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Neighborhood Perceptions Are Associated With Intrinsic Amygdala Activity and Resting-State Connectivity With Salience Network Nodes Among Older Adults

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ABSTRACT

Objective: Neighborhood perceptions are associated with physical and mental health outcomes; however, the biological associates of this relationship remain to be fully understood. Here, we evaluate the relationship between neighborhood perceptions and amygdala activity and connectivity with salience network (i.e., insula, anterior cingulate, thalamus) nodes.

Methods: Forty-eight older adults (mean age = 68 [7] years, 52% female, 47% non-Hispanic Black, 2% Hispanic) without dementia or depression completed the Perceptions of Neighborhood Environment Scale. Lower scores indicated less favorable perceptions of aesthetic quality, walking environment, availability of healthy food, safety, violence (i.e., more perceived violence), social cohesion, and participation in activities with neighbors. Participants separately underwent resting-state functional magnetic resonance imaging.

Results: Less favorable perceived safety ($\beta = -0.33$, $p_{FDR} = .04$) and participation in activities with neighbors ($\beta = -0.35$, $p_{FDR} = .02$) were associated with higher left amygdala activity, independent of covariates including psychosocial factors. Less favorable safety perceptions were also associated with enhanced left amygdala functional connectivity with the bilateral insular cortices and the left anterior insula ($\beta = -0.34$, $p_{FDR} = .04$). Less favorable perceived social cohesion was associated with enhanced left amygdala functional connectivity with the right thalamus ($\beta = -0.42$, $p_{FDR} = .04$), and less favorable perceptions about healthy food availability were associated with enhanced left amygdala functional connectivity with the bilateral anterior insula (right: $\beta = -0.39$, $p_{FDR} = .04$; left: $\beta = -0.42$, $p_{FDR} = .02$) and anterior cingulate gyrus ($\beta = -0.37$, $p_{FDR} = .04$).

Conclusions: Taken together, our findings document relationships between select neighborhood perceptions and amygdala activity as well as connectivity with salience network nodes; if confirmed, targeted community-level interventions and existing community strengths may promote brain-behavior relationships.

Key words: neighborhood, environment, psychosocial stress, amygdala, functional connectivity, social determinants of health.

INTRODUCTION

Neighborhood conditions are important social determinants of health (SDoHs) associated with physical and mental health outcomes including obesity (1,2), cardiovascular disease (3), anxiety (4), and depression (5). Because of structural racism and a history of discriminatory policies, including redlining, that promoted residential segregation, neighborhood factors as SDoH are unevenly

AIC = Akaike information criteria, **BAI** = Beck Anxiety Inventory, **BDI** = Beck Depression Inventory, **FC** = functional connectivity, **FDR** = false discovery rate, **HAM-D** = Hamilton Depression Rating Scale, **MMSE** = Mini Mental State Examination, **MRI** = magnetic resonance imaging, **rsFC** = resting-state functional connectivity, **rsfMRI** = resting-state functional magnetic resonance imaging, **SCID** = Structured Clinical Interview for DSM-IV-TR, **SD** = standard deviation, **SDoH** = social determinants of health, **SN** = salience network , **WTAR** = Wechsler Test of Adult Reading

SDC Supplemental Digital Content

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Received for publication December 22, 2022; revision received November 17, 2023.

Article Editor: David H. Chae

DOI: 10.1097/PSY.0000000000001272

distributed across populations, with minoritized groups being disproportionately impacted by less favorable conditions (3). Recently, we published a health equity-focused framework outlining adverse SDoH as sources of chronic psychosocial and environmental stress, which can influence health outcomes through subsequent biological and psychological sequalae (3); however, the underlying pathways linking neighborhood stress to these health outcomes are not fully understood despite their importance in addressing health disparities. Although the relationship between objectively quantified neighborhood factors and health outcomes is under increasing investigation, less is known about the role of subjective perceptions of neighborhood environment in individual-level health. Given that perceptions of neighborhood conditions may differ from objectively measured neighborhood factors (6), it is important to include subjective measures when considering the interplay between the neighborhood environment and individual-level health. The ways in which individuals perceive their surroundings also have important connections to mental health and psychological symptoms (7), underscoring the importance of incorporating subjective neighborhood measures when examining neural correlates of neighborhood environment. Although neighborhood conditions—measured both objectively and subjectively—have been associated with markers of dysfunctional biological stress responses such as allostatic load (8), stress-related DNA methylation (9), and inflammation (10), the neurobiological associates of less favorable neighborhood conditions, particularly perceived neighborhood environment, require further exploration.

Recent work into neurobiological markers of chronic stress has revealed stress-related changes in amygdala activity and functional connectivity (FC) (11). For example, associations between stressors and alterations in amygdala activity and FC have been demonstrated in the context of prenatal and early life stress and brain development (12–14), psychosocial stress (15,16), emotion and threat processing (17,18), and stress-related disorders such as depression, anxiety, posttraumatic stress disorder, and addiction (11). Moreover, recent studies have shown that exposure to greater neighborhood disadvantage is associated with brain volume changes and altered neural connectivity to regions important for emotion regulation, including the amygdala (19,20). Interestingly, recent resting-state functional magnetic resonance imaging (rsfMRI) studies also found racial discrimination—an important SDoH—associated with higher amygdala activity (15) and enhanced amygdala FC with nodes within the salience network (SN; e.g., anterior insula, thalamus, anterior cingulate) (15,16). Additional studies have also supported psychosocial stress–related associations with amygdala connectivity with SN nodes (21,22). To our knowledge, however, the relationship between neighborhood environment perceptions and resting-state amygdala activity and connectivity with SN nodes has not yet been investigated. We would anticipate a relationship between neighborhood perceptions and amygdala connectivity with SN nodes given the inherent similarities between the SDOH-derived stressors associated with less favorable neighborhood conditions (23) and those psychosocial stressors previously reported to be associated with resting-state amygdala FC to SN nodes.

Given the important role of the amygdala in the stress response (9) and the previous literature, we sought to evaluate the relationship between neighborhood perceptions of aesthetic quality, walking environment, availability of healthy food, safety, violence (i.e., more perceived violence), social cohesion, and participation in activities with neighbors in association with amygdala activity and connectivity with SN nodes in a community-dwelling cohort of older adults. We evaluated neighborhood environment perceptions with a previously validated survey (24–26) and assessed amygdala activity and FC with rsfMRI. We hypothesized that less favorable neighborhood environment perceptions would be associated with higher amygdala activity. Furthermore, we hypothesized less favorable neighborhood environment perceptions would be associated with enhanced amygdala FC with SN nodes specifically associated with threat appraisal and vigilance that may be activated in adverse neighborhood conditions (16). Findings have the potential to inform community-level interventions and identify community strengths and assets that can be leveraged to promote brain-behavior relationships.

METHODS

Study Population

This is a secondary analysis of data from a larger study of cognitive aging and cardiovascular disease risk conducted at the University of Illinois at Chicago (UIC) Department of Psychiatry. The study was approved by the UIC Institutional Review Board and conducted in accordance with the Declaration of Helsinki, with written informed consent obtained from all participants. All requisite institutional review board and institutional data use agreements were in place before data analysis at the National Heart, Lung, and Blood Institute.

As outlined elsewhere (27,28), individuals 60 years or older who self-identified as being from one of three ethnic/racial categories (i.e., non-Latino Black, non-Latino White, or Hispanic/Latino) were recruited via community outreach (e.g., advertisements and fliers) as well as word of mouth between 2012 and 2016. Interested individuals underwent telephone screening conducted in their language of choice (English or Spanish) to determine initial study eligibility. At this screen, exclusion criteria consisted of self-reported current/history of neurological conditions including Alzheimer's or other dementia, mild cognitive impairment, Parkinson disease or other movement disorders, stroke, epilepsy, or Axis I or II disorders, a history of head injury or loss of consciousness, a present/past history of substance abuse or dependence, current psychotropic medication use, or contraindications for magnetic resonance imaging (MRI). A self-reported history of stable (e.g., diabetes) or remitted medical illness (e.g., cancer) was not an exclusionary factor. Individuals were not eligible for this study if they had received cognitive testing in the past year before their participation in this study.

Individuals who passed this telephone screen underwent a more intensive in-person evaluation of inclusion/exclusion criteria in their preferred language. This secondary screening consisted of cognitive and affective screens including the Mini Mental State Examination (MMSE) (29) and a Structured Clinical Interview for DSM-IV-TR (SCID) (30) conducted by a trained research assistant fluent in either English and/or Spanish. This was followed by an evaluation by a psychiatrist, blind to all screening information, who administered the 17-item Hamilton Depression Rating Scale (HAM-D) (31). Final inclusion criteria consisted of an MMSE score ≥24, an absence of psychiatric symptoms based on the SCID, a score ≤8 on the HAM-D, and an absence of subjective memory complaints. All aspects of the study, including MRI visits, were conducted in the participant's preferred language (Spanish or English).

The overall study sample consisted of 121 individuals. Given that the current analyses focused on neighborhood perceptions and rsfMRI, we focused our study on the 84 participants with

neighborhood perception data and the 74 participants who had rsfMRI data. These numbers are reduced, in part because additional funding for the neighborhood data collection came midway through the original project. When taken together, 52 individuals had both neighborhood perception and rsfMRI data. Of these 52 individuals, we excluded 2 participants whose scans showed incidental findings and another 2 participants with quality assurance issues specifically, excess motion (Supplemental Digital Content, Figure S1, http://links.lww.com/PSYMED/A989). Thus, the final analytic sample consisted of 48 participants.

Perceptions of Neighborhood Environment Scale

The Perceptions of Neighborhood Environment Scale was used to assess perceptions of aesthetic quality, walking environment, availability of healthy food, safety, violence, social cohesion, and participation in activities with neighbors. The previously validated survey (24–26) consists of four-point (1 = often, 2 = sometimes, 3 = rarely, 4 = never) and five-point (1 = strongly agree, 2 = agree, 3 = neutral, 4 = disagree, 5 = strongly disagree) Likert scale questions probing seven categories of the neighborhood environment (Supplemental Digital Content Item 1, http://links.lww.com/PSYMED/A989). These included aesthetic quality (e.g., trash, noise, and building quality; 6 questions, scores range from 1 to 5), walking environment (e.g., opportunities to be physically active, built environment characteristics, and neighbor exercise behaviors; 10 questions, scores range from 1 to 5), availability of healthy food (i.e., selection and quality of produce available, availability of low-fat products, and the presence of fast food outlets; 4 questions, scores range from 1 to 5), safety (i.e., feelings of safety in the neighborhood; 3 questions, scores range from 1 to 5), violence (i.e., knowledge of violent crime events in the neighborhood; 4 questions, scores range from 1 to 4), social cohesion (i.e., trust and shared values among neighbors; 4 questions, scores range from 1 to 5), and participation in activities with neighbors (i.e., favors, events, shared advice, and get-togethers; 5 questions, scores range from 1 to 4). Responses were reverse coded as necessary, and scores for each subtype of neighborhood environment perception were calculated by taking the mean of the relevant responses. Across all seven categories, lower scores indicated less favorable perceptions.

Covariates

In addition to participant characteristics of age, self-identified sex (0 = male, 1 = female), and racial/ethnic group (0 = Black, 1 = Hispanic/Latino, 3 = White), we also adjusted for depressive and anxiety symptoms, educational quality, and trauma as outlined hereinafter. These covariates were selected owing to their potential confounding role with either the exposure or the outcome. For example, prior studies have shown that less favorable neighborhood conditions disproportionately impact minoritized racial and ethnic groups (3), and research has also demonstrated that racial discrimination relates to amygdala activity and FC (15,16) and these neural patterns vary by racial and ethnic group (20). Study participants completed the Beck Depression Inventory (BDI-II) (32) and the Beck Anxiety Inventory (BAI) (33) for subjective measures of depressive and anxiety symptoms, respectively. The Wechsler Test of Adult Reading (WTAR) raw score was used as a proxy for educational quality, a more informative means of assessing educational attainment than years of education in racially/ethnically diverse samples (34). The SCID (35) was used to determine the presence (1) or absence (0) of trauma in our participants, given that it is a valid trauma assessment with high positive predictive power compared with the Stressful Life Event Questionnaire (36). As described previously (37,38), presence of trauma required that participants meet both traumatic event Criterion A (1. the person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to physical integrity of self or others, and 2. the person's response involved intense fear, helplessness, or horror).

Neuroimaging

Study Outcome

Given the important role of the amygdala in the stress response (11), we examined the relationship between neighborhood environment perceptions and amygdala activity and amygdala FC. Using a hypothesis-driven approach for the amygdala resting-state FC (rsFC) analyses, we identified nodes of interest within the SN (bilateral insular cortices, bilateral anterior insula, bilateral thalamus, and the anterior cingulate gyrus) based on previously published literature (14,15). We performed ROI-to-ROI analysis by computing the correlation between the amygdala and these ROIs of interest.

Data Acquisition

As described elsewhere (27), participants underwent neuroimaging at UIC's Center for Magnetic Resonance Research. Whole-brain images aligned to the AC-PC line were acquired on a GE MR750 Discovery 3T scanner (General Electric Health Care, Waukesha, Wisconsin) using an eight-channel head coil. Participants were positioned supine on the scanner table with foam pads to minimize head movement and instructed to remain still throughout scanning. Sequences used in the current research included T1-weighted images acquired via Brain Volume (BRAVO) imaging sequence and resting-state fMRI.

The BRAVO imaging sequence included field of view = 22 mm^2, voxel size = 0.42 × 0.42 × 1.5 mm^3, 120 interleaved axial slices, repetition time/echo time = 1200 milliseconds/5.3 milliseconds, and flip angle = 13 degrees. Resting-state functional MR images were acquired with a fast echo-planar imaging sequence with the following parameters: repetition time = 2000 milliseconds, echo time = 30 milliseconds, flip angle = 90 degrees, field of view = 24 × 24 mm, acquisition matrix size = 64 × 64 × 256, slice thickness = 4 mm, gap = 0 mm, and 256 axial slices.

Data Processing

FC data were generated using the resting-state fMRI toolbox, CONN (http://www.nitrc.org/projects/conn) (39). We used CONN's defaultMNI pipeline, and the data were aligned to MNI Space. In brief, raw echo-planar imaging images were realigned, co-registered, normalized, and smoothed before analyses. A smoothing kernel with a full width at half maximum of 6 mm was used. Confounding effects from motion artifact, white matter, and cerebrospinal fluid were regressed out of the signal. Two participants with excess motion attributed to blurring and ringing were identified in structural sequences and were excluded at the time of processing because our fMRI analyses relied on the ROIs defined on structural MRI. Using 132 ROIs defined from the FSL

Harvard-Oxford Atlas and AAL atlas, connectivity between the amygdala and all other ROIs was derived using pairwise blood oxygenation level–dependent signal correlations, which were then converted to z scores using Fisher r-to-z transformation. We then selected FC between the bilateral amygdala and seven ROIs (bilateral insular cortices, bilateral anterior insula, bilateral thalamus, and the anterior cingulate gyrus) for our hypothesis-driven analyses. Amygdala activity was determined by the mean blood oxygenation level–dependent signals for the right and left amygdala, respectively. Amygdala FC data were visualized with the BrainNet Viewer (http://www.nitrc.org/projects/bnv/) (40).

Statistical Analysis

Unadjusted linear regression modeling was used to test the associations between each of the neighborhood perception scores (i.e., aesthetic quality, walking environment, availability of healthy food, safety, violence, social cohesion, and participation in activities with neighbors) and left and right resting-state amygdala activity followed by adjusted models that included age, sex, racial/ethnic group, and WTAR as covariates. We then explored model fit with psychosocial covariates (i.e., BDI, BAI, and trauma history) using the Akaike information criteria (AIC), and the psychosocial covariate that provided the best model fit was selected without a cut point based on lower model AIC. Cronbach α coefficients were used to measure internal consistency of the neighborhood perception measures, with values above 0.7 considered acceptable.

Separate linear regression models were used to determine the relationships between each neighborhood perception category and amygdala FC with each of the following ROIs within the SN: bilateral insular cortices, bilateral anterior insula, bilateral thalamus, and the anterior cingulate gyrus respectively. All models were adjusted for age, sex, racial/ethnic group, WTAR, and the psychosocial covariate that best fit the amygdala activity model as outlined previously. p Values were corrected for false discovery rate (FDR), and $p < .05$ corrected for FDR was considered statistically significant. Two-tailed tests were performed for all analyses. STATA 12 (StataCorp, College Station, Texas) was used for linear regression and AIC analyses, R (R Foundation for Statistical Computing, Vienna, Austria) was used for FDR corrections, and Prism 9.0 (GraphPad, San Diego, California) was used to generate graphs.

RESULTS

Participant Characteristics

Forty-eight older adults (mean age = 68.27 [7.20] years) were included in our analytic sample (Table 1). Consistent with inclusion/exclusion criteria, average MMSE (28.90 [1.32]) and HAM-D (1.12 [1.23]) scores attested to the sample not having dementia or clinical depression. Approximately half of the participants were female (n = 25, 52%), and about half identified as non-Latino Black (n = 23, 48%). Cronbach α coefficients were 0.80 for perceptions of aesthetic quality, 0.87 for walking environment, 0.80 for availability of healthy food, 0.78 for safety, 0.84 for violence (i.e., more perceived violence), 0.82 for social cohesion, and 0.80 for participation in activities with neighbors. There was no evidence of multicollinearity between the neighborhood perception subscores based on variance inflation factors of less than 10 (data not shown).

TABLE 1. Participant Characteristics, 2013–2016

	Cohort (n = 48)[a]
Age, y	68.27 (7.20)
Female, n (%)	25 (52.08)
Race/ethnicity, n (%)	
Non-Latino Black	23 (47.92)
Non-Latino White	24 (50.00)
Hispanic/Latino	1 (2.08)
Education, y	15.63 (2.76)
Psychosocial history	
Beck Depression Inventory	3.02 (3.41)
Beck Anxiety Inventory[b]	2.40 (2.78)
Wechsler Test of Adult Reading raw score	39.67 (9.87)
Trauma history[c,d]	26 (63.41)
Average neighborhood perception scores	
Aesthetic Quality[e]	2.68 (0.58)
Walking Environment[e]	2.14 (0.71)
Availability of Healthy Food[e]	2.07 (0.79)
Safety[e]	2.47 (0.79)
Violence[f]	3.17 (0.69)
Social cohesion[e]	2.37 (0.64)
Participation in Activities with Neighbors[f]	2.39 (0.67)

[a] Values reported in the table as mean (standard deviation) for continuous variables and n (%) for categorical variables.

[b] n = 47.

[c] n = 41.

[d] Determined by the SCID trauma assessment.

[e] Scores range from 1 to 5, with lower scores indicating less favorable perceptions.

[f] Scores range from 1 to 4, with lower scores indicating less favorable perceptions.

Neighborhood Environment Perceptions Are Associated With Intrinsic Amygdala Activity

In unadjusted models, we found that less favorable perceived safety ($\beta = -0.40$, $p_{FDR} = .01$) and participation in activities with neighbors ($\beta = -0.32$, $p_{FDR} = .05$) associated with higher left amygdala activity. No significant associations were found between neighborhood perceptions and right amygdala activity in our study population. We adjusted our models for age, sex, race, WTAR, and BDI-II. BDI-II was selected as the psychosocial covariate instead of BAI or trauma history because the models with BDI resulted in the lowest AIC, indicating the best model fit (Supplemental Digital Content, Table S1, http://links.lww.com/PSYMED/A989). Models adjusted for these factors indicated that every 1 standard deviation (SD) decrease in perceived safety was associated with 0.33-SD higher left amygdala activity ($p_{FDR} = .04$). Similarly, every one SD decrease in perceived participation in activities with neighbors associated with 0.35-SD higher left amygdala activity ($p_{FDR} = .02$; Table 2).

Neighborhood Environment Perceptions Are Related to Left Amygdala rsFC With SN Nodes

Of the seven categories of neighborhood perceptions examined, we identified significant associations between perceived availability of healthy food, social cohesion, and safety and left amygdala FC with a number of ROIs in the SN, with associations remaining significant after FDR correction for multiple comparisons. Namely,

TABLE 2. Perceived Neighborhood Environment Associations With Resting-State Left and Right Amygdala Activity Adjusted for Age, Sex, Race, Wechsler Test of Adult Reading, and Beck Depression Inventory-II Scores, 2013–2016

	Standardized β^a (p_{FDR})^b	
Models (n = 48)	Left Amygdala Activity	Right Amygdala Activity
Aesthetic quality	−0.10 (0.52)	0.12 (0.52)
Walking environment	−0.04 (0.81)	−0.13 (0.81)
Availability of healthy food	−0.04 (0.80)	−0.11 (0.80)
Safety	**−0.33 (0.04)**^{c}	0.08 (0.62)
Violence	0.12 (0.49)	0.11 (0.49)
Social cohesion	−0.25 (0.18)	−0.04 (0.81)
Participation in activities with neighbors	**−0.35 (0.02)**^{c}	0.24 (0.12)

[a] All values are reported as standardized β coefficient (β) and p values from separate linear regression models.

[b] p Values have been corrected for false discovery rate.

[c] p Values in bold represent $p < 0.05$.

less favorable perceptions of the availability of healthy food were associated with higher left amygdala rsFC with the right anterior insula (β = −0.39, p = .016, p_{FDR} = .04), left anterior insula (β = −0.42, p = .003, p_{FDR} = .02), and anterior cingulate gyrus (β = −0.37, p = .016, p_{FDR} = .04; Figure 1, 1A–D). In addition, less favorable perceived safety was associated with higher left amygdala rsFC with the right (β = −0.39, p = .008, p_{FDR} = .04) and left (β = −0.36, p = .018, p_{FDR} = .04) insular cortex and the left anterior insula (β = −0.34, p = .015, p_{FDR} = .04; Figure 1, 2A–D). Finally, every 1-SD decrease in perceived social cohesion was associated with 0.42-SD higher left amygdala rsFC with the right thalamus (p = .006, p_{FDR} = .04; Figure 1, 3A–B). Regression analysis did not reveal significant associations between perceptions of aesthetic quality, violence, or participation in activities with neighbors and the ROIs included in the hypothesis-driven analyses (Supplemental Digital Content, Table S2, http://links.lww.com/PSYMED/A989). We also did not find significant associations when examining relationships between neighborhood perceptions and right amygdala FC with SN nodes (Supplemental Digital Content, Table S3, http://links.lww.com/PSYMED/A989).

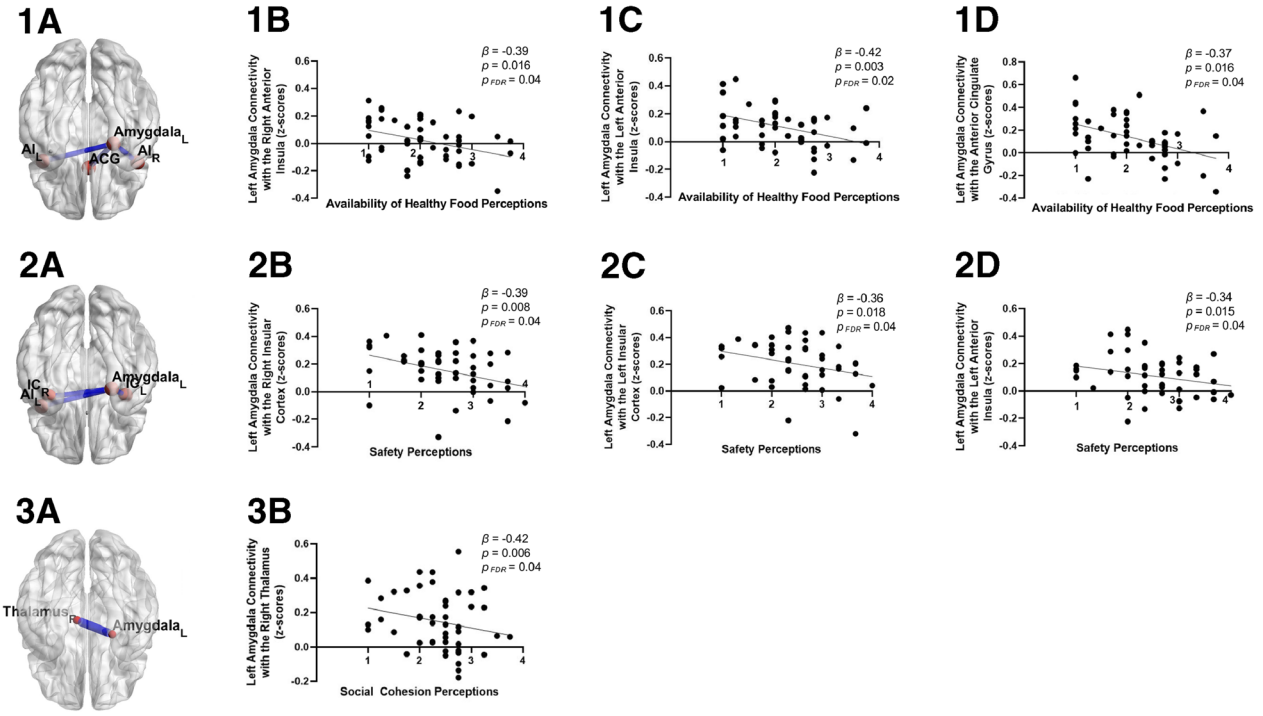

FIGURE 1. 1A, Perceptions of the availability of healthy food were significantly associated with left amygdala rsFC with the (1B) right anterior insula, (1C) left anterior insula, and (1D) anterior cingulate gyrus. 2A, Safety perceptions were significantly associated with left amygdala rsFC with the (2B) right insular cortex, (2C) left insular cortex, and (2D) left anterior insula. 3A, Social cohesion perceptions were significantly associated with left amygdala rsFC with the (3B) right thalamus. Standardized β, p values, and false discovery rate–corrected p values are reported for fully adjusted models. Color image is available online only at the journal website. rsFC = resting-state functional connectivity.

DISCUSSION

To our knowledge, this is the first study to examine the relationship between neighborhood perceptions and amygdala activity and connectivity with SN nodes in a community-dwelling cohort of older adults. We found that two neighborhood perceptions, specifically perceived safety and participation in activities with neighbors, were associated with left resting-state amygdala activity. In addition, less favorable perceptions of the availability of healthy foods, safety, and social cohesion were differentially associated with enhanced left amygdala FC with SN nodes. Taken together, these findings suggest that select neighborhood-level perceptions are associated with amygdala activity and amygdala FC within the SN.

Our findings highlight the importance of not only assessing both objective and subjective neighborhood environment factors (19,20), but also examining a spectrum of neighborhood-level perceptions in relation to markers of neural function. For instance, prior work has shown that perceived neighborhood violence and problems, but not perceived neighborhood social cohesion, were associated with depressive symptoms in a community-based cohort (23), suggesting that unique perceptions may relate to specific psychological stressors. Given that distinct perceptions were associated with resting-state amygdala activity and amygdala FC within SN nodes in our study, there may be different neurobiological pathways by which these perceptions are processed.

Adverse neighborhood conditions disproportionately impact racial and ethnic minoritized populations because of structural racism and discriminatory policies and practices (3). In our study, we aimed to investigate whether neighborhood environment perceptions may be related to amygdala activity and amygdala FC within SN nodes when accounting for other unmeasured social exposures. Here, we use race and ethnicity in our analyses as social constructs and proxies for racialized exposures rather than as measures that imply biological differences between groups. It is well established that race is not biologically relevant and that outcomes associated with race are largely driven by structural and SDoH (41). Although our findings have the potential to identify existing community strengths and inform interventions that can be leveraged to promote brain-behavior relationships, it is crucial to also address upstream structural determinants that impact how neighborhood environment stressors are distributed across populations, unevenly affecting minoritized groups.

Safety and Participation in Activities With Neighbors Are Associated With Left Amygdala Activity in a Community-Dwelling Population of Older Adults

Our findings indicate that less favorable perceived safety and participation in activities with neighbors are associated with higher amygdala activity, which may be a measure of many physiological indicators including chronic stress–related neural activity (42). Heightened resting-state amygdala activity has previously been associated with greater exposure to racial discrimination (15) and chronic stress (43). In addition, recent neuroimaging data demonstrate an association between safety or threat processing and activity in the ventral and dorsal subregions of the human amygdala, which correspond to basolateral and centromedial amygdala regions in rodent models (44). Our work suggests that specific neighborhood perceptions may relate to amygdala activity and the processing of negative stimuli independent of depressive symptoms as a marker of psychosocial stress (15). Future work in larger cohorts should examine if associations between neighborhood perceptions and resting-state amygdala activity remain independent when accounting for anxiety and posttraumatic stress disorder as psychosocial stressors. Future studies in larger, diverse cohorts should also formally examine the mediating role of psychosocial stressors like depression and anxiety in the relationships between neighborhood perceptions and amygdala activity.

Work has demonstrated that chronic psychosocial and environmental stressors can have biological and psychological sequalae and impact subsequent health outcomes, perpetuating health disparities (3). Our findings suggesting that neighborhood perceptions are associated with amygdala activity, if replicated, may provide a potential neurobiological link between sources of environment-related stress and poor health outcomes. For example, greater amygdala activity in response to a stressor is associated with inflammation (45–48) and predicts future psychological vulnerability to life stress (49). In addition, amygdala activity measured by ^{18}Fluorodeoxyglucose-positron emission tomography/computed tomography is associated with vascular inflammation, hematopoietic activity, and future cardiovascular events (43,50). Given the downstream biological associates of elevated amygdala activity, future work is needed to better understand the pathways connecting neighborhood stress to neurobiological outcomes as well as investigate community-level targets to mitigate these relationships and improve health outcomes.

Neighborhood Perceptions Are Related to Left Amygdala rsFC With Nodes in SN

We also demonstrate that elements of neighborhood stress are associated with amygdala FC with SN nodes. Namely, we found less favorable perceptions of safety and availability of healthy foods were associated with enhanced amygdala-insula connectivity. Our findings also indicate a relationship between perceptions of availability of healthy foods and amygdala-anterior cingulate gyrus connectivity as well as social cohesion perceptions and amygdala-thalamus connectivity. Our work connecting neighborhood environment perceptions to amygdala connectivity with SN nodes supports previous research evaluating other psychosocial stressors and amygdala connectivity with SN nodes. For example, previous studies investigating the relationship between racial discrimination and amygdala FC have demonstrated enhanced amygdala FC with nodes within the SN (e.g., anterior insula, thalamus, anterior cingulate) (15,16), with investigators hypothesizing that these neural networks may be related to feelings of heightened self-awareness and represent neural coping mechanisms in anticipation of threats (16). Additional work suggests that enhanced amygdala connectivity with nodes of the SN may indicate an extended state of hypervigilance after psychological stress (21). Thus, it seems that enhanced amygdala connectivity with SN nodes may be associated with stress-related psychological symptoms at both the individual and neighborhood levels. Findings underscore the importance of better understanding these patterns as they relate to individuals' emotions and lived experiences. Results particularly support further investigation into the relationship between the neighborhood environment exposures, stress- and hypervigilance-related neural activity, and downstream physical and mental health outcomes.

Limitations

This was a cross-sectional study, and thus, causality cannot be determined. Furthermore, our study included a small participant sample in one urban geographic area, limiting its applicability to broad geographic regions or rural locations. Because of the limited sample size, our analyses for amygdala FC were hypothesis driven to minimize type II error. Therefore, we may have been unable to detect effects of interest between neighborhood environment perceptions and amygdala FC with other non-SN regions of interest, and future studies are needed in larger samples of racially/ethnically diverse participants to further evaluate patterns outside of the SN. Finally, we were unable to account for socioeconomic position as a potential confounder in our models.

Conclusion

In conclusion, our findings suggest that perceptions of safety and participation in activities with neighbors are associated with left amygdala activity in a community-dwelling cohort of older adults. Furthermore, we found a relationship between neighborhood perceptions of healthy food availability, safety, and social cohesion and amygdala FC with SN nodes. Taken together, these findings help lay the foundation for larger, longitudinal studies of the neurobiological connections through which neighborhood stressors may get under the skin to impact health. In addition, more long term, future studies should further investigate the importance of implementing community-level and multilevel stress reduction interventions to target amygdala activity and FC and promote positive health outcomes in diverse, community-dwelling populations.

Source of Funding and Conflicts of Interest: The Powell-Wiley Lab is funded by the Division of Intramural Research of the National, Heart, Lung, and Blood Institute of the National Institutes of Health and the Intramural Research Program of the National Institute on Minority Health and Health Disparities. Data collection for this project was supported by extramural grants to Dr. Lamar from the National Institute on Aging: R21 AG048176 and K01 AG040192. Dr. Zhan is partially supported by NSF IIS 2045848. The views expressed in this manuscript are those of the authors and do not necessarily represent the views of the National Heart, Lung, and Blood Institute; the National Institute on Minority Health and Health Disparities; the National Institute of Nursing Research; the National Institutes of Health; or the U.S. Department of Health and Human Services. All authors declare that there are no conflicts of interest.

Data Availability Statement: Data are available from the corresponding author upon reasonable request.

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