samples to evaluate the influence of self-reported discrimination. A total of 147 participants contributed samples and measures of Major Life Discrimination scales (MLD-EWAS), which assess discriminatory experiences in adults against demographic factors, while 152 participants contributed samples for analysis based on the Race-Related Events scale (RES-EWAS), which evaluates adult exposure to potentially traumatizing instances of race-related stress.



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The study uncovered several associations between DNA methylation and MLD scores. First, MLD scores were associated with DNA methylation changes at nine cytosine-phosphate-guanine (CpG) sites ($p<0.05$). Secondly, increasing MLD scores correlated with hypomethylation at 77.8% of the identified CpG sites. These results suggest that individuals who reported greater experiences of discrimination per the MLD had decreased DNA methylation on seven CpG gene sites, notably on genes linked to neuropsychiatric function and tumor suppressor genes. For example, the mitotic arrest deficient 1 like 1 (MAD1L1) gene, a tumor suppressor, has been linked to schizophrenia and bipolar depression. The leucine-rich repeat neuronal 3 (LRRN3) gene has been linked to gene expression differences in older age as it relates to neuronal recovery after traumatic brain injury. Additionally, the protein-coding sortilin-related VPS10 domain-containing receptor 1 (SORCS1) gene has been linked to Alzheimer's disease.[18]

Interestingly, there were no statistically significant associations between RES scores and DNA methylation. Therefore, the overall accumulation of discriminatory experiences might play a more critical role than the specific type of discrimination in forecasting long-term mental health outcomes—suggesting a possible distinction between the impact of different types of discrimination experiences on gene expression. Furthermore, the study did not detect an overlap across the top epigenetic changes between the MLD and RES variables when comparing the most significant findings, suggesting the possibility that different forms of discrimination may activate distinct epigenetic pathways.

This analysis highlights the impact of racial discrimination on epigenetic changes, particularly DNA methylation in genes related to neuropsychiatric functions and tumor suppression, among African American women. While major life discrimination correlated with measurable epigenetic changes in this research, race-related stress did not, suggesting that the cumulative effects of discrimination might hold more weight for long-term health effects than specific incidents. These findings are important, as they demonstrate an intersection between race as a social determinants of health and epigenetic modifications in vulnerable populations.

## DISCRIMINATION IS ASSOCIATED WITH NEUROENDOCRINE-RELATED DYSREGULATION DUE TO DNA REGULATORY CHANGES IN STRESS-RELATED GENES[19]

Recent research provides evidence to support an association between DNA methylation changes in loci of stress-regulatory genes during the prenatal period and self-reported scores of racial discrimination over time. In this research, 150 healthy pregnant Latina women aged 18–45 were recruited to provide demographic information and undergo psychological assessments at 24–32-week gestation ("T1") and 4–6 weeks postpartum ("T2"). Experiences of discrimination were surveyed, and blood samples were collected for DNA methylation analysis. To minimize the variability of stress on DNA sample collection, blood samples were collected during routine prenatal visits at T1 and at subsequent visits. Epigenetic analysis focused on CpGs in genes involved in stress regulatory responses, including glucocorticoid receptor gene (NR3C1), glucocorticoid receptor chaperone protein gene (FKBP5), and brain-derived neurotrophic factor gene (BDNF). Covariates, including maternal demographics, depression symptoms, and offspring biological sex, were considered to minimize their impact on study results.

At T1, 43.5% of participants reported experiencing discrimination, with 30.4% specifically attributing discriminatory experiences to their ethnicity at some point in their lives. DNA methylation analyses showed significant negative relationships between self-reported discrimination scores and methylation levels, suggesting a



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possible epigenetic link to discrimination. Specifically, at T1, significant negative correlations were seen across discrimination scores and methylation at CpG sites 1 and 2 of NR3C1 (p=0.008 for site 1, and p=0.004 for site 2). Similar negative correlations were found at CpG sites 6 and 7 of the BDNF promoter (p=0.004, 0.004, respectively). Additionally, a significant negative correlation was noted at CpG site 1 of FKBP5 (p<0.001). At T2, negative associations between discrimination scores and CpG site 2 of NR3C1 (p=0.025) and CpG sites 6 and 7 of BDNF (p=0.025, 0.025, respectively) remained. The analysis also showed negative associations between discrimination scores and CpG site 5 of BDNF (RR=0.86, p=0.025). Further analyses did not reveal significant associations between ethnicity-based discrimination and DNA methylation, suggesting nuanced interplays between discrimination scores and epigenetic modifications.

### RACIAL DISCRIMINATION ASSOCIATED WITH SIGNIFICANT METHYLATION CHANGES AT SELECT CPG SITES

| Gene | CpG Site | EDS at T1 | EDS at T2 |
|---|---|---|---|
| | | *p*-value | *p*-value |
| ***NR3CI*** | Site 1 | 0.008 | 0.891 |
| | Site 2 | 0.004 | 0.025 |
| ***BDNF*** | Site 5 | NS (0.376) | 0.025 |
| | Site 6 | 0.004 | 0.025 |
| | Site 7 | 0.004 | 0.025 |
| ***FKBP5*** | Site 1 | <0.001 | NS (0.442) |

**Table 2.** This table displays the p-values for the association between methylation at specific CpG sites within the NR3C1 and BDNF genes and racial discrimination scores at two time points (T1 and T2), after controlling for demographic variables. NS=nonsignificant. Adapted from Santos, HP Jr, et al. *Psychoneuroendocrinology*. 2018.[19]

Persistent, statistically significant negative associations were found between greater self-reported discrimination scores and methylation at specific CpG sites in NR3C1, FKBP5, and BDNF stress-related genes at T1 and 4–6 weeks postpartum (table 2). This indicates higher discrimination scores associated with altered methylation of genes implicated in stress-related disorders. The study discerned that while some methylation changes were consistent over time (e.g., NR3C1 and BDNF), variations in methylation patterns between T1 and T2 (e.g., NR3C1 and FKBP5) may be attributed to factors such as endocrine changes in the peripartum and postpartum periods or shifts in the social environment in the postpartum period, which could reduce stress associated with discriminatory experiences or enhance social support. Thus, the data suggest that individuals who self-report greater discrimination may exhibit greater sensitivity to social stress. Specifically, the authors conclude from the data on NR3C1 and FKBP5 that hypothalamic-pituitary-adrenal (HPA)-related methylation alterations are linked to experiences of both antenatal and postnatal discrimination, with the dynamics of this relationship potentially changing over time. It is suggested that the stress from discrimination might trigger DNA methylation changes across various genes, which together could reduce stress responsiveness. Additionally, negative correlations were found between BDNF methylation and discrimination scores, particularly at two CpGs analyzed at both time points, suggesting possible enduring discrimination-associated neuroplasticity. This nuanced understanding of epigenetic modifications associated with discriminatory experiences provides insightful implications for the biological impact of noxious social constructs such as racism.

## PARENTAL PSYCHOPHYSIOLOGICAL TRAUMA BEFORE CONCEPTION MAY BE LINKED TO CHANGES OBSERVED IN THEIR CHILDREN[14]

Epigenetic modifications have been observed in children of adults who have experienced psychological trauma. The literature surrounding the long-term effects of the Holocaust on survivors (F0) and their children (F1) alongside controlled counterparts provides compelling evidence to suggest that preconception experiences of trauma are associated with epigenetic modifications in survivors and their descendants. This intergenerational transmission of psychological stress via differential methylation of stress-response genes sheds light on the enduring legacy of psychological trauma.



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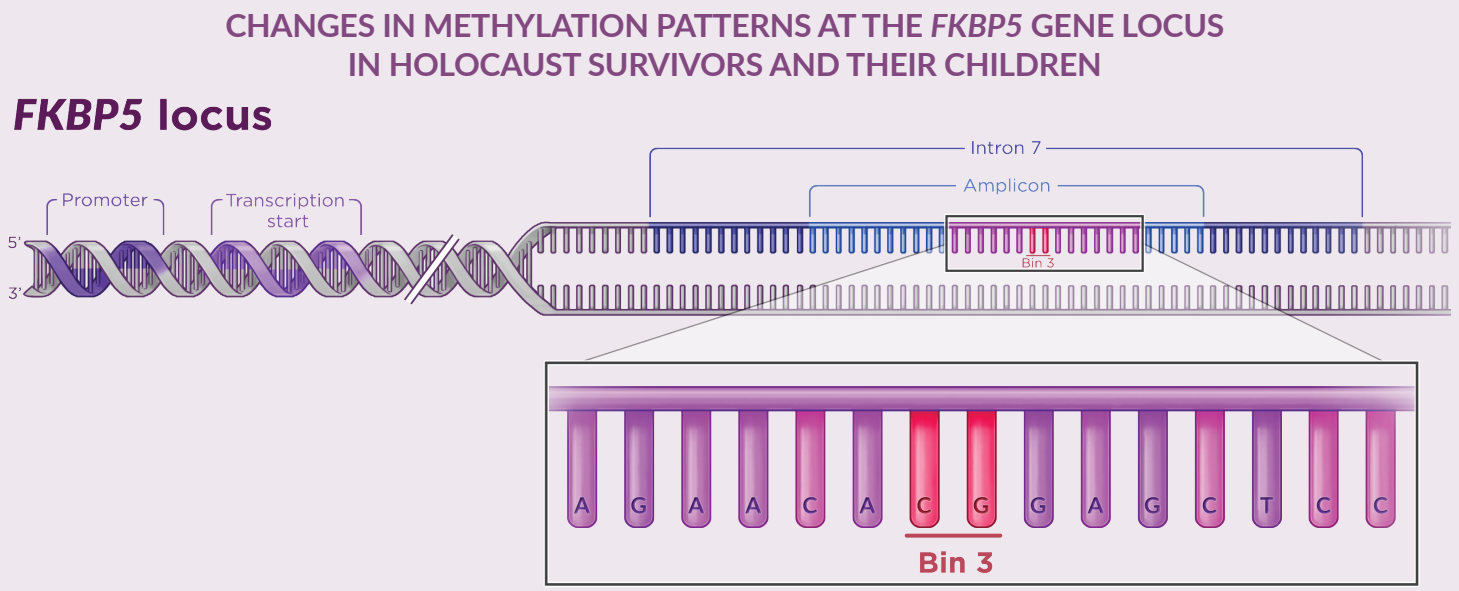


**Figure 9.** Simplified schematic of the region within intron 7 of the FKBP5 gene where methylation changes were observed in opposite directions across parents who survived Holocaust trauma (F0) and adult children of Holocaust trauma survivors (F1). Adapted from Yehuda R, et al. *Biol Psychiatry*. 2016.[14]

*FKBP5* methylation at specific gene sites was studied in the context of intergenerational epigenetic effects of severe psychological trauma following Holocaust exposure. This study surmised that parents who survived Holocaust trauma (F0) would demonstrate differential methylation in specific *FKBP5* sites compared with nonexposed matched Jewish participants in the control arm. They also proposed the adult children of trauma survivors (F1) would exhibit differential methylation in the same *FKBP5* sites as their parents, indicating potential intergenerational transmission. Childhood adversity was measured to account for confounding variables that might influence study results on gene methylation patterns. This study recruited a cohort of Holocaust survivors and their offspring, along with comparison subjects, to explore the intergenerational effects of trauma exposure on DNA methylation. A cohort of Holocaust survivors (F0, n=40) who were interned in Nazi concentration camps, witnessed or experienced torture, or had to flee or hide during World War II were included. Participants who lived outside of Europe during World War II were recruited into the control arm. Inclusion criteria for F1 participants (n=31) included being raised by their biological parents. Psychiatric conditions were diagnosed using structured clinical interviews and validated diagnostic tools, with specific scales used to assess post-traumatic stress disorder (PTSD), depression, and anxiety. F1 participants were asked to complete questionnaires on childhood trauma, parental PTSD symptoms, and severity of parental exposure to the Holocaust. Methylation analysis was conducted to assess parental and child epigenetic modifications via blood DNA, focusing on three regions within *FKBP5* intron 7 known for glucocorticoid response involvement.

Statistical analyses assessed differences in DNA methylation between survivors, offspring, and controls, adjusting for mood disorders, demographic factors, and other relevant variables. The primary analyses focused on comparing methylation differences in the three intron 7 regions between groups of Holocaust survivors or their offspring and comparison subjects. Regression analyses assessed the impact of various factors on *FKBP5* methylation, including parental Holocaust exposure, *FKBP5* methylation in the parents (F0), maternal and paternal PTSD, childhood adversity, and offspring (F1) *FKBP5* genotype to F1 *FKBP5* methylation. Additional analyses explored the impacts of physical and sexual abuse on methylation patterns, particularly in the context of *FKBP5* risk alleles.

Compared to F0 control participants without prior exposure to Holocaust trauma, F0 Holocaust survivors exhibited the presence of PTSD with varying degrees of severity. The F1 adult children of Holocaust survivors reported greater severity of depression, anxiety, and emotional abuse compared to F1 participants in the control group. Epigenetic analysis revealed that Holocaust survivors had 10% greater methylation at bin 3/site 6 compared to controls (p=0.046; figure 9), suggesting that trauma exposure is associated with specific epigenetic

modifications. This effect persisted even after adjusting for PTSD (p=0.049) and *FKBP5* risk allele (p=0.053), indicating that the traumatic exposure itself, rather than a genetic predisposition or the chronic stress of a traumatic experience, may be driving these epigenetic changes. In contrast to F1 control participants, F1 trauma-exposed individuals showed a 7.7% lower methylation at the same bin site as F0 (p=0.034), and this effect appeared to be reduced when adjusting for parental PTSD (p=0.121). This suggests the possibility of a differential intergenerational transmission of methylation patterns, possibly influenced by parental PTSD symptoms.

Further analyses revealed that parental Holocaust exposure was a significant predictor of methylation patterns in their children, overriding other factors such as parental PTSD, *FKBP5* risk allele, childhood adversity, or emotional abuse. Further, a significant correlation was noted between methylation levels of parents who had experienced trauma and their children (p=0.010). Thus, traumatic impact on a parent might substantially influence their children's epigenome more than other potentially confounding variables.

These results demonstrate a relationship between epigenetic changes in regions of *FKBP5* linked to parental preconception traumatic stress effects in Holocaust survivors and their adult children. Notably, methylation changes were observed in the same *FKBP5* site (intron 7 bin 3/site 6) across F0 and F1 generations, albeit in opposite directions, suggesting a potential epigenetic transmission of trauma effects (figure 10). Methylation changes remained significant after adjusting for *FKBP5* genetic risk allele and F1 trauma exposure or psychopathology, suggesting that epigenetic modifications are directly attributable to Holocaust trauma experienced by the prior generation.

The researchers posit that the varied direction of methylation between Holocaust survivors and their descendants shows that *FKBP5* hypermethylation in F0 mothers may result in gene expression changes that affect

## METHYLATION PATTERNS DISPLAY EVIDENCE OF INTERGENERATIONAL IMPACT IN HOLOCAUST SURVIVORS AND THEIR CHILDREN

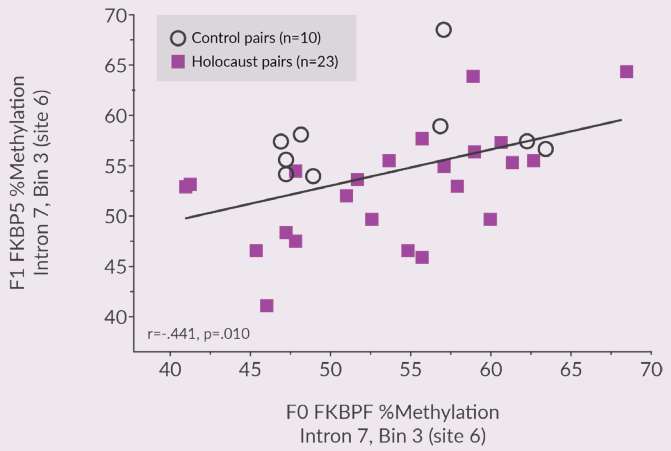


**Figure 10.** A scatter plot showing the association between methylation patterns of FKBP5 intron 7/Bin3 in parents who are Holocaust survivors (F0) and adult children of Holocaust survivors (F1). Circles represent control subject pairs (n = 10), and squares represent parent-offspring pairs among Holocaust survivors (n = 23). Adapted from Yehuda R, et al. *Biol Psychiatry*. 2016.[14]

glucocorticoid receptor sensitivity and circulating levels of glucocorticoids in utero. As a result, these changes may promote demethylation of fetal *FKBP5* to adjust glucocorticoid levels vis-a-vis developmental needs, but preconception and postpartum events may also influence epigenetic modifications. The question remains whether glucocorticoid programming in children results from the direct transmission of altered stress responses from parents who survived severe trauma or if these responses represent the offspring's adaptive glucocorticoid recalibration to external influences. Although the study was not designed to determine the mechanisms of transgenerational epigenetic effects conclusively, the findings suggest intergenerational epigenetic priming of stress responses in F1 of highly traumatized F0, potentially priming their susceptibility to stress, underlying a complex mechanism by which racial trauma, such as the Holocaust, can affect individuals and their descendants through measurable biological markers.



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# RACISM-MEDIATED NEUROENDOCRINE DYSREGULATION ACTS AS A PRENATAL STRESSOR PERPETUATING RACIAL HEALTH INEQUITIES

For pregnant women of minoritized communities, the chronic stress of racial discrimination may also function as a prenatal stressor that impacts fetal development (figure 11).[12,16,17,19] Studies of Holocaust survivors and their descendants reveal associations between prenatal trauma and altered cortisol metabolism in subsequent generations via changes in stress regulatory responses. Women under duress in pregnancy are at risk for transmitting cortisol through the placenta to the fetus, disrupting fetal development. Increased fetal cortisol exposure can alter the developing fetal hypothalamic-pituitary-adrenal (HPA) axis, impacting fetal and infant stress systems and increasing the risk for morbidity over time.[12,15] High levels of cortisol in utero have also been associated with fetal growth restriction, increasing the risk of low birth weight and preterm birth—exacerbating already-existing inequities in birth outcomes in minoritized women.[12,16,17]

Thus, the chronic stress of enduring racism might be biologically imprinted on minoritized individuals. Consequently, this chronic stress functions as a prenatal stressor with long-term implications for maternal, fetal, and child health. Therefore, mental health inequities may originate at conception and persist throughout life, in part due to chronic stress exposure from racism that disproportionately affects minoritized communities and propagates health inequities.[12,16,17]

## RACISM MAY FUNCTION AS A PRENATAL STRESSOR WITH LONG-TERM IMPACTS ON MATERNAL, FETAL, AND CHILDHOOD HEALTH

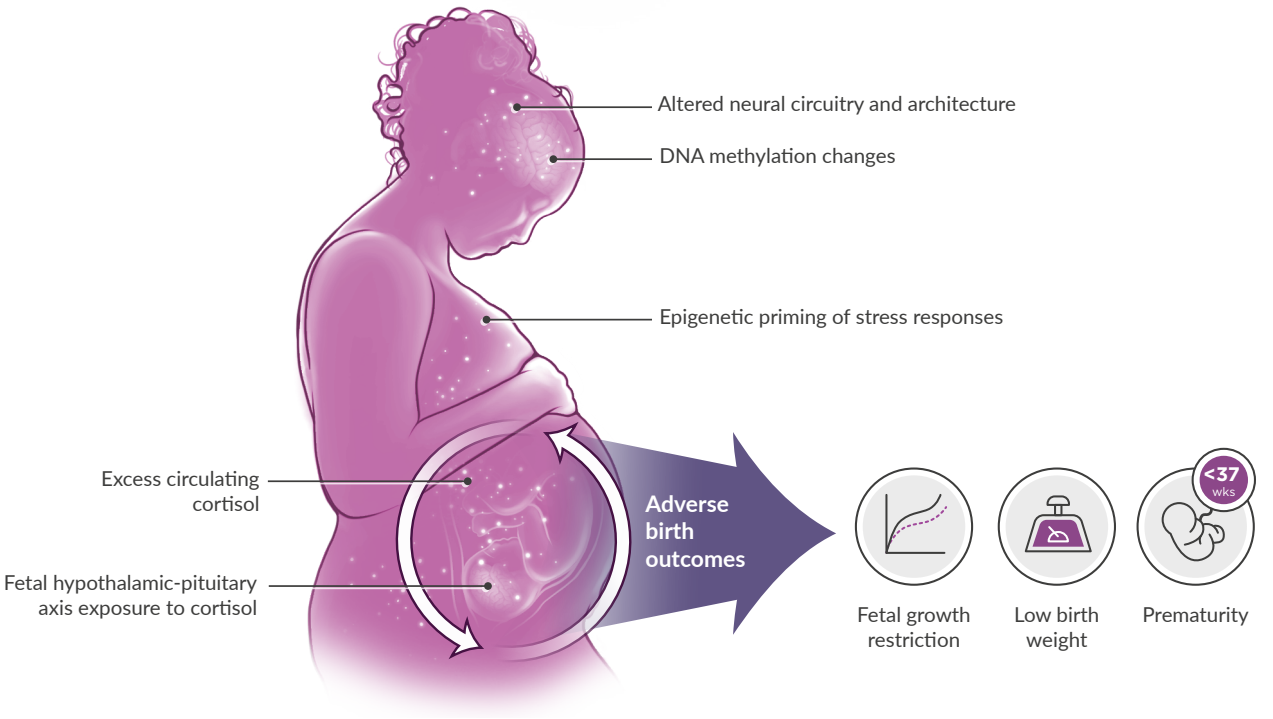


**Figure 11.** The physiological and epigenetic mechanisms through which racial discrimination may act as a prenatal stressor and affect both maternal and fetal health.[5, 12,15-17, 19]



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# RACIAL DISCRIMINATION AS A PRENATAL STRESSOR LINKED TO CHANGES IN THE NEONATAL BRAIN[17]

Preliminary evidence for maternal experiences of discrimination during pregnancy are linked to altered resting-state functional magnetic resonance imaging (rsfMRI) connectivity in newborns. These prenatal experiences of discrimination are associated with changes in the connectivity of threat-related neurocircuitry in their newborns. Strikingly, the results indicate a specificity to experiences of racial discrimination that are independent of other sociodemographic stressors, suggesting that racial discrimination as a prenatal stressor influences threat circuitry in newborns and adults alike, with grave potential for detrimental brain health outcomes across generations.

A predominantly Hispanic cohort (88%) of 165 healthy, nulliparous pregnant adolescent women aged 14–19 was recruited to explore the effects of discrimination and acculturation on rsfMRI of the amygdala in their infants (n=38) six weeks after birth. Participants provided self-reported data at various time intervals during their pregnancy regarding discrimination, acculturation, maternal distress (perceived stress, childhood trauma, and depressive symptoms), and socioeconomic status; the latter was analyzed to isolate these factors from other stressors. A self-reported measure of experiences of discrimination was assessed at weeks 12–14, 24–26, and 34–36 of gestation. An exploratory factor analysis was performed to investigate how discrimination, acculturation, and distress during pregnancy correlate with one another and to differentiate these factors from other stressors. This distinction was then correlated with the rsfMRI connectivity of the infant amygdala.

All women in this study reported being a woman of color or belonging to a minoritized group. Although 88% of the cohort identified as Hispanic/Latinx, discrimination stressors between Hispanic and non-Hispanics were similar. Factor analysis revealed that discrimination and acculturation stressors loaded onto different factors independent of perceived stress, depressive symptoms, trauma, and socioeconomic status, indicating that discrimination factors are distinct from other stressors. Prenatal exposure to discrimination was associated with weaker connectivity between the amygdala and prefrontal cortex (PFC) ($p<0.05$) and stronger connectivity between the amygdala and fusiform gyrus in the infant brain, a phenotype also observed in individuals with PTSD and depression.[5] Although the study did not detect a significant association between discrimination, acculturation stressors, and fetal growth and birth metrics, the findings suggest that discrimination and acculturation factors are distinct from other stressors that can potentially affect fetal brain development.

**MATERNAL DISCRIMINATION DURING PREGNANCY ALTERS NEONATAL BRAIN FUNCTION INDEPENDENTLY OF MATERNAL STRESS AND DEPRESSION, AFFECTING FETAL NEURODEVELOPMENT[17]**



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## RACIAL DISCRIMINATION DURING PREGNANCY LINKED TO ALTERED AMYGDALA CONNECTIVITY IN OFFSPRING

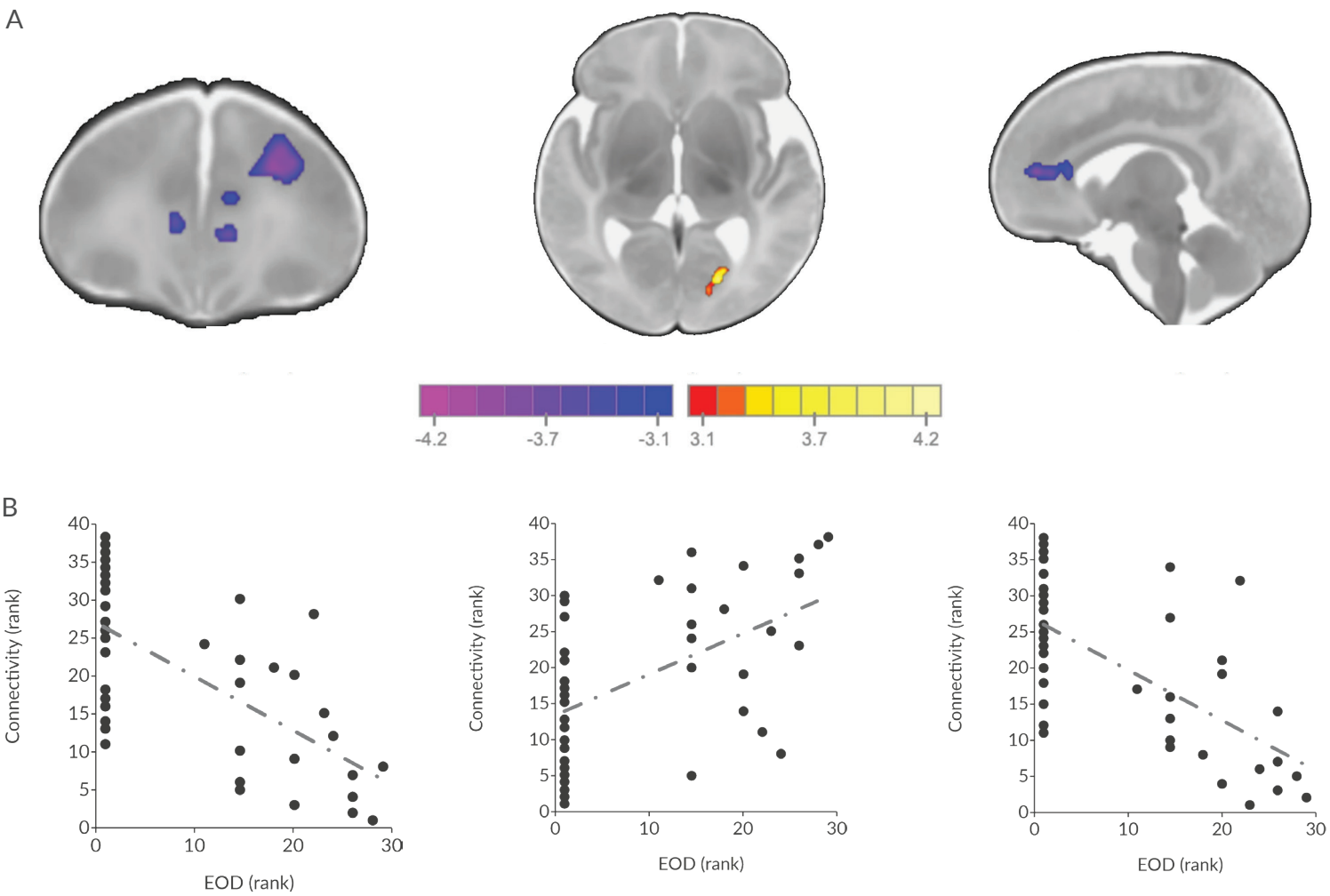


**Figure 12.** Brain scans (A) from babies born to mothers who faced discrimination showed weaker connections between the amygdala and the front parts of the brain but stronger connections with the left side of the brain responsible for recognizing faces. The scatterplots (B) below the brain images show how these connections vary with the level of discrimination the mothers faced. Adapted from Spann MN, et al. *Neuropsychopharmacology*. 2024.[17]

Thus, maternal experiences of discrimination during pregnancy correlate with altered functional connectivity of the neonatal amygdala (figure 12). The effects of discrimination on neonatal amygdala-frontal circuits remain after adjusting for maternal perceived stressors and depressive symptoms, which have also been linked to altered functional connectivity of these neural regions. These data implicate a specificity to discriminatory experiences that are independent of other types of stressors and suggest that exposure to discrimination functions as a prenatal stressor potentially influencing fetal neurodevelopment. These outcomes mirror those observed in adult studies on self-reported discrimination and altered neurocircuitry of threat-related regions, suggesting the effects of racial trauma on amygdala and threat-related neurocircuitry may propagate across generations.

# CONCLUSION

Racism and racial trauma not only initiate changes in neural structure and function but also continue to mold these processes over time. Both acutely and chronically, racism fundamentally alters critical brain circuits and regions involved in threat perception and response. Neural circuits critical for threat detection and emotional processing are recurrently activated during experiences of racial discrimination. Chronic engagement of these regions may have biological impacts with potential negative effects on the brain. Furthermore, the continuous strain from such stressors imposes a significant allostatic load, portending long-term neuropsychiatric implications, including depression, post-traumatic stress disorder (PTSD), and anxiety.[4-9,24,25]

The pernicious influence of racism extends beyond functional, structural, and neuropsychiatric disturbances in individuals and into subsequent generations. Racism may become biologically embedded, intertwined into the very DNA through mechanisms like DNA methylation, altering gene expression in ways that perpetuate disordered stress responses among descendants. This insidious effect begins as early as the prenatal stage, where racism serves as a stark prenatal stressor, disrupting maternal neuroendocrine functions and setting a trajectory of altered neurodevelopment for the unborn. Such early exposures can lead to neuroendocrine dysregulations, which not only predispose individuals to chronic mental health conditions but also alter how stress is perceived and managed across the lifespan.[4,12-19]

The profound effect of racism on biological function across generations is demonstrated in studies showing that racial discrimination during pregnancy is associated with alterations in resting-state functional magnetic resonance imaging (rsfMRI) in the neonatal brain.[17] This evidence suggests that the seeds of mental health inequities may be sown before birth.[12,16] These findings underscore the profound and far-reaching implications of racism across generations, emphasizing a critical avenue for intervention. Understanding and addressing these profound neurobiological impacts may help mitigate the perpetuating cycle of racism and disparate health outcomes in minoritized communities. This narrative underscores not merely physiological and psychological pathways of the noxious impact of racism but also calls to action urging a more conscious and tailored approach to tackling the endemic issue of racism within our health care systems and beyond.



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# CALLS TO ACTION

Racism is pervasive in all aspects of life, which can make driving change feel daunting. However, practical and thoughtful strategies may help mitigate the negative effects of racism that can lead to racial trauma and adverse brain health outcomes among historically underserved, minoritized communities.[53] The following calls to action (CTA) are based on the references indicated and the authors' expertise and experiences. These calls to action are organized by level, starting with individuals and expanding to societal drivers of change.

# CTA FOR INDIVIDUALS: PERSONAL BELIEFS DERIVED FROM SOCIETAL NARRATIVES

For individuals, personal beliefs and biases about race, both explicit and implicit, influenced by culture and society may manifest as prejudices, negative beliefs about one's race or others, beliefs about superiority, or internalized oppression.[26]

**For individuals wanting to challenge their own personal beliefs and biases about race:**

Individuals can reflect on where their beliefs come from and confront internalized biases. Challenging existing beliefs about race and racism requires an openness to learning, commitment to understanding the lived experiences of others, and willingness to make mistakes throughout the process.[58] Actions individuals can take include:

- **Educate oneself:** Learn about the history of racism and systemic oppression to better understand the context of racial trauma. Commit to ongoing learning and personal growth in the journey toward becoming anti-racist.
- **Sustain continuous self-reflection:** Engage in self-reflection to consider how bias or privilege influences everyday life (e.g., choices, opportunities, daily interactions).
- **Engage in conversation:** Share what you have learned with friends, family, and others. Engaging in conversation can help normalize discussions about racism and may provide additional opportunities for education. (Note: Be mindful of imposing conversations about racism on those from minoritized communities. While it is on all of us to understand and address racism, it is often a burden on minoritized communities to educate others about their experiences.)

**For individuals who have experienced racism and racial discrimination:**

Individuals who have experienced racism are encouraged to embrace self-care and seek out support from health care providers that treat the adverse effects of racial trauma. Actions these individuals can take include:

- **Gather resources:** Using tools like books and other resources may help to deal with daily and past experiences of racism, challenge negative thoughts, and manage stress.
- **Practice self-care and self-awareness:** Recognize the signs of racial trauma, which may include anxiety, depression, anger, and hypervigilance. Practice self-awareness to identify how these experiences affect you personally.
- **Seek therapy or counseling:** Consider therapy or counseling with a mental health professional who specializes in racial trauma and understands your unique experiences and challenges.



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# CTA FOR HEALTH CARE SYSTEMS AND PROVIDERS: INSTITUTIONAL SUPPORTS FOR EQUITY

Institutional racism refers to policies and discriminatory practices at an organizational level.[28] Within health care systems, institutional racism may produce inequitable experiences for patients and ultimately result in poorer health outcomes.[53] Integration of these insights into their strategies may help to reduce health inequities and improve outcomes across historically minoritized groups.

**For health care systems:**

Health systems can incorporate intentional strategies, programs, and policies across their organizations to improve cultural understanding, increase diversity and representation, and engage communities to advance mental health equity among historically underserved communities. Actions health systems can take include:

- **Directly engage communities:** Work with local communities to build trust and collaborate on strategies to prevent racial trauma. Community input and partnerships can help health care systems better understand the needs and concerns of the populations they serve.
- **Provide cultural humility training:** Ongoing training in cultural humility and diversity is essential for understanding the lived experiences of historically underserved groups and equipping employees to create a welcoming and supportive environment.
- **Invest in research:** Expand interest and funding for scientific studies into the neurobiological sequelae of racial trauma across various minoritized groups to improve the inclusion of minoritized patients in scientific literature.
- **Prioritize clinical trial diversity:** Expand recruitment of underrepresented groups in clinical trials.
- **Embrace patient-centered care:** Prioritize patient-centricity, which involves engaging patients in shared decision-making and respecting their values, preferences, and lived experiences. This approach ensures that patients' perspectives are valued and reduces the potential for trauma.
- **Enact anti-racist policies:** Implement and enforce anti-racist policies and practices that actively work to identify and eliminate racism within the system. This includes addressing systemic inequities and promoting health equity.
- **Advance workforce diversity:** Foster a more inclusive environment by creating a diverse workforce that reflects the communities it serves. A diverse staff can provide better care and reduce the likelihood of racial trauma.

**For individual practitioners:**

Identifying ways to reduce the impact of racial discrimination can enhance healing practices. Practitioners should consider using approaches such as liberation psychology and Black Feminist methods to address racial trauma. These strategies suggest that incorporating activism and building social support networks into treatment plans might help reduce the negative effects of racial discrimination for Black American adults.

- **Evaluation of individual-level factors:** Before starting this work, it is important for practitioners to understand what influences a person's coping strategies, including past trauma and stress related to their identity. Therapists should consider personal situations, such as their client's power at work and social support, to weigh the benefits and any potential downsides of including activism in treatment.
- **Implement culturally relevant therapy models:** While encouraging activism and social involvement fits well with therapies like cognitive-behavioral therapy, it is also important to consider culturally relevant approaches. For example, the Critical Consciousness of Anti-Black Racism model (Mosley et al., 2020) provides guidance on addressing racial discrimination in therapy and encourages activism as part of the healing process, making therapy a place for recovery and rejuvenation.



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# CTA FOR SOCIETY: CULTURAL AND STRUCTURAL DRIVERS OF CHANGE

Systemic and structural racism refers to racism found in societal systems and structures, such as laws, policies, ideologies, cultural narratives, and more, which reinforce discriminatory beliefs.[53] Fostering empathy and active listening to better understand the experiences of minoritized communities is crucial to changing societal beliefs and dismantling pervasive narratives that undermine equity.

**For society:**

Society can work to ensure that communities impacted by racial trauma have equitable access to mental health support and practice continual self-reflection to identify and prevent viewing historically underserved, minoritized communities through the lens of their biases. Actions to address racism at a societal level may include:

- **Facilitate mental health support:** Ensure that mental health services are accessible and culturally competent so individuals who experience racial trauma can seek help. Reduce the stigma around mental health in minoritized communities.
- **Increase representation and inclusion:** Promote diversity and inclusion in all sectors of society, including government, education, media, and corporate leadership. Ensure minoritized communities have a voice in decision-making processes and policy development.
- **Support allyship and solidarity:** Support people, organizations, and narratives encouraging individuals to be allies and stand in solidarity with minoritized communities.

While the evidence to support the physiological impact of racism grows, it is clear there is an urgent need to address mental and cognitive health among minoritized communities. The role of racial trauma and its impact on the brain is only beginning to be understood. Additional research to understand the mechanisms by which trauma affects the brain is needed, as well as widespread interventions to reduce the impacts of racism at all levels of society. The pervasive nature of racism can make driving change seem daunting; however, practical and thoughtful strategies at individual, systemic, and societal levels may help mitigate its negative effects, particularly those leading to racial trauma and adverse brain health outcomes in minoritized communities. Individuals can challenge internalized biases through education, self-reflection, and conversation. Health care systems can implement policies to promote equity, enhance cultural understanding, and engage communities meaningfully. Society must work towards increasing representation, ensuring equitable access to mental health support, and fostering empathy and active listening to dismantle discriminatory narratives. By addressing racism at every level, we can begin to create a more inclusive and supportive environment for all.



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# APPENDIX

# KEY LEXICON

To discuss and progress toward health equity, we must establish a common health equity language in the space. The following are definitions for key health equity terms utilized by the Centers for Disease Control and Prevention (CDC), American Psychological Association (APA), and American Medical Association (AMA) used throughout the report.

- **Cultural humility:** Cultural humility involves a lifelong commitment to self-evaluation and addressing power imbalances in health care for underserved, minoritized communities.[59]
- **Discrimination:** The unfair or prejudicial treatment of individuals or groups based on characteristics such as race, ethnicity, gender, age, religion, disability, sexual orientation, or other attributes.[60] This includes direct and indirect discrimination, incidences of discrimination (perceived), and simulated discrimination.[59]
- **Epigenetics:** Epigenetics is the study of how your behaviors and environment can cause changes that affect how your genes work.[61] More specifically, the chemical marker for a gene may be changed rather than the gene itself.[61,62] According to the theory of intergenerational trauma, trauma experienced by the older generation is translated into an epigenetic change that can be passed on to successive generations.[62]
- **Equity:** Equity means recognizing that we do not all start from the same place.[59]
- **Health equity:** Health equity can be described as the state in which everyone, regardless of history or personal experiences, has fair and just opportunities to attain their highest level of health.[59]
- **Historically underserved, minoritized, or excluded:** Minoritization exists when a person or group is considered subordinate or less than a more dominant group or its members. Groups that are referred to as minorities have been "minoritized" and excluded by the dominant, majority culture that holds power.[59]
- **Health inequities:** Health "inequities," in contrast, are explicitly defined as differences in health outcomes that are avoidable, unnecessary, unfair, and unjust.[59]
- **Intergenerational trauma:** The transmission of trauma or its legacy, in the form of a psychological consequence of an injury or attack, poverty, and so forth, from the generation experiencing the trauma, for example, mother or birthing person, to subsequent generations.[62]
- **Justice:** Justice requires us to perform actions to ensure that no harm befalls communities, and when harm is inflicted, methods of recourse and mitigation are expeditiously implemented.[59]
- **Made vulnerable:** Describing people or communities as vulnerable overlooks the fact that their vulnerability is often a result of socially constructed systems, structures, and processes. These factors determine the resources and power available to these groups, affecting their ability to cope with and be resilient to the forces that create vulnerability and poverty. People and communities are not inherently vulnerable; rather, they are made vulnerable by these external systems.[59]
- **Race:** A system of categorizing people that arises to differentiate groups of people in hierarchies to take advantage of some and disadvantage others. Stated another way, race is a social construct or "a symbolic category [actively created and recreated, rather than pre-given], based on phenotype or ancestry and constructed to specific racial and historical contexts, that is misrecognized as a natural category."[59]
- **Racial discrimination:** The differential treatment of individuals because of their membership in a particular racial group. Discrimination is, in most cases, the behavioral manifestation of prejudice and, therefore, involves unfair, negative, hostile, or injurious treatment.[63]
- Racial trauma: Racial trauma refers to the psychological and emotional response resulting from repeated exposure to racism and racial discrimination.[31] Racial trauma is inclusive of the emotional impact of stress related to racism, racial discrimination, and race-related stressors, such as being affected by stereotypes, hurtful comments, or barriers to advancement.[31] Racial trauma can refer to a specific incident of racial discrimination or the ongoing, harmful emotional impact of racial discrimination that builds up over time.[31] People can experience racial trauma from something that happens directly to them or from seeing others mistreated because of their race.



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- Racism: Racism is a system of structuring opportunity and assigning value based on phenotype ("race") that unfairly disadvantages some individuals and communities, unfairly advantages other individuals and communities, and saps the strength of the whole society through the waste of human resources. Racism can operate at different levels: structural, institutional, interpersonal, and internalized.[59]
- Transgenerational trauma: Transgenerational trauma refers to the generally subconscious transmission of traumatic experiences to subsequent generations and to society. People in the next generation find themselves showing the symptoms of trauma without having experienced the trauma themselves.[12]
- Trauma: Any disturbing experience that results in significant fear, helplessness, dissociation, confusion, or other disruptive feelings intense enough to have a long-lasting negative effect on a person's attitudes, behavior, and other aspects of functioning. Traumatic events include those caused by human behavior (e.g., rape, war, industrial accidents) as well as by nature (e.g., earthquakes) and often challenge an individual's view of the world as a just, safe, and predictable place.[64]

# HISTORICAL AND MODERN-DAY RACISM

Around the world, minoritized communities have historically faced racial discrimination. For example, indentured Africans endured systemic dehumanization, forced labor, and violent oppression under the pervasive institution of slavery in the United States, Europe, Latin America, and the Caribbean; during World War II, people of Jewish ancestry suffered the atrocities of the Holocaust in Europe; and Japanese Americans endured forced relocation and were placed in internment camps in the United States; and Indigenous populations across the globe have encountered perpetual violence, cultural assimilation policies, dispossession of land, and forced relocation.[65-68]

Racism has negatively impacted minoritized populations for generations, leading to discrimination, lost economic opportunities, incarceration, and, in many instances, premature death.[1] Modern racism persists today, so much so that the Director of the Centers for Disease Control and Prevention declared, "racism a serious public health threat that directly affects the well-being of millions of Americans."[2] Racism manifests both overtly and through institutional structures.[28] Some recent events illustrate its ongoing impact:

- Anti-Asian Hate Crimes in 2020: In 2020, anti-Asian hate crimes surged by 145% in major U.S. cities, fueled by false associations of COVID-19 originating among Asian communities. This led to widespread harassment and violence, creating additional harm and fear in Asian communities.[48]
- The murder of George Floyd: The murder of George Floyd, an unarmed Black man, by a white police officer in 2020 ignited nationwide protests against racial discrimination and police brutality. This highlighted systemic racism in law enforcement and prompted calls for police reform and federal policies that address racial inequality.[49]
- Israel-Hamas War in 2023: The Israel-Hamas war in 2023 intensified antisemitism and anti-Muslim hate speech and violence against Middle Eastern, Islamic, and Jewish communities globally.[50]
- The murder of Laken Riley in 2024: In 2024, Laken Riley was murdered by Venezuelan citizen Jose Ibarra near the University of Georgia. Ibarra's illegal entry into the U.S. was politicized and resulted in increased anti-immigration rhetoric, both on campus and on a national scale.[51,52]



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# ABBREVIATIONS

| | |
|---|---|
| ACC | anterior cingulate cortex |
| ADHD | attention deficit hyperactivity disorder |
| AMA | American Medical Association |
| APA | American Psychological Association |
| ASD | autism spectrum disorder |
| BDNF | brain-derived neurotrophic factor |
| BOLD | blood-oxygen-level-dependent |
| caCC | caudal anterior cingulate cortex |
| CB | cingulum bundle |
| CC | cingulate cortex |
| CDC | Centers for Disease Control and Prevention |
| CEN | central executive network |
| CoC | corpus callosum |
| CpG | cytosine-phosphate-guanine |
| dACC | dorsal anterior cingulate cortex |
| DMN | default mode network |
| DNA | deoxyribonucleic acid |
| EDS | Everyday Discrimination Scale |
| EWAS | epigenome-wide association study |
| FA | fractional anisotropy |
| fMRI | functional magnetic resonance imaging |
| FKBP5 | FKBP prolyl isomerase 5 |
| GAD | generalized anxiety disorder |
| HPA | hypothalamic-pituitary-adrenal |
| HIV | human immunodeficiency virus |
| ILF | inferior longitudinal fasciculus |
| KFF | Kaiser Family Foundation |
| LRRN3 | leucine-rich repeat neuronal 3 |
| MAD1L1 | mitotic arrest deficient 1 like |
| MD | mean diffusivity |
| MLD | EWAS - Major Life Discrimination-EWAS |
| NR3C1 | nuclear receptor subfamily 3 group C member 1, or glucocorticoid receptor |
| pACC | perigenual anterior cingulate cortex |
| PCC | posterior cingulate cortex |
| PFC | prefrontal cortex |
| PTSD | post-traumatic stress disorder |
| rACC | rostral anterior cingulate cortex |
| RES-EWAS | Race-Related Events-EWAS |
| rsfMRI | resting state functional MRI |
| SD | standard deviation |
| SDOH | Social Determinants of Health |
| SLF | superior longitudinal fasciculus |
| SN | salience network |
| SORCS1 | protein-coding sortilin-related VPS10 domain-containing receptor |
| SUD | substance use disorder |
| UF | uncinate fasciculus |
| vmPFC | ventromedial prefrontal cortex |
| VPS10 | vacuolar protein sorting 10 |



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