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Experiences of Discrimination Are Associated With Greater Resting Amygdala Activity and Functional Connectivity

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ABSTRACT

BACKGROUND: Social discrimination, a type of psychological stressor, is associated with poorer physical and mental health outcomes, yet we have little understanding of how discrimination affects neural functions in marginalized populations. By contrast, the effects of psychological stress on neural functions are well documented, with evidence of significant effects on the amygdala—a neural region that is central to psychosocial functions. Accordingly, we conducted an examination of the relation between self-reported discrimination exposure and amygdala activity in a diverse sample of adults.

METHODS: Seventy-four adults (43% women; 72% African American; 23% Hispanic; 32% homosexual/bisexual) completed self-report ratings of discrimination exposure. Spontaneous amygdala activity and functional connectivity were assessed during resting-state functional magnetic resonance imaging.

RESULTS: Greater discrimination exposure was associated with higher levels of spontaneous amygdala activity. Increases in discrimination were also associated with stronger functional connectivity between the amygdala and several neural regions (e.g., anterior insula, putamen, caudate, anterior cingulate, medial frontal gyrus), with the most robust effects observed in the thalamus. These effects were independent of several demographic (e.g., race, ethnicity, sex) and psychological (e.g., current stress, depression, anxiety) factors.

CONCLUSIONS: Collectively, our findings provide the first evidence that social discrimination is independently associated with elevations in intrinsic amygdala activity and functional connectivity, thus revealing clear parallels between the neural substrates of discrimination and psychological stressors of other origins. Such results should spur future investigations of amygdala-based networks as potential etiological factors linking discrimination exposure to adverse physical and mental health outcomes.

Keywords: Amygdala, Psychosocial stressors, Social discrimination, Social marginalization, Stress, Thalamus

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Exposure to social discrimination is a well-established environmental risk factor for mental health disorders, including depression, anxiety, and posttraumatic stress disorder (PTSD) (1–13). Yet, we have little understanding of the neural substrates that may contribute to these effects, as surprisingly few studies have examined the neural correlates of discrimination or social exclusion in marginalized populations (14–17). The current study, conducted in a diverse sample of adults, helps to address this gap in the literature by examining links between social discrimination—a type of psychological stressor—and amygdala function.

The amygdala is a central component of the neural networks that support complex psychosocial behavior (18,19). A wealth of evidence implicates aberrant amygdala activity in stress-related mental health disorders and in the response to psychological stressors (20–26). Findings from both the human and animal literature reveal increased amygdala reactivity in the context of stress (27–36). Recent studies have also linked elevations in spontaneous amygdala activity (at rest) to psychological stress. Data from these studies indicate that individuals with stress-related disorders, such as PTSD, as well as those with high current stress levels exhibit elevated levels of spontaneous amygdala activity (21,22). Such data align with the amygdala's role in mediating basic affective processes, including vigilance regulation, fear conditioning, associative learning, and threat detection (18,37,38).

Humans, in general, are highly social, with strong motivations to be included by others; hence, acts of social exclusion are experienced as acute psychological stressors (39–43). Consistent with these data, increased amygdala reactivity has been observed in individuals who are the targets of acute social exclusion (44,45). Researchers have identified several attributes of psychological stressors (e.g., social exclusion) that elevate the stress response (46). Social discrimination shares many of these attributes—it is unpredictable, is uncontrollable, and involves threats to the social self—but in many ways it is also unique (42,43,46). For example, social discrimination often involves subtle, sometimes conflicting,

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social cues that can generate a sense of ambiguity in the target (42,43). In marginalized individuals, the physiological effects that occur in response to subtle acts of discrimination are often equal to, and sometimes greater than, those that occur in response to overt discrimination (43,47–49), suggesting that ambiguity contributes to the stress-related effects of common "everyday" forms of social discrimination (e.g., via negative internal attributions) (49–51). Notably, the amygdala is also known to play a role in processing ambiguity, consistent with its involvement in associative learning (52–56).

Building on the evidence implicating the amygdala in the stress response, in our first aim we sought to examine the association between social discrimination and spontaneous amygdala activity at rest. We assessed spontaneous amygdala activity using resting-state functional magnetic resonance imaging (fMRI) and examined the fractional amplitude of low-frequency fluctuations (fALFF) in the blood oxygen level–dependent (BOLD) signal as a marker of intrinsic amygdala activity. fALFF is a computationally derived index of resting-state fMRI data; it is thought to reflect dynamic fluctuations in spontaneous neural activity (57,58). LFFs are fundamental characteristics of the resting brain. The magnitude of these LFFs, as measured by fALFF, is known to differ between brain regions and across individuals (58–60). Additionally, fALFF correlates with relative glucose uptake as assessed by fluorodeoxyglucose positron emission tomography (61), further supporting its use as a marker of individual differences in intrinsic brain activity. Guided by findings from studies of PTSD and chronic stress (21,22), we hypothesized that greater levels of social discrimination would be associated with greater spontaneous activity within the amygdala.

Furthermore, we also conducted amygdala resting-state functional connectivity (rsFC) analyses to assess whether discrimination-related effects were present not only in spontaneous amygdala activity, but also within the broader network of brain regions associated with amygdala function. Hence, our second aim was to examine whether amygdala connectivity strengths correspond to levels of discrimination exposure. We hypothesized that greater discrimination exposure would correlate with stronger rsFC between the amygdala and several brain regions, particularly those within the salience network. This hypothesis was informed by recent studies that have demonstrated stronger connectivity between the amygdala and several regions associated with the salience network in response to stress (62–64). The salience network is responsible for attending to and responding to behaviorally salient stimuli (65–67). The amygdala is an important subcortical hub within this network (68); additional regions include the anterior insula, dorsal anterior cingulate, medial prefrontal cortex, striatum, and thalamus (66-70). Altogether, these analyses aim to improve our understanding of whether and how experiences of social discrimination relate to a neural network that is intricately involved in social behavior and emotional well-being (18,19).

METHODS AND MATERIALS

Participants

We included 90 adults from the New York City area enrolled in MRI studies of stress and human immunodeficiency virus (HIV). The Icahn School of Medicine at Mount Sinai's Institutional Review Board approved this research. All participants gave their informed consent and were financially compensated for their time. Inclusion criteria required that participants were between 21 and 70 years of age, had completed ≥10 years of education, and were native English speakers. All participants achieved a score of ≥25 points on the Mini-Mental State Examination (71). All HIV-positive participants were prescribed antiretroviral medications. Exclusion criteria included reported history of left-handedness, uncorrected abnormal vision, developmental disability, learning disability, major psychiatric illness (e.g., schizophrenia, bipolar disorder), primary neurological disorder (e.g., stroke, epilepsy), opportunistic brain infection, head injury with loss of consciousness >10 minutes, and severe medical conditions (e.g., cirrhosis of the liver). Individuals who met criteria for current major depressive disorder or PTSD diagnosis via the Mini-International Neuropsychiatric Interview Plus (version 5) (72) were excluded. Substance use exclusion criteria were reported current alcohol or substance dependence within the past 12 months (Mini-International Neuropsychiatric Interview) and positive urine toxicology before MRI assessment (cocaine, amphetamine, methamphetamine, methadone, opiates, barbiturates, benzodiazepine, tricyclic antidepressants, buprenorphine); however, individuals who tested positive for marijuana use (n = 12) were not excluded. Fifteen participants were excluded due to excessive head motion during the fMRI scan (see MRI Data Processing). An additional participant was excluded due to MRI data loss. Accordingly, we present demographic, imaging, and psychosocial data for the remaining 74 participants only. This group was diverse, with respect to several demographic and social factors previously linked to elevated risk of discrimination exposure (73–91), including HIV status, age, sex, race, ethnicity, and sexual orientation. Demographic data are reported in Table 1.

Measures of Discrimination and Psychosocial Function

The Everyday Discrimination Scale (EDS) (92) assessed the frequency of unfair treatment during common everyday situations. The EDS has been widely used across a diversity of samples (differing by age, sex, race, ethnicity, sexual orientation), with high levels of internal consistency and convergent and divergent validity (93–96). This 9-item self-report questionnaire measures social discrimination across multiple domains. Respondents indicate how often in their "day-to-day life" they experience different forms of social mistreatment. Sample items include "You are treated with less courtesy than other people," "You receive poorer service than other people at restaurants or stores," and "You are threatened or harassed." The frequency of each item was rated using a 4-point Likert-type scale with responses ranging from 0 (never) to 3 (often). These types of "everyday" experiences of discrimination contribute to a type of chronic stress that has been linked to adverse health effects, which have been observed across a range of racial, ethnic, and social groups (13,97–102). For each participant, scores were summarized across items resulting in a highest possible EDS score of 27.

Table 1. Participant Demographics, Discrimination Levels, and Psychosocial Functions (*N* = 74)

Age, Years, Mean ± SD	47.46 ± 10.95
Over 55 years of age, %	25.7
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
Nadir CD4, cells/μL, Mean ± SD	286.12 ± 256.95
Current CD4, cells/μL, Mean ± SD	679.38 ± 299.45
Current HIVL, copies/mL, Mean ± SD	1689.92 ± 8006.91
HIVL below 50 copies/mL, %	65.4
Length of HIV infection, Years, Mean ± SD	15.08 ± 6.92
ARV regimens, *n*	
PI + II	1
PI + NRTI	7
PI + NRTI + II	1
NRTI + II	3
NRTI + NNRTI	11
NRTI + NNRTI + II	3
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

ARV, antiretroviral; BAI, Beck Anxiety Inventory; CD4, cluster of differentiation 4; CES-D, Center for Epidemiologic Studies Depression Scale; EDS, Everyday Discrimination Scale; HIV, human immunodeficiency virus; HIVL, human immunodeficiency virus viral load; II, integrase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PCLC, Posttraumatic Stress Disorder Checklist–Civilian Version; PI, protease inhibitor; PSS, Perceived Stress Scale; PTSD, posttraumatic stress disorder.

Levels of current stress, depression, anxiety, and PTSD-related symptomology were assessed using the Perceived Stress Scale (103), the Center for Epidemiologic Studies Depression Scale (104), Beck Anxiety Inventory (105), and PTSD Checklist–Civilian Version (106), respectively. Discrimination exposure is associated with increases in neuropsychiatric symptoms, including depression, anxiety, and PTSD-related symptoms (2–7). Notably, current stress, depression, anxiety, and PTSD-related symptoms are known to affect spontaneous amygdala activity (20–22,107). Accordingly, the Perceived Stress Scale, Center for Epidemiologic Studies Depression Scale, Beck Anxiety Inventory, and PTSD Checklist–Civilian Version were used to evaluate whether the relation between perceived discrimination and amygdala activity was specific, and not confounded by the effects of current stress or neuropsychiatric symptoms on amygdala activity.

MRI Image Acquisition

MRI scans were completed before administering the questionnaires described above. Whole-brain echo-planar BOLD fMRI was conducted during a 5-minute resting-state scan (eyes open, no visual fixation point) (108). BOLD images were acquired in the axial plane with anterior–posterior phase encoding using a Siemens MAGNETOM Skyra 3T scanner (Siemens Corp., Erlangen, Germany) (echo time/repetition time = 35/1000 ms, matrix = 108 × 108, 2.1 mm slices, field of view = 228 × 228 mm) equipped with a 32-channel head coil. This procedure yielded 305 whole-brain volumes with a spatial resolution of 2.1 mm^3 per voxel. Whole-brain high-resolution T1 images were acquired in the sagittal plane before fMRI for anatomical reference (echo time/repetition time = 2.07/2400 ms, 0.8 mm^3, field of view= 256 × 256 mm).

MRI Data Processing and Statistical Analysis

Image Processing. All fMRI dataset processing was performed with Analysis of Functional NeuroImages (AFNI) software (109). For each participant, the functional dataset was despiked, slice-timing corrected, spatially aligned to the sixth volume (to minimize movement artifact), coregistered to high-resolution anatomical volumes, and transformed into standard stereotaxic space (110) before applying a three-dimensional 4-mm Gaussian kernel. The first three volumes were removed to allow the scanner to reach steady state. Motion correction was conducted using regression analysis in which the six motion parameters (demeaned) and their temporal derivatives were included as regressors of noninterest. Participants exhibiting excessive movement (i.e., >2 mm maximum displacement in any x, y, or z axis, or >2° maximum rotation) were excluded from the sample, as noted above. Bandpass filtering was applied to remove low- and high-frequency noise (0.01–0.10 Hz), only after calculating the fALFF.

Spontaneous Amygdala Activity. fALFF values were calculated on a voxelwise basis for each participant as the sum of amplitudes across the low-frequency range (0.01–0.10 Hz), divided by that of the entire detectable frequency range (0–0.25 Hz) (57). An a priori region-of-interest (ROI) analysis was conducted within the right and left amygdala to assess spontaneous amygdala activity levels and their relation to discrimination exposure. ROIs were drawn as spheres with a 5-mm radius centered on Talairach coordinates for the amygdala (x = ±23, y = 5, z = −15). For each participant, overlap between the ROI spheres and the right and left amygdala was verified before calculating mean fALFF within each ROI. Extracted data thus represent mean fALFF within the right and left amygdala, separately, for each participant. These data were utilized in subsequent analyses conducted in SPSS (version 23, IBM Corp., Armonk, NY). As an initial validation

step, we verified that significant spontaneous activation was observed within the a priori ROIs using one-sample *t* tests (vs. a hypothetical mean of zero). Next, to assess our first aim, linear regression analysis was used to examine the relation between spontaneous amygdala activity and EDS scores, controlling for levels of current stress, depression, anxiety, and PTSD-related symptoms. In this model, mean fALFF values within the right and left amygdala were entered as independent variables and EDS scores were entered as the dependent variable; the Perceived Stress Scale, Center for Epidemiologic Studies Depression Scale, Beck Anxiety Inventory, and PTSD Checklist–Civilian Version scores were included as covariates. Multicollinearity checks were run for all regression models to ensure that correlations between predictor variables did not exceed acceptable limits (tolerance <0.2) (111).

Resting-State Functional Connectivity. Whole-brain seed-based correlation analyses were conducted in AFNI. Separate analyses were conducted for the right and left amygdala; these a priori ROIs were defined using a 5-mm radius sphere centered on Talairach coordinates for the amygdala (x = ±23, y = 5, z = −15). As a control, we also examined posterior cingulate cortex (PCC) connectivity using a 5-mm radius ROI seed centered on the PCC (x = −2, y = 51, z = 27) (112), a major hub of the default mode network (112–114). For each participant, we extracted the mean time series of activity across voxels in each ROI, which was then used as a temporal predictor in whole-brain correlation analyses; the resulting *r* values were converted to normalized *Z* scores using the Fisher *r*-to-*Z* transformation. *Z*-score maps were entered into group-level analyses, which involved regressing EDS scores (discrimination measure) against whole-brain amygdala connectivity on a voxelwise basis, thus assessing our second aim. Associations between EDS scores and whole-brain PCC connectivity were assessed in an identical manner. Because this is the first study to examine the neural correlates of discrimination using rsFC, to protect against type II error, we applied a liberal whole-brain voxelwise significance threshold of $p < .05$, with a cluster-level correction for multiple comparisons across the entire brain (cluster volume ≥568 voxels), which corresponds to a familywise error–corrected *p* value of .05, as determined by Monte Carlo simulations (AFNI 3dClustSim; non–Gaussian-shaped spatial autocorrelation function).

RESULTS

Discrimination Frequency and Psychosocial Functions

Table 1 lists group mean scores on the EDS and all psychosocial measures. Pearson correlations assessed the relation between EDS scores and psychological symptoms. Results revealed that higher discrimination exposure was significantly associated with higher levels of current stress ($r_{74} = .48$, $p < .001$), depression ($r_{74} = .53$, $p < .001$), anxiety ($r_{74} = .44$, $p < .001$), and PTSD-related ($r_{74} = .58$, $p < .001$) symptoms.

For descriptive purposes, demographic-related differences in EDS scores were assessed using Mann-Whitney *U* tests (Table 2). Mean levels of perceived discrimination were higher in participants who were HIV positive (vs. HIV negative), 55 years of age or older (vs. younger than 55 years of age), men (vs. women), white (vs. nonwhite), non-Hispanic (vs. Hispanic), and homosexual/bisexual (vs. heterosexual); however, none of these group differences were significant (all *p*s > .05). Interpretation of these group differences is further limited by the fact that groups were not prospectively matched on potentially confounding factors (e.g., men and women were not matched according to ethnicity, sexual orientation), as the aim of this study did not involve assessing group differences in discrimination exposure.

Spontaneous Amygdala Activity and Discrimination Frequency

Our first aim examined whether greater discrimination exposure was associated with spontaneous amygdala activity. We first confirmed that robust levels of spontaneous activity were observed within the amygdala (left [$t_{73} = 76.82$, $p < .001$], right [$t_{73} = 70.29$, $p < .001$]), and that amygdala activity levels in those with and without positive marijuana toxicology did not differ significantly (left [$t_{72} = 0.89$, $p = .37$], right [$t_{72} = 0.20$, $p = .84$]). In testing our first aim, the regression model controlling for levels of current stress, depression, anxiety, and PTSD-related symptoms revealed a significant positive association between spontaneous left amygdala activity and EDS scores ($\beta = .33$ [$t = 2.08$, $p = .041$]) (Figure 1), whereas associations in the right amygdala were nonsignificant ($\beta = -.26$ [$t = -1.64$, $p = .106$]). The association between left amygdala activity and EDS scores remained significant ($\beta = .36$, $p = .039$), even when

Table 2. Mean Levels of Self-reported Discrimination (EDS Scores) Within the Sample When Grouped by Six Different Demographic and Social Factors

	Group 1		Group 2		
Demographic Category (Group 1 vs. Group 2)	Mean ± SD	*n*	Mean ± SD	*n*	*p*
HIV Status (HIV Positive vs. HIV Negative)	7.27 ± 5.68	26	6.54 ± 5.22	48	.640
Age (55 Years of Age or Older vs. Younger Than 55 Years of Age)	7.47 ± 5.50	19	6.56 ± 5.34	55	.563
Sex (Female vs. Male)	6.16 ± 5.14	32	7.29 ± 5.53	42	.380
Race (Nonwhite vs. Caucasian/White)	6.54 ± 5.37	67	9.29 ± 4.92	7	.230
Ethnicity (Hispanic vs. Non-Hispanic)	5.06 ± 5.72	17	7.32 ± 5.19	57	.089
Sexual Orientation (Homosexual/Bisexual vs. Heterosexual)	8.21 ± 5.45	24	6.12 ± 5.24	50	.143

Everyday Discrimination Scale (EDS) scores are listed for descriptive purposes only; groups were not prospectively matched with respect to factors that may influence discrimination exposure (e.g., men and women were not matched with respect to ethnicity, sexual orientation), which limits the interpretation of any observed group differences in discrimination ratings.

HIV, human immunodeficiency virus.

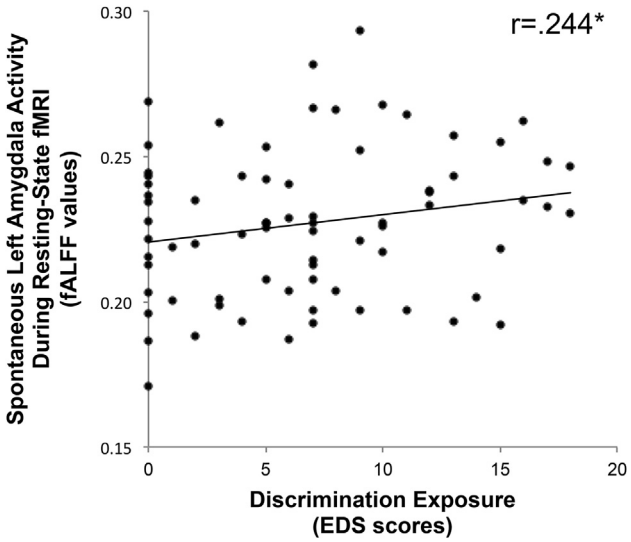

Figure 1. Association between spontaneous left amygdala activity (at rest) and self-reported discrimination exposure. *$p < .05$, controlling for right amygdala activity, current levels of depression, stress, anxiety, and posttraumatic stress disorder–related symptoms. EDS, Everyday Discrimination Scale; fALFF, fractional amplitude of low frequency fluctuations.

controlling for HIV status, age, sex, race, ethnicity, sexual orientation, and urine toxicology results (Table 3). This result was also replicated when excluding the 12 participants with positive marijuana toxicology (left [$\beta = .37$, $p = .055$], right [$\beta = -.26$, $p = .165$]). Similarly, although HIV infection has been shown to impact brain structure and function (115–123), the observed effects did not differ based on HIV status (see the Supplemental Results).

Table 3. Results from the Regression Analysis Assessing the Association Between Discrimination Exposure (EDS Scores; Dependent Variable) and Intrinsic Amygdala Activity Levels, Controlling for Several Psychological, Social, and Demographic Factors

Predictor	β	*t*	*p*
Left Amygdala (fALFF)	.36	2.11	.039
Right Amygdala (fALFF)	−.32	−1.88	.066
Current Stress (PSS)	.06	0.36	.719
Current Depression (CES-D)	.12	0.63	.535
Current Anxiety (BAI)	−.01	−0.05	.964
Current PTSD-Related Symptoms (PCLC)	.46	2.24	.029
HIV Status	.00	0.02	.987
Age	.08	0.72	.473
Sex	−.10	−0.87	.387
Race	.01	0.10	.922
Ethnicity	−.15	−1.41	.164
Sexual Orientation	−.02	−0.12	.905
Urine Toxicology	.02	0.14	.887

BAI, Beck Anxiety Inventory; CES-D, Center for Epidemiologic Studies Depression Scale; EDS, Everyday Discrimination Scale; fALFF, fractional amplitude of low-frequency fluctuations; HIV, human immunodeficiency virus; PCLC, Posttraumatic Stress Disorder Checklist–Civilian Version; PSS, Perceived Stress Scale; PTSD, posttraumatic stress disorder.

Amygdala rsFC and Discrimination Frequency

Our second aim examined whether greater discrimination exposure was associated with stronger amygdala rsFC. The results focus on analyses of the left amygdala rsFC, given that significant associations were observed between EDS scores and spontaneous activity in the left amygdala only. In addition, the control analysis, which examined associations between EDS score and PCC rsFC, did not reveal significant results ($p > .05$, familywise error corrected).

The whole-brain regression analysis of left amygdala connectivity revealed that higher levels of discrimination were associated with stronger rsFC between the left amygdala and three clusters encompassing several salience network regions (left anterior insula, left putamen, bilateral caudate, bilateral anterior cingulate, bilateral medial frontal gyrus, bilateral thalamus), as well as the left parahippocampal gyrus, bilateral lingual gyrus, and right cerebellum (Figure 2A, B; Table 4). Applying a more stringent threshold (voxelwise $p < .005$; cluster size >90 voxels; $p < .05$, familywise error corrected) revealed that the most robust associations were observed within a cluster centered on the left thalamus (126 voxels; central coordinate: x = 12, y = 9, z = 15).

Mean connectivity strengths were extracted from the initial three clusters for further analysis in SPSS; results revealed that the association between discrimination exposure and mean amygdala connectivity levels across these three regions remained significant ($\beta = .33$, $p = .003$) even when controlling for current stress, depression, anxiety, PTSD-related symptoms, HIV status, age, sex, race, ethnicity, sexual orientation, and urine toxicology results (Table 5). This result was replicated when excluding the 12 participants with positive marijuana toxicology ($\beta = .33$, $p = .006$). Similarly, the observed effects did not differ based on HIV status (see the Supplemental Results).

DISCUSSION

To our knowledge, this is the first study to examine whether self-reported discrimination exposure corresponds to resting-state brain activity in marginalized adults. This study thus serves as a complement to the extant task-based fMRI literature (16) in this nascent area of research. In the current study, we examined the relation between self-reported discrimination exposure and spontaneous amygdala activity at rest. As predicted, we observed that greater discrimination exposure was associated with higher levels of spontaneous amygdala activity. These effects were observed in the left amygdala only, aligning with data implicating the left amygdala in the processing of negative stimuli (124,125) and the right amygdala in emotional well-being (126). However, because lateralized valence effects have not been consistently observed (127) and we did not have specific hypotheses regarding laterality, firmer conclusions regarding these lateralized findings require additional investigation.

Prior studies have linked elevated levels of spontaneous amygdala activity to increases in affective symptoms, including higher levels of current stress, depression, anxiety, and PTSD-related symptoms (20–22,107). Yet, in the current study, the association between spontaneous amygdala activity and discrimination was independent of current stress,

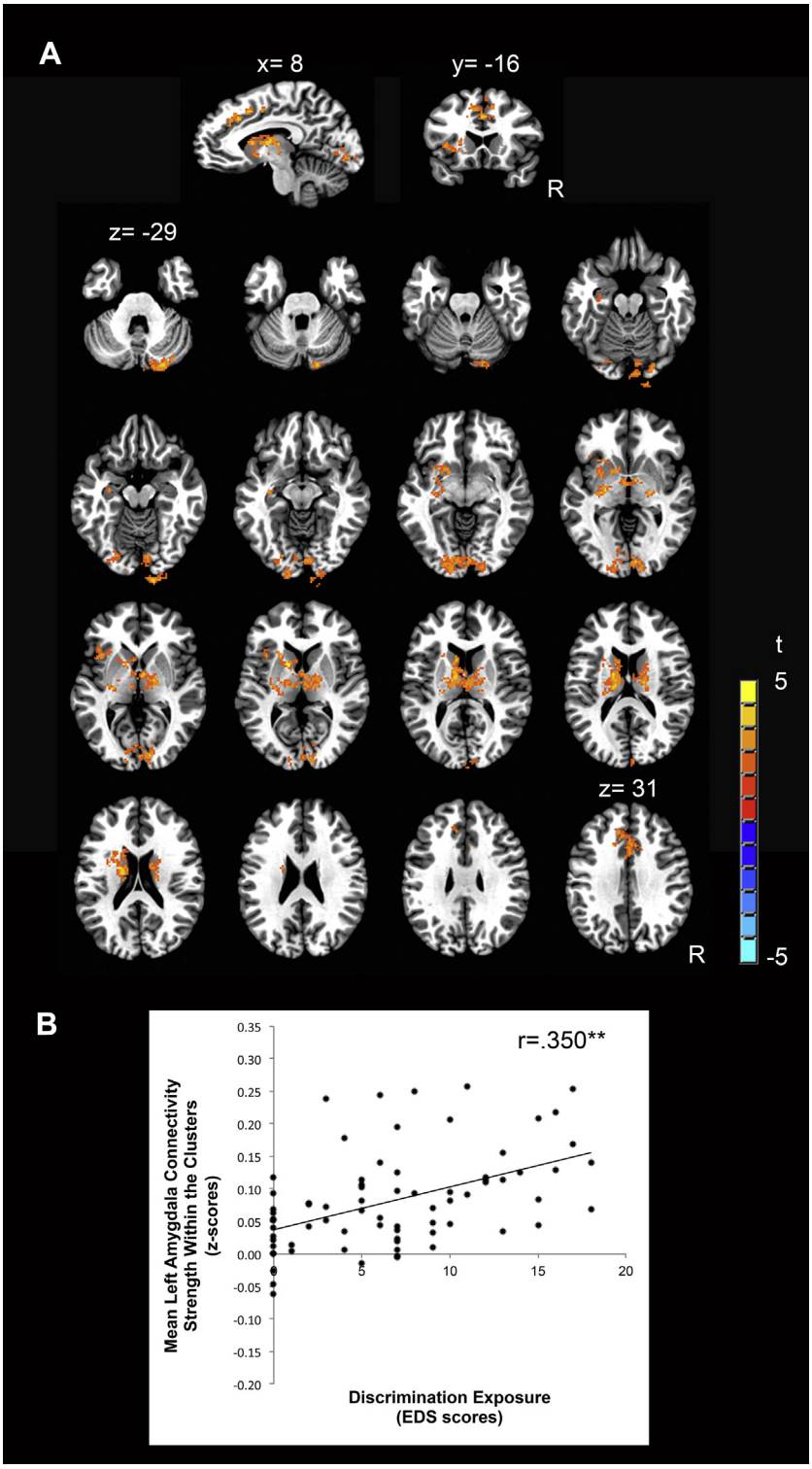

Figure 2. **(A)** Regions where left amygdala functional connectivity strength is associated with discrimination exposure (Everyday Discrimination Scale [EDS] scores) ($p < .05$, familywise error corrected). One sagittal image (upper left), one coronal image (upper right), and 15 axial images are shown. For the sagittal image, x = 8; for the coronal image, y = −16; axial images begin at z = −29 and increase in 4-mm increments. **(B)** Association between self-reported discrimination exposure and mean left amygdala connectivity strengths within the clusters shown in panel **(A)**. $^{**}p < .01$, controlling for current levels of depression, stress, anxiety, and post-traumatic stress disorder–related symptoms. R, right.

depression, anxiety, and PTSD-related symptoms. This suggests that the relation between discrimination exposure and amygdala function is distinguishable from several of the affective symptoms that frequently accompany discrimination. There is strong evidence that discrimination has an independent effect on physical and mental health outcomes (1–4,8–13). Our data thus suggest that these effects extend to the level of neural function.

Table 4. Regions Where the Strength of Functional Connectivity With the Left Amygdala Is Associated With Discrimination Exposure

Peak Region	BA	Coordinates (x, y, z)	Cluster Size (Voxels)	Mean *t*	*p*
L Caudate		15, 5, 18	1681	2.536	.013
R Lingual Gyrus	18	−3, 83, −4	1314	2.447	.017
R Cingulate Gyrus	32	−1, −15, 34	580	2.481	.015

Peak voxel coordinates are listed using the Talairach and Tournoux atlas.

BA, Brodmann area; L, left; R, right.

Having found discrimination-related effects on spontaneous left amygdala activity, we then examined patterns of spontaneous amygdala connectivity to determine whether discrimination-related effects were also observed within a broader network of amygdala function. Our results revealed an independent effect of discrimination on intrinsic amygdala connectivity. Specifically, we found that greater discrimination exposure was associated with stronger connectivity between the left amygdala and several brain regions (e.g., anterior cingulate, anterior insula, thalamus). Prior research indicates that marginalized adults, relative to nonmarginalized adults, exhibit stronger anterior cingulate connectivity during acute stress induction (16). Extending this finding, our data reveal that discrimination-related effects on neural connectivity are evident even in the absence of an exogenous stress-related trigger. Interestingly, results from our control analyses of PCC connectivity suggest that the observed effects involving amygdala connectivity are specific, and do not simply reflect general discrimination-related increases in connectivity across all rsFC networks (e.g., default mode network).

As noted above, we observed stronger rsFC between the left amygdala and several brain regions, including many associated with the salience network (i.e., anterior insula, putamen, caudate, anterior cingulate, medial frontal gyrus, thalamus) (66–70). The amygdala is an important hub within this network (68), which is responsible for detecting and responding to behaviorally salient stimuli (65–68). Hyperconnectivity between the amygdala and salience network regions has been reported in individuals with PTSD (23–25) and single-episode depression (26). In addition, stronger coupling within this system has been shown to correlate with increases in physiological arousal and vigilance (64,128,129). With regard to the thalamus, where the most robust effects were observed, prior studies indicate that the amygdala and thalamus are functionally as well as anatomically connected (130–133). These two structures play a large role in the detection of threats in the environment, and they are also critically involved in associative learning processes, such as fear conditioning (37,134–137). Taken as a whole, these findings suggest that an important goal for future studies will be to determine whether discrimination-related elevations in amygdala connectivity reflect greater physiological arousal, vigilance, threat-related processing, and/or associative learning processes.

Table 5. Results From the Regression Analysis Assessing the Association Between Discrimination Exposure (EDS Scores; Dependent Variable) and Amygdala Connectivity Levels Across the Three Clusters, Controlling for Several Psychological, Social, and Demographic Factors

Predictor	β	*t*	*p*
Left Amygdala rsFC (Across the Three Clusters)	.33	3.04	.003
Current Stress (PSS)	.01	0.05	.964
Current Depression (CES-D)	.11	0.60	.551
Current Anxiety (BAI)	.02	0.12	.909
Current PTSD-Related Symptoms (PCLC)	.37	1.88	.065
HIV Status	.04	0.32	.751
Age	.10	0.96	.340
Sex	−.04	−0.33	.746
Race	.07	0.66	.514
Ethnicity	−.15	−1.50	.140
Sexual Orientation	.03	0.26	.798
Urine Toxicology	−.03	−0.33	.746

BAI, Beck Anxiety Inventory; CES-D, Center for Epidemiologic Studies Depression Scale; EDS, Everyday Discrimination Scale; HIV, human immunodeficiency virus; PCLC, Posttraumatic Stress Disorder Checklist–Civilian Version; PSS, Perceived Stress Scale; PTSD, posttraumatic stress disorder; rsFC, resting-state functional connectivity.

While our correlational findings cannot establish causality, results from investigations that involve controlled modulation of acute stress levels raise the possibility that frequent discrimination exposure could contribute to the observed differences in amygdala function. These studies show that increased connectivity between the amygdala and several salience network nodes occurs in response to acute stress induction (62–64), whereas decreased amygdala connectivity is observed following administration of corticosteroids (138) and anxiolytic agents (64,139). Moreover, elevations in amygdala activity and connectivity can persist even after the precipitating stressor has subsided, as is evident in individuals with PTSD and other stress-related conditions (21,23–26). Collectively, such findings lend greater support to the possibility that frequent, repeated exposure to discrimination could perhaps contribute to the observed differences in amygdala function.

Our sample included a diverse group of individuals who, based on a variety of demographic and social factors (race, ethnicity, sex, sexual orientation, HIV status, age) and their potential intersectionalities are at increased risk of discrimination (73–91). Yet, the observed associations between self-reported discrimination exposure and amygdala function were evident even after accounting for these factors. Such data suggest that the observed results were not driven by one particular demographic or social group. Hence, results from this study have implications for our understanding of the effects of discrimination on neural and health-related outcomes across several marginalized groups (140–143). For example, frequent discrimination exposure has been associated with a wide range of adverse health effects, including increased risk of cardiovascular disease and hypertension (9–11). As described above, we observed discrimination-related elevations in spontaneous amygdala activity. Notably, recent findings have directly linked stress-related elevations in spontaneous amygdala activity to increases in cardiovascular events (22). Future studies that investigate the possibility that discrimination-related elevations in spontaneous amygdala activity may have similar effects on cardiovascular outcomes appear warranted. Accordingly, our findings may offer valuable information to a range of medical and mental health

professionals working with marginalized individuals, as our data suggest that experiences of social discrimination can be placed within a neurobiological model akin to other types of psychological stressors.

Several issues merit further consideration. First, self-report studies are limited by reporting biases. For instance, some individuals may perceive less discrimination than may exist (minimization bias), while others may perceive more discrimination than may exist (vigilance bias) (144). It is thus possible that elevations in amygdala activity and rsFC reflect innate individual differences that facilitate the detection, perception, and/or recollection of discriminatory acts (144–146), as well as factors unexamined in the current study [e.g., attribution tendencies (50), distress tolerance (147), resilience capacity, coping strategies]. Future prospective or longitudinal studies may help to clarify the question of causal effects, which remain obscure owing to the cross-sectional nature of our study. Nevertheless, strong parallels between our discrimination-related results and those observed in association with current stress (22), PTSD (21,23–25), and single-episode depression (26) lend greater validity to our findings, and further suggest shared commonalities in the neural response to stress of various origins. Second, although the duration of our resting-state scan was similar to prior studies [e.g., (21,112,148)], there is some evidence (149) that scans of longer duration (>6 minutes) generate rsFC metrics with even greater reliability [however, see also (108)]. Future studies employing complementary approaches (analyses of longer resting-state scans, task-based studies, etc.) are expected to provide greater contextualization of the observed results.

In summary, we report that frequent exposure to "everyday" forms of discrimination (i.e., relatively minor social mistreatment) is associated with observable differences in brain function. Specifically, we found that greater self-reported discrimination was associated with elevated intrinsic amygdala activity and connectivity. The observed effects were independent of those related to current stress, depression, anxiety, or PTSD-related symptoms. Our data thus suggest that social discrimination affects brain function in a manner that is similar to, but still distinct from, other types of psychological stressors. Prior studies have linked increases in intrinsic amygdala activity and connectivity to higher levels of stress, physiological arousal, and vigilance (22,64,128,129), as well as negative health outcomes (22,150–156). Taken together, these findings indicate that amygdala-based neural networks warrant future examination among marginalized individuals and should be further investigated as a potential etiological pathway connecting discrimination exposure to adverse physical and mental health outcomes.

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