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Neural impact of neighborhood socioeconomic disadvantage in traumatically injured adults

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ABSTRACT

Nearly 14 percent of Americans live in a socioeconomically disadvantaged neighborhood. Lower individual socioeconomic position (iSEP) has been linked to increased exposure to trauma and stress, as well as to alterations in brain structure and function; however, the neural effects of neighborhood SEP (nSEP) factors, such as neighborhood disadvantage, are unclear. Using a multi-modal approach with participants who recently experienced a traumatic injury (N = 185), we investigated the impact of neighborhood disadvantage, acute post-traumatic stress symptoms, and iSEP on brain structure and functional connectivity at rest. After controlling for iSEP, demographic variables, and acute PTSD symptoms, nSEP was associated with decreased volume and alterations of resting-state functional connectivity in structures implicated in affective processing, including the insula, ventromedial prefrontal cortex, amygdala, and hippocampus. Even in individuals who have recently experienced a traumatic injury, and after accounting for iSEP, the impact of living in a disadvantaged neighborhood is apparent, particularly in brain regions critical for experiencing and regulating emotion. These results should inform future research investigating how various levels of socioeconomic circumstances may impact recovery after a traumatic injury as well as policies and community-developed interventions aimed at reducing the impact of socioeconomic stressors.

1. Introduction

The role environmental context (e.g., social milieu, natural and built environments, etc.) plays in biological functioning and subsequent behavior cannot be overstated: in nearly every society, relative socioeconomic position (SEP) is tied to health status (Farah, 2017, 2018; Hackman and Farah, 2009). Although individual and neighborhood socioeconomic position, iSEP and nSEP respectively, are associated with a host of psychiatric conditions, including depression (Panaite et al., 2019; Richardson et al., 2015) and post-traumatic stress disorder (PTSD; Nayback, 2008; Shalev et al., 2019), the neural impact of such indicators is poorly defined. Substantial societal emphasis on the individual has influenced neuroscience research, and historically bypassed the impact of community characteristics (and more broadly the environment) in favor of focusing on how iSEP (e.g., education, income) impacts neural functioning (Brito and Noble, 2014; Diez Roux and Mair, 2010; Farah, 2018; Gianaros and Hackman, 2013; Hackman and Farah, 2009; Harnett, 2020; Johnson et al., 2016).With nearly fourteen percent of Americans living in a socioeconomically disadvantaged neighborhood (Kneebone, 2014), it is imperative to identify whether there are neural effects of nSEP and how these variables compare to the known effects of individual characteristics.

The mechanisms by which the environment impacts the brain and concurrent behavior have not been fully elucidated (Harnett, 2020;

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Hong, 2021; Lenroot and Giedd, 2008). Residents of disadvantaged communities may be exposed to adverse factors, such as environmental toxins, known to have a detrimental neural impact (de Prado Bert et al., 2018; Marshall et al., 2020; Pujol et al., 2016). Physical geography may also dictate an individual's exposure to crime and police violence as well as the availability of educational or employment opportunities, all of which are known risk factors for stress-related psychopathology (McCoy et al., 2016; Shalev et al., 2019; Sun et al., 2020). Critically, processes that are highly correlated with residing in poorer communities, including childhood trauma (Baglivio et al., 2017; Maguire-Jack and Font, 2017), biological aging (as indexed by shorter telomere length; Massey et al., 2018; Needham et al., 2014) and altered immune system activation (Finegood et al., 2020; Janusek et al., 2017; Karb et al., 2012), can trigger modifications to brain regions involved in necessary everyday function, including emotion regulation, attention, and memory (Hägg et al., 2017; Marusak et al., 2015; Weaver et al., 2002).

Notably, all of the aforementioned biological processes (e.g., immune system activation) are significantly associated with mental health outcomes, including PTSD (Baker et al., 2012; Daskalakis et al., 2018; Hietbrink et al., 2006; Li et al., 2017; Neigh and Ali, 2016). Trauma exposure is wide-spread – nearly 90% of American adults will experience a traumatic event in their lifetime, but individuals who live in disadvantage neighborhoods are at an elevated risk of both trauma exposure and developing PTSD (Collins et al., 2010). Given the prevalence of trauma, past work on the relationships between iSEP, nSEP, and the biological systems subserving stress responding may have been confounded by the presence of trauma. Conversely, research on trauma and stress-responding, in trauma-exposed or healthy participants, may have captured the effects of chronic stress related to nSEP or iSEP (e.g., Harnett et al., 2019).

Neuroscience literature uses the term 'chronic stress' to encompass prolonged exposure to a multitude of psychological and physiological stressors (e.g., poverty, sensory deprivation, maternal separation, physical insult, etc.), however, the convergence of neural consequences from the different modes of stress is noteworthy (Jaggi et al., 2011; McEwen, 2000; Uys et al., 2003; Veenema, 2009). To summarize: exposure to chronic stress, *including lower socioeconomic circumstances*, elicits prolonged neuroendocrine and stress system responding (Carlson and Chamberlain, 2005; McEwen, 2000, 2012). Regions in the medial temporal lobe (i.e., amygdala and hippocampus) and prefrontal cortex, which underlie processing and regulating response to biologically relevant stimuli, appear highly vulnerable to stressors. Chronic stressors are associated with reduced size and atypical functioning (as assessed by fMRI) of these regions (McEwen et al., 2012; Sandi and Pinelo-Nava, 2007).

These regions are also susceptible to the psychological consequences of a traumatic injury (i.e., a physical injury, not synonymous with traumatic brain injury; Liberzon and Sripada, 2007; Shin, 2006), further complicating researcher's ability to parse apart the unique effects of socioeconomic circumstances and that of specific traumatic experiences. This nuance is critical: if analyses with iSEP or nSEP are also capturing individual trauma exposure then those effects must be parsed out. It remains unclear whether the neural effects of different types of socioeconomic circumstances (e.g., iSEP and nSEP) can be disentangled from a trauma exposure and the resulting psychological sequalae. The present study sought to test whether neighborhood disadvantage (a nSEP indicator) uniquely impacts the brain and does so *beyond* iSEP and the effects of a recent traumatic injury.

1.1. Socioeconomic circumstances and trauma: convergent effects on the brain

Both the impact of socioeconomic stressors and the psychological consequences of trauma are strongly linked to greater "input" of negative events (e.g., attentional-biases and frequency of stimuli detection), subsequent evaluation and responsivity to the stressor(s), and aberrant recall of negative information (e.g., flashbacks in PTSD; Carretié et al., 2009; Kim et al., 2013; Luethi et al., 2009; McEwen, 2000; McEwen et al., 2016; Taylor et al., 2006). Although the neural mechanisms delineated in studies on chronic and acute stress are not exclusively activated during negative events, they are recognized as critical for detecting, processing, and responding to dangerous and unpleasant stimuli (reviewed in Carretié et al., 2009).

The structures essential for evaluation of and regulation of response to unpleasant stimuli include the amygdala and insula, as well as the ventromedial prefrontal cortex (vmPFC; Carretié et al., 2009; McEwen et al., 2016; Motzkin et al., 2015; Shin, 2006). The amygdala and insula interact to generate appropriate responses to salient information, while the vmPFC exhibits top-down control over the subcortical structures (e.g., Carretié et al., 2009; Jeong et al., 2019; Koch et al., 2016). Although the effects of chronic stress may vary across development and interact with biological (e.g., age) and social variables (e.g., race and ethnicity), there is a significant body of research that has examined how stress, including iSEP, impacts the functioning and morphology of these regions across the lifespan (LeWinn et al., 2017; Tooley et al., 2020).

In children, lower perceived parental social standing (Gianaros et al., 2008a,b) and family income-to-need ratio (Javanbakht et al., 2015) are independently associated with increased amygdala reactivity to threatening stimuli, after controlling for various individual factors. Individual differences in amygdala activation track with variations in structural morphology (Hartley et al., 2011; Kanai and Rees, 2011; Llera et al., 2019). For instance, smaller amygdala volume is significantly associated with higher rates of stress reactivity and abnormal fear learning (e.g., impaired fear extinction, overgeneralization of fear to non-threatening stimuli; Gianaros et al., 2008a,b; Hartley et al., 2011). In addition, amygdala and vmPFC volume reductions are significantly associated with exposure to childhood trauma, lower iSEP (in both childhood and adulthood), and exposure to environmental toxins (Calderón-Garcidueñas et al., 2011; de Prado Bert et al., 2018; Merz et al., 2018; Morey et al., 2016).

The anterior insula is involved in reappraisal and salient-stimuli processing (Carlson and Mujica-Parodi, 2010; Simmons et al., 2011; Singer et al., 2009). The structure underlies a variety of socio-emotional behaviors, including affective interoceptive awareness (Uddin, 2015), and is connected, both functionally and anatomically, to the amygdala (Kandilarova et al., 2018) and hippocampus (Ghaziri et al., 2018). Similar to findings related to amygdala volume, lower iSEP is associated with smaller insula cortical volume and reduced surface area in adults and children, respectively (Ansell et al., 2012; Noble et al., 2015). To our knowledge, no studies have examined how nSEP factors alter the insula.

Another region that is particularly vulnerable to chronic stress is the hippocampus (McEwen et al., 2012, 2016). Although the majority of the brain is likely responsible for some aspect of affective memory, the hippocampus is crucial for both working and long-term memory (Battaglia et al., 2011). Hippocampal reductions are significantly associated with lower iSEP (Hanson et al., 2011; Hunt et al., 2020). In children, hippocampal volume is negatively related to parental income (Hanson et al., 2011) and lower childhood SEP predicts smaller adult hippocampal volume (Hanson et al., 2011; Staff et al., 2012). In adults, larger hippocampal volume as well as fewer microstructural changes (i.e., mean diffusivity) are significantly associated with education attainment (Piras et al., 2011).

The aforementioned work substantiates the claim that iSEP has identifiable neural "marks", which are similar to those related to a recent trauma exposure. Although investigations into nSEP factors are more scarce, recent developments have suggested the neural elements described above are likewise impacted by nSEP indicators (Ansseau et al., 2008; Finegood et al., 2017; Harnett et al., 2019; Saxbe et al., 2018; Tomlinson et al., 2020; Tooley et al., 2020). For example, reduced hippocampal volume is linked to greater community violence in adolescents (Saxbe et al., 2018) and greater neighborhood disadvantage in adulthood (Hunt et al., 2020). In adults, neighborhood disadvantage is

associated with diminished amygdala reactivity to threat (Harnett et al., 2019). In children, growing up in a disadvantaged neighborhood contributes to wide-spread functional alterations in brain networks (Tooley et al., 2020) and deficits in behavioral response inhibition (Tomlinson et al., 2020), suggesting adolescents growing up in these neighborhoods have disrupted development (Tooley et al., 2020).

These initial studies highlight the important role that socioeconomic context beyond the individual and household can have on brain structure and function. Immersion in a disadvantaged neighborhood may affect neural circuits supporting adaptive stress-responding over and above iSEP factors. Crucially, the majority of previous studies have selected either brain structure *or* function to examine in relation to socioeconomic circumstances; herein, we describe multi-modal associations between PTSD symptoms related to a recent traumatic injury, iSEP, and nSEP.

1.2. Current study

Over two-hundred adult participants were recruited from a metropolitan area following a traumatic injury. We assessed how a nSEP variable, derived through geocoding, uniquely impacted brain structure as well as functional connectivity at rest. Based on previous studies, we expected to identify a neural mark of nSEP, after adjusting for two iSEP indicators (education and income), age, gender, and PTSD symptoms. We hypothesized neighborhood disadvantage would uniquely impact neurocircuitry critical for emotion regulation *and* that these effects would remain significant after accounting for the symptoms related to a recent clinically significant traumatic event.

In light of mounting evidence implying lower nSEP and iSEP are independent chronic stressors (Ross and Mirowsky, 2008), we anticipated greater neighborhood disadvantage would be uniquely associated with smaller amygdala, vmPFC, and hippocampus volumes (e.g., Morey et al., 2016; Noble et al., 2012; Saxbe et al., 2018). We hypothesized greater neighborhood disadvantage would be associated with decreased resting state functional connectivity (rsFC) between the amygdala and insula-prefrontal cortex as well as reduced hippocampus-prefrontal cortex rsFC. By demonstrating this in a traumatically injured sample at the outset and examining how nSEP affects the brain *beyond* symptoms of the indexed trauma, future work may feel more confident that acute trauma and socioeconomic circumstances are distinct factors. This paves the way to continue probing how nSEP and iSEP interact to alter trauma outcomes.

2. Results

2.1. Structure

Zero-order correlations between ADI and regional brain volumes are depicted in Fig. 1; results of GLMs are presented in Table 1). After adjusting for estimated intracranial volume, individual education, individual income, and PCL-5 total scores, higher ADI rankings (indicative of greater neighborhood disadvantage) were significantly associated with smaller bilateral hippocampus (B = −0.01, $t(159) = -2.20$, $p = .030$; full model: $R^2 = 0.27$) and smaller vmPFC volume (B = −0.01, $t(159) = -2.05$, $p = .042$; full model: $R^2 = 0.47$). Higher individual income and PCL-5 total scores were also significantly associated with larger vmPFC volume, B = 0.06, $t(159) = 2.50$, $p = .014$ and B = 0.01, $t(159) = 2.11$, $p = .036$, respectively. There was no significant relationship between neighborhood disadvantage and bilateral amygdala (B < −0.01, $t(159) = -1.19$, $p = .239$; full model: $R^2 = 0.35$), or bilateral anterior insula volume (B < −0.01, $t(159) = -0.31$, $p = .761$; full model: $R^2 = 0.50$).

2.2. Resting-state functional connectivity

Results of the rsFC analysis are presented in Table 2. Higher ADI rankings were significantly associated with increased bilateral amygdala connectivity with the left inferior parietal lobule (IPL), even after adjusting for individual education, individual income, gender, age, and PCL-5 total scores (MNI coordinates x: −40, y: −58, z: 28; cluster size $k = 84$; pFDR = .030; Fig. 2A). After controlling for covariates, greater connectivity between bilateral anterior insula and right ventrolateral prefrontal cortex was associated with higher ADI rankings (MNI coordinates: x: 36, y: 52, z: −6; cluster size $k = 88$; pFDR = .048; Fig. 2B).

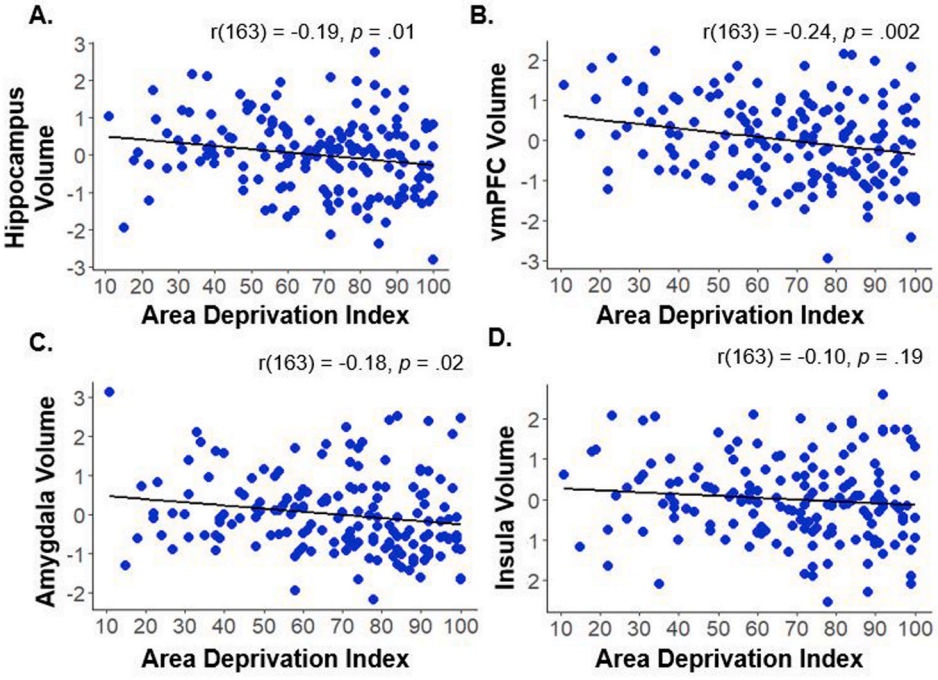

Fig. 1. Bivariate relationship between neighborhood socioeconomic disadvantage and bilateral A) hippocampus, B) ventromedial prefrontal cortex (vmPFC), C) amygdala, and D) insula, structural volumes (mm^3). *Note:* Zero-order correlation coefficients (r) are provided on the figure.

Table 1
Structural volumes (mm3) general linear model results.

Bilateral Amygdala	B	t-statistic	p
Intercept	0.62	1.06	.289
Individual Education	−0.04	−1.04	.302
Individual Income	0.04	1.70	.091
ADI	<-0.01	−1.19	.238
ICV	**0.54**	**8.43**	**<.001***
PCL-5	<-0.01	−0.33	0.741
Bilateral Hippocampus			
Intercept	1.09	1.75	.082
Individual Education	−0.04	−1.04	.298
Individual Income	<-0.01	−0.02	0.981
ADI	**−0.01**	**−2.20**	**.030**
ICV	**0.48**	**6.94**	**<.001***
PCL-5	<-0.01	−0.09	.925
Bilateral Insula			
Intercept	0.49	0.95	.345
Individual Education	−0.03	−1.10	.282
Individual Income	0.02	1.07	.288
ADI	<-0.01	−0.31	.761
ICV	**0.69**	**12.03**	**<.001***
PCL-5	<-0.01	−0.70	.487
Bilateral vmPFC			
Intercept	0.80	1.50	.135
Individual Education	−0.10	−1.82	.071
Individual Income	**0.06**	**2.50**	**.014***
ADI	**−0.01**	**−2.05**	**.042***
ICV	**0.59**	**10.09**	**<.001***
PCL-5	**0.01**	**2.11**	**.036***

Note. ***p* < .05**, **B,** estimated coefficient, **ADI,** Area Deprivation Index; **PCL-5,** total score from the PTSD Checklist for DSM-5, **ICV**, estimated intracranial volume, **vmPFC**, ventromedial prefrontal cortex. **N = 165.**

There were no significant main effects between ADI rankings and bilateral hippocampus rsFC or vmPFC rsFC.

3. Discussion

In traumatically injured adults, we have shown neighborhood disadvantage is a unique chronic stressor that is associated with aberrations in neurocircuitry, as evidenced by both altered structure and function. We identified associations with neighborhood disadvantage in regions central for emotion regulation, including the vmPFC, hippocampus, amygdala, and insula. Remarkably, the effects of ADI rankings were significant even after adjusting for individual education and income as well as acute PTSD symptoms, suggesting there are discernible effects of varying levels of socioeconomic circumstances on brain structure and function. To our knowledge, previous work has not tested whether the effects of nSEP or iSEP could also be capturing effects of a recent trauma exposure. This is practically important because post-trauma outcomes can be influenced by both individual-level (e.g., education) and neighborhood-level factors (Cross et al., 2016; Shalev et al., 2019; Sun et al., 2020).

The structural findings replicated previous work and further support the need to systematically implement both individual- and neighborhood-level variables in neuroscience research (Gianaros and Hackman, 2013). Perhaps least surprising of our results was that hippocampal volumes were smaller in individuals who live in more disadvantaged neighborhoods (Hunt et al., 2020) given the plethora of articles indicating the hippocampus is highly vulnerable to chronic stress (McEwen et al., 2016). In the context of trauma outcomes, smaller hippocampal volume is thought to be a prominent risk factor of PTSD (Astur et al., 2006; Hendler and Admon, 2015). Smaller vmPFC structure was also significantly associated with lower individual income and acute PTSD symptoms, adding to the claim that the effects of iSEP and nSEP are independently identifiable. In other words, vmPFC is impacted by neighborhoods, even after considering individual factors. Smaller vmPFC is associated with emotion dysregulation (Palacios-Barrios and Hanson, 2019) and also a range of psychiatric conditions, including PTSD (Keding and Herringa, 2015; Kühn and Gallinat, 2013; Morey et al., 2016).

If both neighborhood socioeconomic disadvantage and lower individual income independently and negatively impact the vmPFC, a prefrontal region that modulates affective responses and underlies memory consolidation (Bonnici et al., 2012; Carretié et al., 2009; Gyurak et al., 2011; Phelps et al., 2004), perhaps this is one mechanism by which socioeconomic disadvantage can influence psychopathology and respond adaptively to stressors (Motzkin et al., 2015; Palacios-Barrios and Hanson, 2019). Together, these findings imply acutely traumatically injured individuals who live in a disadvantaged neighborhood may already be at heightened risk of poor post-trauma outcomes – though this requires additional investigation. That said, this work clearly highlights how understanding the influence of both individual and neighborhood factors may be especially important for research with traumatically injured samples, where effects may be more challenging to disentangle without this information.

Participants living in higher ADI areas had greater bilateral anterior insula connectivity with the vlPFC, a section of the PFC thought to underlie affect appraisal and emotion regulation (Benelli et al., 2012; Prater et al., 2013; Zhao et al., 2021). Both the anterior insula and vlPFC are key nodes in the emotional salience network, an intrinsic connectivity network that is present during rest and anti-correlated with the default mode network (Chai et al., 2011). Greater connectivity between these two regions broadly suggests individuals from more disadvantaged neighborhoods may have not only a heightened neural disposition to identify, discriminate, and attend to biologically-relevant stimuli but also difficulties downregulating these initial affective responses (Gyurak et al., 2011).

Greater neighborhood disadvantage was also associated with greater connectivity between the amygdala and IPL. Increased amygdala-IPL resting-state connectivity may be indicative of greater attentiveness to emotional information (Rive et al., 2013). The IPL is recruited during automatic attention (i.e., attention not consciously-directed) to emotional information (Rive et al., 2013). For example, activation of the IPL with transcranial magnetic stimulation is significantly associated with greater processing of fearful body expressions (Engelen et al., 2015). Both the amygdala and IPL are recruited when emotional faces are processed and assessed (Sarkheil et al., 2013; Troiani and Schultz, 2013). Neighborhood disadvantage may be altering neural systems supporting evaluation of biologically salient stimuli. However, we did not explore task-based fMRI data and it is possible that compensatory processes may protect against the effects of lower nSEP. As resting-state connectivity analyses do not provide direct information on brain-behavior relationships (Poldrack, 2011), additional studies (such

Table 2
Altered functional connectivity associated with neighborhood disadvantage after adjusting for relevant individual variables.

ROI	Contrast	Brain Region	No. of voxels	$p_{FDR\text{-}corrected}$	Peak Coordinates (MNI)		
					X	Y	Z
Amygdala	Positive	Inferior Parietal Lobule L	84	**.030***	−40	−58	28
Insula	Positive	Ventrolateral PFC R	88	**.048***	36	52	−6

Note. **Covariates:** Education, Income, Age, Gender, PCL-5 scores; ****pFDRcorrected* < .05**, **L,** left; **R,** right; **PFC**, prefrontal cortex; **ROI:** seed region of interest, **N = 165.**

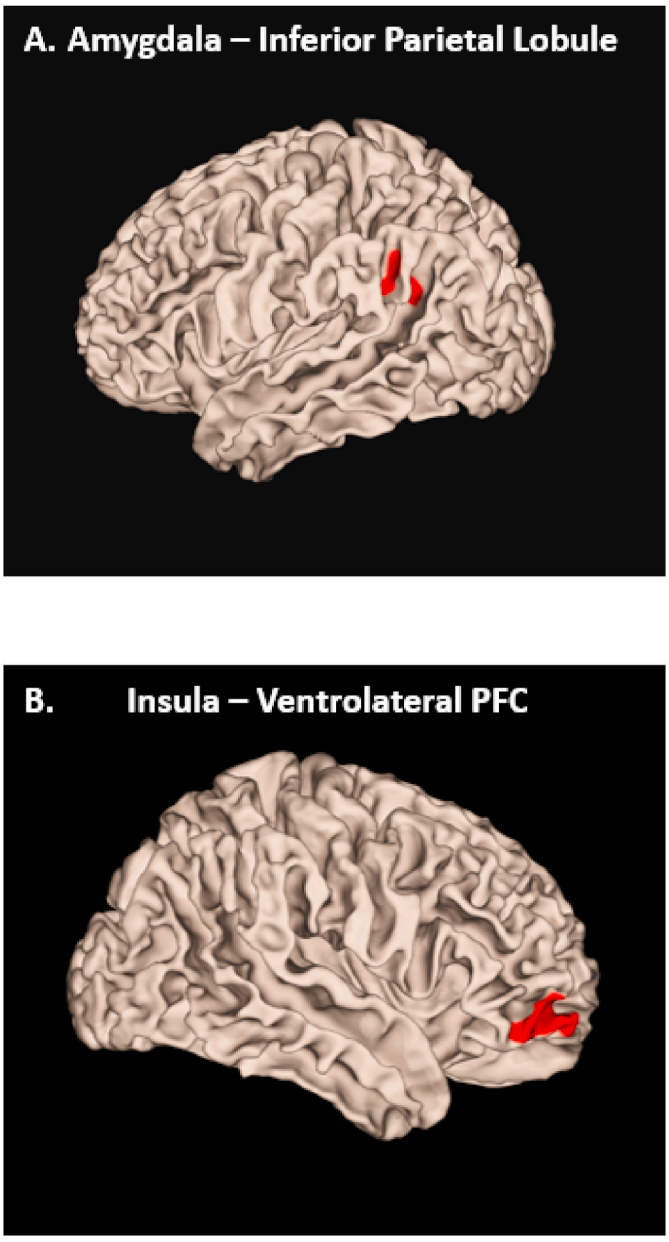

Fig. 2. Results of seed-to-voxel analyses revealed greater neighborhood socioeconomic disadvantage was significantly associated with A) increased connectivity between bilateral amygdala and left inferior parietal lobule (IPL; MNI coordinates x: −40, y: −58, z: 28; cluster size $k = 84$; pFDR = .030) B) greater connectivity between bilateral anterior insula and right ventrolateral prefrontal cortex (vlPFC; 36, 52, −6; cluster size $k = 88$; pFDR = .048).

as Tomlinson et al., 2020) should explore how different levels of socioeconomic circumstances interact to modulate neural activation during affective tasks and the associated behavioral measures.

These findings indicate the effects of chronic stressors, both nSEP and iSEP, as well as recent trauma can be disentangled in both structural and functional (i.e., rsFC) neuroimaging data. Our results, however, are tempered by the fact our sample is limited geographically. Individuals were largely from urban neighborhoods and therefore the implications of our results may not apply to those experiencing resource deprivation in rural areas or even urban settings with different characteristics. In addition, the sample consisted of individuals who had recently experienced a traumatic injury and did not include a non-trauma control group. As such these relationships may not be identical to those found in a sample of non-injured adults. Furthermore, this study was observational and cross-sectional, meaning we did not consider other important variables such as residential instability and childhood socioeconomic position.

McLaughlin and Sheridan (2017) proposed a comprehensive theory that adversity (originally conceptualized as childhood adversity but extended to adults here), is multi-dimensional. Although many experiences are described as "chronic stress", this model better encapsulates the events by distinguishing experiences by low versus high threat (e.g., typical environment versus physical abuse) and low versus high deprivation (e.g., physical abuse versus institutionalization; (McLaughlin and Sheridan, 2016). Dimensionality of adversity may be an important consideration in our study. For example, despite a significant association between ADI rankings and structure, we did not find an effect of ADI rankings on hippocampal or vmPFC rsFC; however, the rsFC of these particular regions may be more associated with other variables, such as exposure to community violence (e.g., higher threat but lower deprivation), police presence, or air pollution (e.g., Saxbe et al., 2018). Future directions include leveraging large data consortiums to examine multiple neighborhood-level measures.

Nevertheless, we have presented a multi-modal investigation which documents the neural features of neighborhood disadvantage. The brain regions critical for emotion regulation are susceptible to the effects of nSEP. Beyond iSEP indicators *and* acute PTSD symptoms from a recent trauma, ADI rankings were significantly associated with altered structure and functional connectivity. It is noteworthy, that after accounting for these individual-level measures (e.g., individual education and income, and stress symptoms), which researchers widely recognize as potent factors underlying individual differences in psychopathology, the circumstances of where people live are independently associated with brain circuits regulating emotion in trauma-exposed individuals. Although the overarching goal should be to reduce and eliminate systems which generate and maintain poverty, our work suggests that while these steps are being taken, clinicians and scientists should consider the role socioeconomic circumstances are playing in their patients' and participants' lives.

4. Methods

4.1. Participants

Two hundred and fifteen participants were recruited from an Emergency Department (ED) at an urban Level 1 trauma center as part of a longitudinal observational study investigating neurobiological and socioenvironmental predictors of PTSD (study name: iSTAR; Webb et al., 2020; Bird et al., 2021; Weis et al., 2021). Briefly, individuals were considered eligible if they were English-speaking, between the ages of 18–65 years old, and had experienced a traumatic injury. Full inclusion/exclusion criteria can be found in Table 3. All participants provided written consent and were financially compensated for their time. Study procedures were approved by the local Institutional Review Board at the Medical College of Wisconsin.

Of the recruited participants, 198 completed a structural and resting-state scan two-weeks post-injury. Not all participants could be successfully geo-coded (required to derive neighborhood SEP); of the 185 participants who had useable resting-state and structural scans, 165 had complete demographic and geo-coded data.

4.2. Individual measures

Sample characteristics can be found in Table 4. Individual demographics (gender, age, income, and education) were self-reported at the first study visit. Household income and educational attainment (two iSEP variables) were assessed on a semi-continuous scale. Acute PTSD symptoms were assessed using the PTSD-Checklist Scale for DSM-5 (PCL-5; Blevins et al., 2015) which consists of 20 items that evaluate the presence and severity of PTSD symptoms corresponding to

Table 3
Recruitment criteria.

Inclusion	Exclusion
Experienced a traumatic injury that led to ED visit	Moderate to severe traumatic brain injury (Glasgow Coma Scale[b] Score of <13)
18–65 years of age	Suffered a spinal cord injury with neurological deficits
English-speaking	Apparent (as indicated by medical records) substance abuse disorder
Ability to schedule a study appointment within 2-weeks of trauma	Visit to ED was a result of suicide or self-harm
A minimum score of 3 on the Predicting PTSD Questionnaire[a] (indicative of elevated risk of future PTSD)	Active psychosis, or history of psychotic or manic symptoms, or current prescription of antipsychotic medication
Note: a. Rothbaum et al. (2014) b. Sternbach (2000). Of the 215 recruited participants, 165 had useable structural and resting-state fMRI data and were successfully geocoded.	On police hold following traumatic injury
	MRI incompatible (e.g., presence of ferromagnetic material in body, claustrophobic, pregnant, etc.)

Table 4
Sample characteristics (N = 165).

Variable	Mean (SD) or %
Age (years)	32.30 (10.45)
Sex	
Female	55%
Individual Education	
Did not complete high school	10%
High school/GED	32%
Some post-secondary education/college	41%
Bachelor's degree	12%
Master's degree, JD, MD, PhD	5%
Individual Income	
$0–10,000	21%
$10,000–20,000	15%
$20,000–30,000	15%
$30,000–40,000	9%
$40,000–50,000	9%
$50,000–60,000	7%
$60,000–70,000	6%
$70,000–80,000	7%
$80,000–90,000	<5%
$90–100,000	<5%
$100,000 and above	6%
Race and Ethnicity	
African American and/or Black	58%
White	27%
Hispanic or Latino	8%
Other racial/ethnic identity*	10%
Not reported	5%
Mechanism of Injury	
Motor vehicle crash	67%
Physical assault	16%
Other	17%
Acute PTSD Symptoms (PCL-5)	26.75 (17.86)

Note: PCL-5, PTSD Checklist for DSM-5. * Due to small sample sizes, additional self-reported racial identities have been combined.

diagnostic criteria (American Psychological Association, 2013).

4.3. Neighborhood socioeconomic disadvantage

Neighborhood socioeconomic disadvantage, the nSEP variable, was measured using the Area Deprivation Index (ADI; Kind and Buckingham, 2018). Participants provided their home address at the same study visit that they underwent neuroimaging. This address was then used to derive ADI rankings from a publicly available dataset hosted by the University of Wisconsin School of Medicine and Public Health https://www.neighborhoodatlas.medicine.wisc.edu/ (downloaded February 2020, geocoding completed approximately 3 months after all data was collected) which provides census block-group ADI rankings from data collected during the National 2014–2018 American Community Survey (ACS; Hu et al., 2018; Kind et al., 2014; Kind and Buckingham, 2018; Singh, 2003). Block-group is the smallest ACS geographic area and represents a maximum of 3,000 people or 1,200 housing units (U.S. Census Bureau, 2020).

Briefly, National ADI rankings, which range from 1 (most advantaged) to 100 (most disadvantaged), are factor-based percentile scores representing 17 variables (see Singh, 2003 for more information on development of this index and a list of exact variables). ADI rankings incorporate measurements of income, education, housing, and employment (Kind et al., 2014). In this way, the individually reported education and income of all the neighborhood's residents were averaged within each block-group. These averages were then incorporated as components of the block-group's ADI ranking.

ADI rankings range from 1 to 100. A score of 50 indicates, compared to that specific block-group, approximately half of the neighborhoods in the nation are more disadvantaged and approximately half are more advantaged. The current sample was largely disadvantaged (mean ADI = 68, standard deviation = 22), though the range in ADI rankings was sufficient to test hypotheses (see Fig. 3 for distribution).

4.4. MRI data acquisition

All images were collected on a General Electric Discovery MR750 3.0 T scanner with a 32-channel head-coil (Waukesha, WI). For co-registration with functional images and structural analysis, T1-weighted high-resolution anatomical scans were acquired (FOV = 240 mm; matrix = 256 × 224; slice thickness = 1 mm; 150 slices; TR/TE = 8.2/3.2; flip angle = 12°, voxel size = 0.9375 × 1.071 x 1). Resting-state images were obtained during an 8-min scan (240 vol) with the following parameters: FOV = 22.4 mm; matrix = 64 × 64; slice thickness = 3.5 mm; 41 sagittal slices; repetition time (TR)/echo time (TE) = 2000/25 ms; flip angle = 77°.

4.5. MRI data preprocessing and analytic strategy

4.5.1. Structure

Freesurfer was used to perform volumetric quantification of regions of interest (v5.30; Fischl, 2012). Prior to extracting volumetric measurements, each participant's image was visually inspected and manual edits were performed as needed. As we had no specific hypotheses regarding laterality, left and right ROI measurements were combined. Volume measures (mm^3) were extracted for the amygdala, hippocampus, and insula. As previously done, bilateral vmPFC volumes were created by summing the left and right medial orbitofrontal and lateral orbitofrontal cortices (Desikan et al., 2006; Morey et al., 2016).

Univariate outliers (±3 standard deviations) were removed (N = 6)

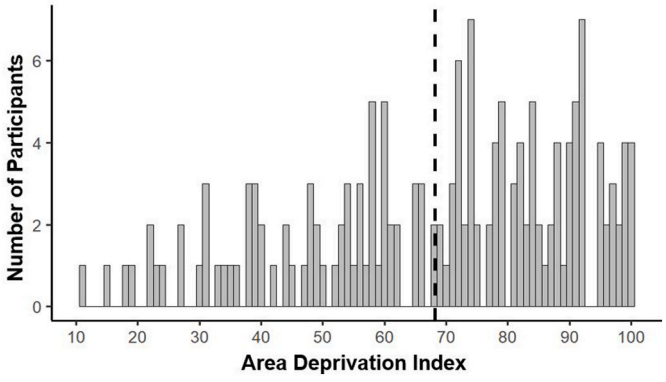

Fig. 3. Histogram of neighborhood socioeconomic disadvantage (national ADI; Mean ADI ranking in current sample = 68 [vertical dashed line], standard deviation = 22; N = 165).

from all structural analyses and volumes were *z*-standardized. Four separate General Linear Models (GLM) were conducted in R ('glm' function) to evaluate the relationship between sub-cortical (bilateral amygdala and hippocampus) and cortical volumes (grey matter volume; vmPFC and insula), individual education, individual income, acute PTSD symptoms (PCL-5 scores), and ADI rankings. Individual estimated intracranial volume (ICV) from Freesurfer was used as covariate of no interest (Morey et al., 2016). An example of one of the statistical models is as follows:

$$\text{Amygdala volume} \sim \text{education} + \text{income} + \text{PCL} - 5 \text{ scores} + \text{ICV} + \text{ADI}$$

Although both biological sex and age can impact structural volumes, we had no specific hypothesis regarding these demographic characteristics, and after controlling for estimated intracranial volume, these variables were not significant and therefore excluded from final reported models. As these were *a priori* analyses, alpha was set at 0.05, uncorrected.

4.5.2. Resting state

Images were preprocessed using the Matlab-based (version 2019b; Mathworks) SPM (version 12) CONN toolbox (

Whitfield-Gabrieli and Nieto-Castanon, 2012; version 20; http://www.nitrc.org/projects/conn). Default preprocessing steps included: discarding the first three TRs, motion correction using a six-parameter linear transformation, normalization to Montreal Neurological Institute (MNI 152) template, and spatial blurring with a 4-mm full-width-at-half-maximum smoothing kernel. To address any confounding effects of motion, volumes with frame-wise displacement over 0.3 mm were excluded from analysis. Nuisance covariates (head motion parameters and their first-order derivatives, white matter signal, and cerebrospinal fluid signal) were regressed out during first-level analysis. Participants were removed from analyses (both structural and functional) if more than 20% of the resting-state volumes were scrubbed. This criterion excluded seven participants (final N = 165).

The default ROIs provided in the CONN toolbox (AAL atlas) for the bilateral hippocampus, amygdala, and anterior insula, were used as seed regions for separate GLMs. As the vmPFC is not clearly defined by discrete anatomical boundaries, we opted to use a vmPFC seed obtained from NeuroSynth (http://neurosynth.org/; Chen et al., 2020). We conducted seed-to-voxel analyses in which the mean BOLD signal from each ROI was correlated with all other voxels in the brain. In the group-level GLMs, individual education, individual income, gender, age, and acute PTSD symptoms (PCL-5 total scores) were included in the model as covariates. The effect of interest was the association between ADI (independent variable) and resting-state connectivity of the two seed regions. The rsFC statistics were thresholded at $p < .05$, with a height threshold of $p < .001$ uncorrected and a cluster-size threshold of an adjusted $p < .05$ false discovery rate (FDR) corrected.

4.5.3. Sensitivity analyses

To determine whether the results were driven by the most disadvantaged neighborhoods, we excluded the top 10% of participants with the highest ADI rankings (n = 19) and reran all analyses (N = 146). More information on these follow-up tests and the results are included in the supplementary materials.

Author contributions

E.K.W., C.N.W., T.A.D., C.L.L. conceptualized this study; E.K.W., C.N.W., A.A.H., J.M.F., K.B., C.M.B., E.A.P., M.D., T.M., J.K., collected the data; E.K.W. and C.N.W. conducted the analysis and wrote the original draft; E.K.W., C.N.W., A.A.H., J.M.F., K.B., C.M.B., E.A.P., M.D., T.M., J.K., T.A.D., and C.L.L., reviewed and edited the manuscript. T.A.D., and C.L.L. supervised the project and acquired funding.

Declaration of competing interest

The authors report no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ynstr.2021.100385.

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