

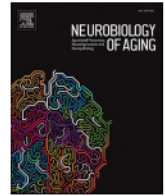


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The relationship between racial discrimination and white matter among Black older adults

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ABSTRACT

Black older adults experience worse brain and cognitive aging than White older adults, on average. Racially patterned psychosocial stressors may contribute to these disparities. Maintaining white matter health is important for cognitive aging, particularly among Black older adults, and it is uniquely vulnerable to stress. Examining associations between racial discrimination and white matter may elucidate mechanisms of disparities. A sample of Black older adults in the Washington Heights-Inwood Columbia Aging project were included (N = 217). Everyday and major life discrimination were self-reported on well-validated scales. Diffusion tensor imaging quantified white matter fractional anisotropy (FA). Multivariable regressions revealed more major life discrimination was associated with lower FA in the cingulum cingulate gyrus, forceps major, forceps minor, and inferior fronto-occipital fasciculus but greater FA in the superior longitudinal fasciculus temporal projection. Everyday discrimination was not associated with FA. Findings suggest that institutional racism may have a stronger effect on white matter tracts corresponding to cognitive and emotional/affective processing than interpersonal racism. White matter health may be a mechanism through which racially patterned stressors contribute to disparities in brain and cognitive aging.

1. Introduction

1.1. Racial inequities in brain and cognitive aging

Black older adults experience accelerated brain aging and a disproportionate burden of cognitive impairment with age compared to White older adults, on average. For example, Black older adults show greater levels of white matter hyperintensity (WMH) burden, indicative of cerebrovascular disease, than White older adults (Brickman et al., 2008). Racial disparities in brain health (Turney et al., 2023) and cognitive health (Zahodne et al., 2016) are evident across mid- and late life. As the aging population continues to increase, it is necessary to identify pathways for risk and resilience within these communities.

Socioeconomic factors (e.g., education) and physical health (e.g., hypertension, diabetes, stroke) are well studied contributors to brain

and cognitive aging that play a major role in racial disparities through direct and indirect pathways (Beydoun et al., 2022; Marebwa et al., 2018). However, disparities continue to persist after controlling for education and health risk factors, with Black and Hispanic older adults being twice as likely to develop clinical Alzheimer's disease compared to White older adults (Mayeda et al., 2016; Tang et al., 2001). Racial health disparities exist at every level of socioeconomic status (Braveman et al., 2010), underscoring the need to examine additional modifiable factors. There is a growing body of literature supporting the unique contribution of psychosocial factors in health disparities (Adler, 2009; Bailey et al., 2017). Psychosocial stressors that disproportionately affect Black older adults could contribute to racial health disparities. Discrimination is one racially patterned psychosocial stressor that appears to have implications for brain and cognitive aging (Zahodne et al., 2019, 2023).

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1.2. Discrimination & pathways of influence

The biopsychosocial model of racism by Clark et al., (1999) posits that racial discrimination can negatively affect health outcomes and increase disparities through multiple stress-related pathways. Findings from several studies support this model and suggest that racial discrimination is a determinant of health (Krieger, 2014; Mays et al., 2007; Williams et al., 2019).

Williams and colleagues (2008) conceptualized racial discrimination in the form of acute (i.e., major life experiences of discrimination) and chronic (i.e., everyday discrimination) stressors. As a stressor, racial discrimination activates physiological stress responses, leading to downstream long-term health effects. Specifically, discrimination is associated with increased levels of inflammatory biomarkers (e.g., C-reactive protein; Lewis et al., 2010), alterations in activity of the hypothalamic-pituitary-adrenal axis (Busse et al., 2017) and sympathetic-adrenal-medullary axis (Grasser and Jovanovic, 2022), and increased red blood cell oxidative stress (Szanton et al., 2012). These pathways of stress-related physiological dysregulation enable racial discrimination to impact numerous health outcomes including mental health (e.g., depression, anxiety; Berger and Sarnyai, 2015; Paradies et al., 2015), cardiovascular health (e.g., stroke, hypertension; Javed et al., 2022), and premature mortality (Muscatell et al., 2022). Black adults are disproportionately burdened by each of these health outcomes, and discrimination may be a mechanism contributing to these disparities (Williams and Mohammed, 2009). Disparities in cardiovascular health are particularly pronounced and have critical consequences for brain and cognitive aging.

1.3. White matter health

White matter, which is composed of myelinated axonal projections, is important for cognitive aging due to its role in forming cortical connections (Madden et al., 2012). The formation of white matter helps promote cognitive processes in development and sustain cognitive efficiency in aging. Changes to white matter health have been associated with premature brain aging, making it a critical brain metric to evaluate (Busby et al., 2022). The structure and health of white matter can be evaluated with diffusion magnetic resonance imaging (Bullock et al., 2022).

White matter is highly vulnerable to downstream effects of cardiovascular disease, including cerebral small vessel disease (Cortes-Canteli and Iadecola, 2020; Purkayastha et al., 2014; Rastogi et al., 2021), which can be visualized as WMHs on magnetic resonance imaging (MRI). Black adults are at an increased risk for cardiovascular health concerns (Graham, 2015), which puts them at greater risk of developing WMHs (Farkhondeh and DeCarli, 2024). Increased white matter abnormalities have been shown to be associated with lower cognitive functioning cross-sectionally and over time (Wang et al., 2020). Thus, white matter may be a particularly important indicator of brain and cognitive health for this group. Indeed, white matter abnormalities appear to be a better predictor of cognition (Zahodne et al., 2015) and have a stronger association with cortical thinning in areas related to the progression of Alzheimer's disease (Rizvi et al., 2021) in Black older adults compared to White older adults.

White matter may also be a critical brain health outcome to investigate in relation to discrimination because of its unique vulnerability to stress-related physiological dysfunction (Lupien et al., 2009; McEwen, 2007). Greater experiences of racial discrimination are associated with faster accumulation of WMHs over time, indicating greater cerebrovascular burden (Zahodne et al., 2023). Similarly, more discrimination is associated with greater white matter lesion volume (Beatty Moody et al., 2019). However, additional measures of white matter health may be important to investigate.

Specifically, white matter fractional anisotropy (FA) is theorized to be a more sensitive measure of early white matter changes compared to

WMHs (Seiler et al., 2018). White matter FA can be used to grossly reflect white matter organization and damage via directional diffusion of water along axons (Bullock et al., 2022). FA can be used to measure white matter tracts, which help form connections between different regions of the brain. For example, the corpus callosum is a major white matter tract that connects both cerebral hemispheres and is important for interhemispheric communication (Bullock et al., 2022). Abnormal FA (i.e., low values of FA) may indicate macroscopic disorganization, reflecting white matter abnormalities (Ranzenberger and Snyder, 2022). Reductions in white matter FA are associated with increased WMH volume (Vemuri et al., 2021) as well as additional underlying white matter pathology (e.g., demyelination) and neurodegeneration (i.e., Alzheimer's disease; Wen et al., 2019). FA has also been shown to mediate the association between WMH and cognition (Chen et al., 2023). A prior study with trauma-exposed Black women found experiences of racial discrimination to be negatively associated with white matter FA (Fani et al., 2022), further indicating its potential role in brain health disparities.

1.4. The current study

Relative to other health outcomes, brain health has been understudied in relation to racial discrimination. The current study addressed this gap by evaluating the relationship between racial discrimination and white matter (i.e., mean FA), a particularly important brain health metric in Black older adults that is believed to roughly reflect the integrity of axons. Both everyday and major life experiences of discrimination were evaluated to identify pertinent forms of discrimination that may be differentially related to brain health. Due to prior limited research on the relationship between discrimination and white matter health, this study conducted exploratory analyses evaluating several white matter tracts to expand the knowledgebase of potential mechanistic pathways of the impact of discrimination through white matter health. We aimed to examine the associations between racial discrimination and 1) whole brain white matter FA (i.e., mean FA of identified white matter tracts) and 2) within individual white matter tracts. Based on theoretical and empirical evidence linking discrimination with worse brain health, we hypothesized that experiencing more racial discrimination would be associated with lower white matter FA (i.e., compromised white matter health).

2. Methods

2.1. Participants and procedures

Participants were drawn from the Washington Heights-Inwood Columbia Aging Project (WHICAP), which is a diverse sample of community dwelling residents aged 65+ in northern Manhattan, New York (Tang et al., 2001). A subsample of participants who underwent an MRI (Brickman et al., 2008) and completed the psychosocial questionnaire introduced in 2017 were included in the study (Zahodne et al., 2018). Because of the unique conceptualization of discrimination across race and the emphasis on disproportionate brain and cognitive morbidity among Black older adults, we conducted a within-group analysis of non-Hispanic Black older adults from WHICAP who had imaging and psychosocial data available. Participants with research diagnoses of dementia at the time of administration of the psychosocial questionnaire were excluded due to concerns for validity of self-report. In WHICAP, dementia diagnoses are determined through a consensus conference with neurologists, psychiatrists, and neuropsychologists based on full neuropsychological and functional data; the Diagnostic and Statistical Manual of Mental Disorders 4th edition (American Psychiatric Association, 1994) and the Clinical Dementia Rating scale were used (Morris, 1993). Fig. 1 details the process for determining the final analytic sample of 217.

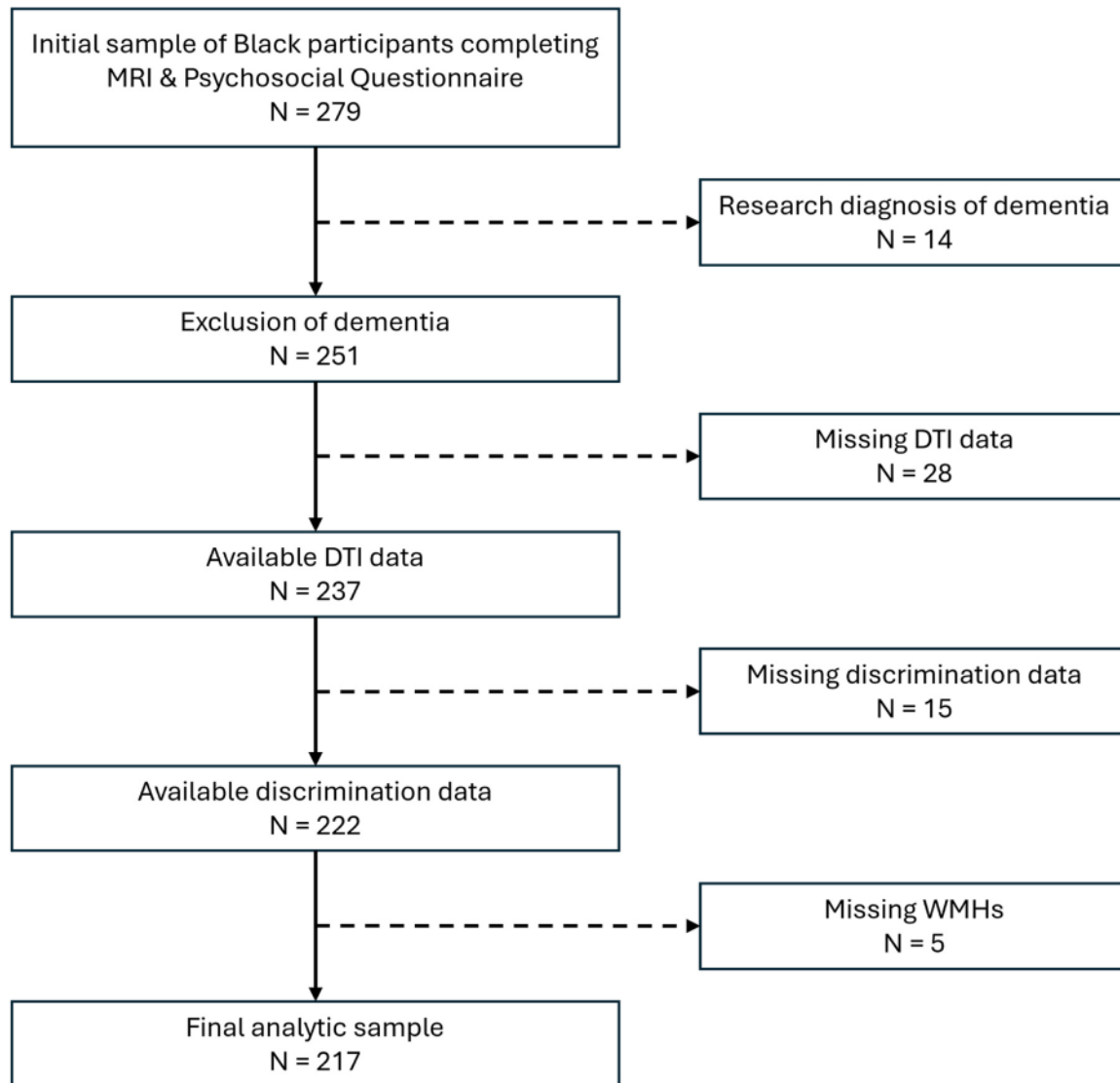


Fig. 1. Flow Chart of Sample Size. Flow chart depicting the steps taken to achieve the final analytic sample.

2.2. Discrimination

Discrimination was operationalized through self-reported everyday and major life experiences of discrimination. The Everyday Discrimination scale (Williams et al., 1997) and Major Life Experiences of Discrimination scale (Williams, González et al., 2008) were used. The Everyday Discrimination scale includes a series of 10 questions with a 6-point scale ranging from “Never” to “Almost every day” that attempts to capture day-to-day experiences of interpersonal discrimination (e.g., “You are treated with less respect than other people”; “You are called names or insulted”); there is no time scale incorporated with this measure. Scores were reverse coded then averaged so that higher values corresponded to more discrimination (“Never” coded as 1; range 10–60). The Major Life Experiences of Discrimination scale includes a series of 9 yes or no questions that capture lifetime experiences of discriminatory events. Included questions may reflect experiences of interpersonal and/or institutional discrimination (e.g., “At any time in your life, have you ever been unfairly fired from a job?”; “Have you ever been unfairly stopped, searched, questioned, physically threatened or abused by the police?”). Participants were asked to report what they believed was the main reason for their experiences of everyday discrimination and for each major life experience of discrimination (e.g., ancestry, gender, race, age, skin color); racial discrimination was operationalized as the

sum of different items attributed to race or skin color.

2.3. Neuroimaging

T1-weighted MRI scans were conducted using a 3.0 T Philips Achieva scanner at Columbia University Medical Center beginning in 2011 ($n = 208$; repetition time (TR) = 6.6 ms, echo time (TE) = 3.0 ms, flip angle = 8° , field of view (FOV) = $256 \times 256 \times 165$, slice thickness = 1 mm, resolution = $1.00 \times 1.00 \times 1.00 \text{ mm}^3$). T2-weighted FLAIR images were acquired axially (TR = 8000 ms, TE = 332 ms, flip angle = 90° , inversion time (TI) = 2400 ms, FOV = $240 \times 240 \times 180$, slice thickness = 1 mm, resolution = $1.00 \times 1.00 \times 1.00 \text{ mm}^3$; Brickman et al., 2013; Rizvi et al., 2020). Scans after February 2020 were conducted on a 3.0 T GE Signa Premier scanner ($n = 9$; TR = 7.2 ms, TE = 3.0 ms, flip angle = 11° , field of view $256 \times 256 \times 182$, slice thickness = 1 mm, resolution = $1.00 \times 1.00 \times 1.00 \text{ mm}^3$). T2-weighted FLAIR images were acquired axially (TR = 8000 ms, TE = 106 ms, TI = 2095 ms, field of view = $256 \times 256 \times 166$, slice thickness = 1 mm, resolution = $0.88 \times 0.88 \times 1 \text{ mm}^3$).

Whole brain diffusion imaging (matrix field of view = $224 \times 224 \text{ mm}^2$, reconstruction matrix = 112×112 , contiguous slices, slice thickness = 2 mm, TR = 8185 ms, TE = 69 ms) was acquired along 16 gradient directions ($n = 107$; b-value = 800 s/mm^2 ; Lao et al., 2019). Diffusion

images collected from 2016 to February 2020 were acquired along 32 gradient directions ($n = 101$; $b\text{-value} = 1000 \text{ s/mm}^2$, $TR = 9225$, $TE = 70 \text{ ms}$, dimensions = $112 \times 112 \times 75$, resolution = $2.00 \times 2.00 \times 2.00 \text{ mm}^3$). Diffusion images collected following February 2020 were acquired along 64 gradient directions ($n = 9$; $b\text{-value} = 1000 \text{ s/mm}^2$, $TR = 6000$, $TE = 56 \text{ ms}$, dimensions = $256 \times 256 \times 256$, resolution = $0.88 \times 0.88 \times 2.00 \text{ mm}^3$). All data are single shell DTI. Regions of interest were derived from the JHU-ICBM-DTI-81 white matter label atlas (Hua et al., 2008; Mori et al., 2008). White matter health was approximated via mean FA. FA reflects a scalar value that ranges from 0 to 1 with higher values corresponding to greater directional restriction of water diffusion. White matter FA maps were constructed for each participant after eddy current and susceptibility corrections in FSL. Tract specific mean FA (11 bilateral tracts: anterior thalamic radiation, cortical spinal tract, cingulum cingulate gyrus, cingulum hippocampus, forceps major, forceps minor, inferior fronto-occipital fasciculus, inferior longitudinal fasciculus, superior longitudinal fasciculus, superior longitudinal fasciculus temporal projection, uncinate fasciculus) and total white matter FA (i.e., mean FA of tract-based ROIs) were assessed using tract-based spatial statistics.

2.4. Covariates

Age and sex/gender were included as covariates due to their potential to confound the association between racial discrimination and brain health. Age was recorded at the time of DTI acquisition. Sex/gender was self-reported and operationalized dichotomously (Male, Female). Intracranial volume was controlled to account for differences in head size and was calculated via FreeSurfer v5.1 (<http://surfer.nmr.mgh.harvard.edu/>). To evaluate the effects of discrimination on white matter FA independent of other measures of white matter health, WMHs were included as an additional covariate. WMH volume was estimated via T2-FLAIR weighted images; voxels 2.5 standard deviations above the image mean were identified as hyperintense; additional methodology is described previously (Brickman et al., 2009, 2011). Analyses were adjusted for differences in scanner parameters (e.g., diffusion directions, scanner manufacturer).

2.5. Statistical analyses

Multivariable regression models were used to evaluate the unique effects of everyday and major life experiences of discrimination on white matter FA. Separate models were run for total white matter FA and tract-specific mean FA. Both everyday and major life experiences of discrimination were included as simultaneous predictors. Initial models controlled for age, sex/gender, intracranial volume, white matter hyperintensities, and differences in scanner parameters. A subsequent sensitivity analysis controlled for years of education due to its potential role as a confounder or mediator of the relationship between discrimination and brain health.

3. Results

Descriptive statistics are displayed in Table 1. On average, participants were around 73 years-old and female (66.40 %) with approximately 14 years of education, primarily reporting never experiencing everyday discrimination (mean = 12.69 [range = 10–46]) and less than 1 major life discrimination event (mean = 0.63 [range = 0–7]). The average time between the date of MRI and psychosocial data collection was 2.71 years (standard deviation = 2.34). Primary results are displayed in Table 2 and Fig. 2. Everyday discrimination and major life experiences of discrimination were not associated with total white matter mean FA. More major life experiences of discrimination were associated with lower mean FA of the left cingulum cingulate gyrus, forceps major, forceps minor, and bilateral inferior fronto-occipital fasciculus. Conversely, more major life experiences of discrimination

Table 1
Sample Characteristics (N = 217).

	Mean / %	SD
Age (62–93)	73.30	6.10
Gender (% Female)	66.40 %	–
Education (6–20)	13.88	2.77
Everyday Racial Discrimination (10–46)	12.69	5.66
Major Life Racial Discrimination Events (0–7)	0.63	1.21
Whole Brain Mean Fractional Anisotropy	0.51	0.02
Left Anterior Thalamic Radiation	0.45	0.03
Right Anterior Thalamic Radiation	0.43	0.03
Left Corticospinal Tract	0.61	0.03
Right Corticospinal Tract	0.60	0.03
Left Cingulum Cingulate Gyrus	0.57	0.04
Right Cingulum Cingulate Gyrus	0.53	0.04
Left Cingulum Hippocampus	0.55	0.06
Right Cingulum Hippocampus	0.52	0.05
Forceps Major	0.65	0.04
Forceps Minor	0.47	0.03
Left Inferior Fronto-Occipital Fasciculus	0.49	0.03
Right Inferior Fronto-Occipital Fasciculus	0.48	0.03
Left Inferior Longitudinal Fasciculus	0.46	0.03
Right Inferior Longitudinal Fasciculus	0.46	0.03
Left Superior Longitudinal Fasciculus	0.47	0.03
Right Superior Longitudinal Fasciculus	0.47	0.03
Left Superior Longitudinal Fasciculus Temporal Part	0.53	0.05
Right Superior Longitudinal Fasciculus Temporal Part	0.54	0.04
Left Uncinate Fasciculus	0.47	0.03
Right Uncinate Fasciculus	0.49	0.04
Total White Matter Hyperintensity Volume (cm^3)	5.24	5.40
Total Intracranial Volume (mm^3)	1382344.51	174696.00

Note. Mean fractional anisotropy ranges from 0 to 1, with higher values reflecting greater restriction of water diffusion.

were associated with greater mean FA of the right superior longitudinal fasciculus temporal projection. Everyday experiences of discrimination were not associated with tract-specific mean FA.

A sensitivity analysis controlling for years of education followed a similar pattern of tract-specific results with some variations noted. Importantly, higher education was correlated with more everyday ($r = .16$, $p = .02$) and major life ($r = .30$, $p < .001$) experiences of discrimination. A full correlation matrix is provided in Supplementary Table 1. Sensitivity analyses are presented in Supplementary Table 2. Major life experiences of discrimination were no longer associated with the forceps major or left inferior fronto-occipital fasciculus. All other prior significant associations remained. While these white matter tracts showed the most statistically reliable associations, other tracts showed similar effect sizes (e.g., anterior thalamic radiation, uncinate fasciculus).

4. Discussion

This within-group study of older non-Hispanic Black adults living in northern Manhattan, New York provides evidence for the potential negative association between discrimination and white matter FA. The pattern of results indicated that major experiences of lifetime discrimination had a stronger and more consistent relationship to white matter FA than everyday discrimination. These associations appear to be tract-specific with some evidence for lateralization, providing insight into potential pathways by which racial discrimination could influence cognitive aging and brain health with functional implications. The interpretations below are made conservatively to avoid overinterpretation of findings in relation to the limitations of the measurement of white matter health via fractional anisotropy.

4.1. Major life experiences of discrimination & white matter FA

Consistent with hypotheses, more major life experiences of racial discrimination were associated with lower mean FA of the left cingulum

Table 2
Standardized Regression Estimates of Associations Between Discrimination and Mean Fractional Anisotropy.

	Everyday Discrimination		Major Life Discrimination	
	β	95 % CI	β	95 % CI
Total White Matter Fractional Anisotropy	0.041	(−0.076 – 0.157)	−0.090	(−0.204 – 0.024)
Left Anterior Thalamic Radiation	−0.009	(−0.128 – 0.111)	−0.108	(−0.225 – 0.009)
Right Anterior Thalamic Radiation	0.084	(−0.033 – 0.201)	−0.104	(−0.218 – 0.011)
Left Corticospinal Tract	−0.021	(−0.153 – 0.111)	−0.018	(−0.148 – 0.112)
Right Corticospinal Tract	0.063	(−0.065 – 0.191)	0.054	(−0.072 – 0.179)
Left Cingulum Cingulate Gyrus	−0.013	(−0.135 – 0.109)	−0.182	(−0.301 – −0.064)*
Right Cingulum Cingulate Gyrus	−0.020	(−0.142 – 0.103)	−0.100	(−0.220 – 0.020)
Left Cingulum Hippocampus	0.000	(−0.131 – 0.130)	−0.047	(−0.175 – 0.081)
Right Cingulum Hippocampus	0.094	(−0.039 – 0.226)	−0.055	(−0.185 – 0.075)
Forceps Major	−0.020	(−0.138 – 0.097)	−0.116	(−0.231 – −0.001)*
Forceps Minor	−0.005	(−0.117 – 0.107)	−0.151	(−0.260 – −0.041)*
Left Inferior Fronto-Occipital Fasciculus	0.001	(−0.110 – 0.111)	−0.121	(−0.229 – −0.013)*
Right Inferior Fronto-Occipital Fasciculus	0.055	(−0.053 – 0.163)	−0.139	(−0.245 – −0.033)*
Left Inferior Longitudinal Fasciculus	0.024	(−0.097 – 0.144)	−0.074	(−0.191 – 0.044)
Right Inferior Longitudinal Fasciculus	0.009	(−0.111 – 0.130)	−0.095	(−0.213 – 0.023)
Left Superior Longitudinal Fasciculus	0.009	(−0.122 – 0.141)	−0.065	(−0.194 – 0.064)
Right Superior Longitudinal Fasciculus	−0.015	(−0.142 – 0.113)	−0.021	(−0.146 – 0.104)
Left Superior Longitudinal Fasciculus Temporal Part	0.099	(−0.036 – 0.235)	0.108	(−0.025 – 0.241)
Right Superior Longitudinal Fasciculus Temporal Part	0.070	(−0.063 – 0.203)	0.138	(0.008 – 0.267)*
Left Uncinate Fasciculus	0.069	(−0.056 – 0.195)	−0.116	(−0.238 – 0.007)
Right Uncinate Fasciculus	0.040	(−0.086 – 0.166)	−0.108	(−0.231 – 0.015)

Note. White matter was measured as mean fractional anisotropy via diffusion tensor imaging. Each tract was evaluated unilaterally in independent models. Everyday discrimination and major life discrimination were evaluated simultaneously. Age at time of MRI, sex/gender, intracranial volume, white matter hyperintensities, and differences in scanner parameters were controlled for in all models.

* $p < .05$

cingulate gyrus, forceps major, forceps minor, and bilateral inferior fronto-occipital fasciculus. Counter to hypotheses, more major life experiences of racial discrimination were associated with greater mean FA of the right superior longitudinal fasciculus temporal projection. These findings show similarities and differences with prior research. For example, Fani and colleagues (2022) found a negative association between self-reported experiences of racial discrimination (i.e., interpersonal and institutional discrimination measured via Experiences of Discrimination Scale; Krieger et al., 2005) and mean FA of the corpus callosum, left anterior cingulum bundle, and right superior longitudinal fasciculus among trauma exposed Black women. Current findings noted within the corpus callosum (forceps minor), cingulum, and superior longitudinal fasciculus indicate some overlap; however, discrimination was positively associated within the right superior longitudinal fasciculus in the current study, specifically within the temporal projection. Notable differences in study design (i.e., younger age, female only sample, trauma exposure, measurement of discrimination) may account for differential findings. Consideration of the corresponding connectivity and posited functionality of these identified tracts may lead to a better understanding of how discrimination may disrupt cognitive and functional processes through white matter and increase disparities in cognitive and brain aging.

4.1.1. Specific white matter tracts & their potential implications

Major life experiences of racial discrimination were associated with lower white matter FA in tracts that are involved in emotion processing such as fear (i.e., cingulum cingulate gyrus, inferior fronto-occipital fasciculus). These tracts connect threat-response regions that are affected by psychological stressors through the hypothalamic-pituitary-adrenal axis and sympathetic-adrenal-medullary axis (Busse et al., 2017; Grasser and Jovanovic, 2022). Specifically, the cingulum cingulate gyrus connects portions of the medial orbito-frontal and temporal lobes (Wycoco et al., 2013) and is implicated in affective processes through the Papez circuit (Bubb et al., 2018). Further, the inferior fronto-occipital fasciculus shares connections within the insula (Mori and van Zijl, 2007), which is involved in self-awareness, subjective feeling, and emotion recognition (Uddin et al., 2017). Thus, stress and additional exposures derived from experiences of discrimination that leave a psychological and physiological toll may uniquely influence

these white matter tracts due to their roles in affective pathways and emotional processing.

With regard to potential functional implications of these findings, several of the identified white matter tracts are involved in important cognitive processes and form integral connections including tracts associated with memory (forceps major; Voineskos et al., 2012; cingulum; Wycoco et al., 2013), executive functioning (forceps minor; Mamiya et al., 2018; forceps major; Voineskos et al., 2012), and language processing (inferior fronto-occipital fasciculus; Wycoco et al., 2013). Therefore, decreased white matter FA within these tracts could lead to or indicate accelerated cognitive aging and worse cognitive health. Indeed, a previous study found that cognitive abilities involving fronto-occipital connections (e.g., executive functioning) were negatively impacted by discrimination, aligning with recent findings from structural imaging (Zahodne et al., 2020). Additionally, the inferior fronto-occipital fasciculus shares connections with the posterior temporal stem; thus, degradation of this tract could increase risk for temporal lobe syndromes such as Alzheimer's disease (Wycoco et al., 2013). Individuals with Alzheimer's disease have been shown to have decreased white matter FA within the cingulum, corpus callosum, and superior longitudinal fasciculus, among others (Mayo et al., 2017). The corresponding processes and connections of the implicated tracts may reflect cognitive and functional vulnerabilities resulting from exposure to major life experiences of racial discrimination.

Conversely, more experiences of major life experiences of discrimination were associated with greater FA of the right superior longitudinal fasciculus temporal projection. While this finding was contrary to hypotheses, it should be interpreted with caution because the superior longitudinal fasciculus features a high level of crossing fibers, and FA may not accurately reflect white matter in the presence of crossing fibers. This portion of the superior longitudinal fasciculus projects from the posterior temporal lobule to the superior parietal lobule (Kamali et al., 2014). This tract shares connections between the superior temporal gyrus and the intraparietal sulcus. The superior longitudinal fasciculus temporal projection has been understudied and little is known about its function (Kamali et al., 2023). Future research is needed to uncover functional and behavioral implications of this association.

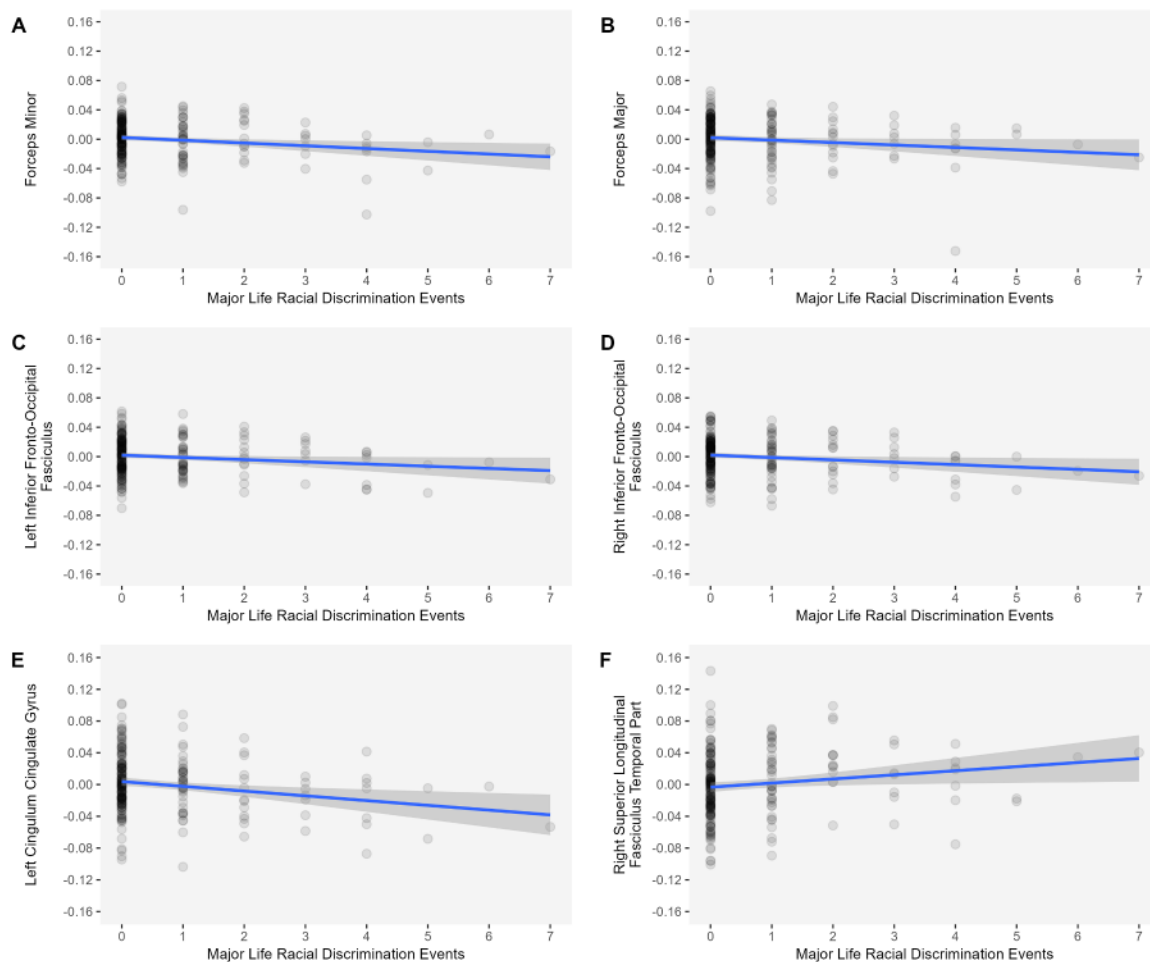


Fig. 2. Association Between Major Life Discrimination and Mean Fractional Anisotropy. Unstandardized residual of mean fractional anisotropy (accounting for age at time of scan, gender, total intracranial volume, white matter hyperintensities, and differences in scanner parameters) for A) forceps minor, B) forceps major, C) left and D) right inferior fronto-occipital fasciculus, E) left cingulum cingulate gyrus, F) right superior longitudinal fasciculus temporal projection as a function of major life racial discrimination events.

4.1.2. Consideration of education

In the literature, there is conflicting evidence regarding the relationship between discrimination and education. Some studies find more discrimination (Das, 2020), as well as an exacerbation of its effects (Ward et al., 2019; Zhang and Hong, 2013), at higher levels of education, while other evidence points to higher levels of education as a buffer against the harmful effects of discrimination (Johnson-Lawrence et al., 2020). One potential explanation for the positive correlation between education and discrimination in the current study is that Black adults with higher education may be exposed to more discrimination due to a greater likelihood of living and/or working in predominantly White spaces.

While results were mostly unchanged when considering education, there was some evidence of both weaker and stronger associations between discrimination and specific tracts. The association between more discrimination and lower FA of the forceps major and left inferior fronto-occipital fasciculus *decreased* in magnitude when controlling for education and became non-significant; non-significant negative correlations between these tracts and education ($p > .05$) could account for a decrease in effect. Findings within the left cingulum cingulate gyrus, forceps minor, right inferior fronto-occipital fasciculus, and right superior longitudinal fasciculus temporal projection appear to be the most robust as they remained significant with and without education in the model. Taken together, this pattern of results suggests that education serves as an exposure that may influence experiences of discrimination on health outcomes, and considering education may provide a more

accurate depiction of the association between discrimination and white matter FA. Future research should seek to clarify the complex relationships between discrimination, education, and brain health to better understand potential causal phenomena.

4.2. Everyday discrimination

In contrast to major experiences of lifetime discrimination, everyday discrimination was not associated with white matter FA in our sample. This somewhat differs from a prior study including the same sample of older adults from WHICAP that found everyday discrimination was associated with faster accumulation of WMHs over time (Zahodne et al., 2023). Notably, everyday discrimination was not associated with WMHs at baseline; thus, measuring changes in FA over time may yield differential associations and should be evaluated in the future. Additionally, the lack of association in the current study may reflect the tendency for older adults to report less everyday racial discrimination compared to younger adults (Kessler et al., 1999; Wheaton et al., 2018). Indeed, the current sample aligned with this prior finding with minimal reporting of everyday discrimination, potentially limiting the ability to capture an effect due to restricted variance. The observation that older adults report less everyday discrimination than younger adults may be related to the social structures with which individuals engage. While the everyday discrimination scale does not explicitly identify a time frame, the items are worded to elicit current, ongoing experiences. Therefore, the scale may not capture discrimination in early life when individuals are more

likely to be involved with institutions where discriminatory practices persist. Older adults may not be actively involved in the education system, workforce, housing market, or other institutions that may lead to increased experiences of everyday discrimination. Future studies should consider potential differences in the association between white matter health and discrimination in younger compared to older adult samples.

Importantly, major experiences of lifetime discrimination may reflect discrimination experienced on an institutional level (e.g., housing, employment). Thus, exposure to institutional levels of discrimination may pose more negative effects to brain health in later life than interpersonal levels of discrimination alone. Major experiences of discrimination may be more salient and life altering than everyday discrimination as these experiences have the potential to affect social standing and mobility more directly (e.g., denial of a bank loan). The accumulation of these discriminatory events across the life course do not happen in isolation and can cause compounding effects with additional stressors. Furthermore, as people age, they become more selective of relationships and prioritize emotionally rewarding social ties (i.e., socioemotional selectivity theory; Carstensen, 1995; Carstensen et al., 1999), potentially limiting the chances of interacting in discriminatory spaces on a day-to-day basis. Thus, the association between everyday discrimination and brain health could be dynamic over the life course and should be evaluated across multiple timepoints.

5. Strengths, limitations, & future directions

The current study had notable strengths. Specifically, the study incorporated a large imaging dataset of community dwelling older Black adults. A within-group analysis was performed to explicitly evaluate the unique effects of everyday and major life experiences of discrimination among older Black adults, allowing for comparison between more interpersonal and institutional levels of discrimination. The consideration of WMHs in the current study helps to extend prior research that linked discrimination to white matter abnormalities; future research should distinguish differential mechanisms of influence through white matter FA compared to WMHs (e.g., physiological stress influences, cardiovascular health) as well as their temporality and relationship (e.g., FA precipitating WMHs). The inclusion of several white matter tracts also allows for more targeted future research on tracts related to experiences of discrimination and potential pathways of disparities in cognitive and brain health.

The current study also had some limitations that may influence interpretation of findings. The change of MRI scanners during the study complicates findings due to the sensitivity of diffusion imaging to differences in scanning parameters. Scanners with more directions and higher resolution provide better estimates of diffusion directionality and allow for investigation of smaller tracts. However, we attempted to address this limitation by controlling for changes in scanner parameters in all analyses. The cross-sectional design precludes causal interpretations of relationships between discrimination and white matter FA. Further, capturing the timing and chronicity of discrimination should be prioritized in future studies to refine intervention strategies due to potential differential impact of discrimination based on age of exposure (Wheaton et al., 2018). Additionally, MRI acquisition and psychosocial data collection did not occur at the same timepoint, leading to some participants undergoing an MRI prior to or after experiences of discrimination were measured. However, this limitation is believed to have had minimal effect on our findings since discrimination is not thought to fluctuate rapidly, and there is no theoretical basis supporting reverse causation between white matter FA and experiences of racial discrimination. Due to the exploratory nature of our analyses, we did not apply multiple comparison corrections. This choice was made given the lack of prior research and the goal of providing direction and informing hypotheses for future studies. We were unable to control for potential individual differences in brain development which could impact white

matter microstructure (Bottenhorn et al., 2023). We also used a subset of participants in WHICAP who participated in the imaging portion of the study, which could introduce selection bias (e.g., differences in education and health status for imaging subsample).

There were additional limitations within the measures of this study. Both discrimination scales were self-reported, limiting our ability to capture additional experiences of institutional discrimination. Current self-report methods for capturing discrimination are likely to underestimate the impact of racism on health (Krieger, 2012). Future work should continue to build on measurements of discrimination by adding cognitive interviews to capture experiences more fully (Harnois, 2022) and attempting to measure multiple levels and forms of discrimination that include structural factors across the life course (Bailey et al., 2017; Cuevas and Boen, 2021). Additional factors such as income and occupation should be explicitly considered as potential mediators in future research. We also did not account for intersectional identities that may lead to greater exposure and compounding effects of discrimination (e.g., gender; Crenshaw, 1989), which is an important direction for future research that was outside the scope of the current study.

Additionally, FA is a crude measure of white matter health because it is unable to capture the complex nature of crossing fibers within white matter microstructure. Thus, due to methodological limitations, a lower value of FA does not necessarily equate to compromised white matter health in all cases, so findings should be interpreted with caution. The tensor model of white matter used to compute FA values renders it difficult to discern between overlapping tracts (e.g., superior longitudinal fasciculus, arcuate fasciculus; Wang et al., 2016). Notably, white matter tracts involving the corpus callosum (e.g., forceps major, forceps minor) and superior longitudinal fasciculus, which were highlighted in the current study, include high levels of crossing fibers. Future studies should incorporate additional measures of white matter tracts when possible, such as fixel-based analysis, which allows for a more accurate measurement of white matter microstructure for better clinical application (Dhollander et al., 2021).

6. Conclusion

The current study adds to recent evidence linking racial discrimination and brain health in older adults. White matter health may be a mechanism through which racially patterned psychosocial stressors contribute to racial disparities in cognitive aging. The most robust findings were noted within the left cingulum cingulate gyrus, forceps minor, right inferior fronto-occipital fasciculus, and the right superior longitudinal fasciculus temporal projection as they remained significant after controlling for education. Evaluating these white matter tracts revealed overlap with literature highlighting the impacts of discrimination on areas of the brain known to be involved in emotional and affective processes as well as cognitive processes important for healthy cognitive aging. More research is needed to continue evaluating how racially patterned psychosocial stressors impact specific regions of the brain. This study can help support regional or tract-specific hypotheses for future work. Our findings highlighted the importance of evaluating institutional level discrimination. The development of more robust measures for institutional and structural levels of racial discrimination across the life course is needed to continue to promote research that can motivate health equity policy and reduce racial disparities.

CRedit authorship contribution statement

Zahodne Laura B: Writing – review & editing, Writing – original draft, Supervision, Methodology, Formal analysis, Conceptualization. **Ji Hyun Lee:** Writing – review & editing, Data curation. **Brickman Adam M:** Writing – review & editing, Supervision, Methodology, Investigation, Funding acquisition. **Palms Jordan D:** Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Lao Patrick J:** Writing – review & editing, Methodology. **Manly Jennifer J:**

Writing – review & editing, Supervision, Investigation, Funding acquisition. **Morales Clarissa D:** Writing – review & editing, Methodology, Data curation. **Alshikho Mohamad J:** Writing – review & editing, Methodology. **Walters Monica E:** Writing – review & editing. **Scambray Kiana A:** Writing – review & editing. **Morris Emily P:** Writing – review & editing, Validation. **Ketlyne Sol:** Writing – review & editing.

Disclosures

The authors have nothing to disclose.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.neurobiolaging.2025.07.017.

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