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Shaped By the Environment: The Influence of Childhood Trauma Exposure, Individual Socioeconomic Position, and Neighborhood Disadvantage on Brain Morphology

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SHAPED BY THE ENVIRONMENT: THE INFLUENCE OF CHILDHOOD TRAUMA
EXPOSURE, INDIVIDUAL SOCIOECONOMIC POSITION, AND NEIGHBORHOOD
DISADVANTAGE ON BRAIN MORPHOLOGY

by

Elisabeth K. Webb

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ABSTRACT

SHAPED BY THE ENVIRONMENT: THE INFLUENCE OF CHILDHOOD TRAUMA EXPOSURE, INDIVIDUAL SOCIOECONOMIC POSITION, AND NEIGHBORHOOD DISADVANTAGE ON BRAIN MORPHOLOGY

by

Elisabeth K. Webb

The University of Wisconsin-Milwaukee, 2020
Under the Supervision of Professor Christine Larson

The relationship between an individual's socioeconomic position (SEP) and their overall physical and mental health has been well demonstrated. Far less is known about how area-level factors, such as neighborhood disadvantage, "get under the skin". Previous research indicates lower SEP and childhood trauma negatively effects brain structure and function. The hippocampus, amygdala, and ventromedial prefrontal cortex (vmPFC) are particularly vulnerable to adversity. The current study investigated how individual SEP, childhood trauma, and neighborhood disadvantage impact these structures. Two-hundred and fifteen individuals were recruited from an Emergency Department in southeastern Wisconsin. Two-weeks post-traumatic injury, participants completed a structural magnetic resonance imaging scan and various self-report measures. Area Deprivation Index (ADI), a measure of a neighborhood's socioeconomic disadvantage, and neighborhood homicide rates were derived from participants' addresses. Results of hierarchical multiple linear regression analyses revealed ADI was associated with hippocampal volume, over and above individual variables while vmPFC was significantly impacted by individual income but not neighborhood disadvantage. Interestingly, amygdala volume was only related to gender. In an exploratory analysis, we used Structural Equation Modeling to investigate how a model with individual and neighborhood factors would interdependently relate to brain structure. Neighborhood

variables were significantly correlated with Individual SEP measures. Similar to the regression analysis, we demonstrated that vmPFC volume is significantly associated with individual SEP but not neighborhood factors. This study provides additional support that neuroscience has an imperative role in identifying and addressing health disparities and help fuel the development of interventions targeting at-risk populations.

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For Jamie,
who learned how to pronounce *all* of the brain regions in this document.
Thank you for always being open to conversing about science,
and cheering me on.

TABLE OF CONTENTS

Introduction	1
How Environments “Get Under the Skin”: Theoretical Approaches	1
Defining Individual and Neighborhood SEP: Composite or Component?	4
A Neuroscientific Approach to Health Disparities	7
Impact of Individual- and Area-Level Variables on Brain Structure and Function	8
The Current Study	12
Methods	14
Participants	14
Procedure	15
Self-Report Measures	16
Area-Level Derived Measures	16
Imaging Acquisition	19
Image Analysis	19
Statistical Analysis	19
Exploratory Structural Equation Modeling	20
Results	21
Relationships Between Study Measures	25
Unique Contribution of ADI in the Explanation of ROI Volumes	29
Factors Impacting Hippocampal Volume	29
Factors Impacting Amygdala Volume	30
Factors Impacting vmPFC Volume	31
Exploratory Aim: Structural Equation Modeling	32
Discussion	37
Exploratory Structural Equation Modeling	42
Conclusions	43
References	45

LIST OF FIGURES

Figure 1. Distribution of Area Deprivation Index Rankings

Figure 2. Distribution of Area Deprivation Index Rankings by Racial Group (A) and Sex (B).

Figure 3. Bivariate Relationship between Area Deprivation Index and Region of Interest Volumes

Figure 4. Schematic Representation of Structural Equation Model (Amygdala)

Figure 5. Schematic Representation of Structural Equation Model (Hippocampus)

Figure 6. Schematic Representation of Structural Equation Model (vmPFC)

LIST OF TABLES

Table 1. Sample Characteristics

Table 2. Correlation Coefficients Between Study Variables

Table 3. Hierarchical Linear Regression of Hippocampal Volume

Table 4. Hierarchical Linear Regression of Amygdala Volume

Table 5. Hierarchical Linear Regression of vmPFC Volume

Table 6. Fit Indices for Exploratory Structural Equation Models

LIST OF ABBREVIATIONS

ACTH	Adrenocorticotrophic Hormones
ACS	American Community Survey
ADI	Area Deprivation Index
AVP	Arginine Vasopressin
CFI	Comparative Fit Index
CRF	Corticotropin-Releasing Factor
CTQ	Childhood Trauma Questionnaire
EA	Emotional Abuse
ED	Emergency Department
EN	Emotional Neglect
HPA	Hypothalamic-Pituitary-Adrenal Axis
PA	Physical Abuse
PN	Physical Neglect
PTSD	Post-Traumatic Stress Disorder
ROI	Region of Interest
RMSEA	Root Mean Square Error of Approximation
SA	Sexual Abuse
SEM	Structural Equation Modeling
SEP	Socioeconomic Position
vmPFC	ventromedial Prefrontal Cortex

Shaped by the Environment: The Influence of Childhood Trauma Exposure, Individual Socioeconomic Position, and Neighborhood Disadvantage on Brain Morphology

How Environments “Get Under the Skin”: Theoretical Approaches

For hundreds of years, researchers and philosophers have theorized about which factors influence human development and individual characteristics. Socrates and Plato first explored whether ideas stemmed from innate concepts that all humans were born with (nature) or from acquired knowledge (nurture; see review by Ariew and Shorey, 2001). In a scientific context, nature and nurture are understood as the influence of genes and of the environment, respectively (Meaney, 2001). A plethora of studies have demonstrated nature and nurture interact to alter behavior and genes within an individual’s lifespan (Meaney, 2001). It is well known that genetic predisposition of disease, individual behavior, and social milieu, are variables that interdependently influence an individual’s health status and outcomes (Rose, 2001); however, genuine environmental (e.g. area-level) factors have not always been considered in the study of mental health.

Theories of disease distributions, which attempt to identify factors that confer disease risk or resilience, have historically neglected the importance of assessing an individual’s environment (Frohlich and Potvin, 2008; Krieger and Zierler, 1996). For example, the life-style theory (Frohlich and Potvin, 2008; Krieger and Zierler, 1996), suggests specific behavioral-traits (e.g. risk-taking) explain the occurrence of disease. Psychologists, in parallel, also developed theories to explain psychiatric illnesses that emphasized the individual (Turner and Lehning, 2007). Critically, the life-style theory -

and those akin to it - disregard the frameworks forged by economic, social, and political structures. Area-level factors associated with low socioeconomic position (SEP), such as higher rates of neighborhood crime (Curry, Latkin, & Davey-Rothwell, 2008), greater racial discrimination (Ong and Burrow, 2018), and employment satisfaction/job stress (Iacovides, Fountoulakis, Kaprinis, & Kaprinis, 2003), increase the likelihood of depressive symptoms. These are examples of factors the individual may not be directly responsible for; therefore, they cannot be classified as entirely behavioral/individual traits. Beginning in the 1980's, psychologists expanded their vision and broadened theories to include contextual-level factors that aid in the creation and maintenance of low SEPs (Turner and Lehning, 2007).

As research established that lower SEP was associated with poorer mental health outcomes, including higher rates of depression (Assari, 2017; Lorant et al., 2007; Wang, Schmitz, & Dewa, 2010), schizophrenia (Werner, Malaspina, & Rabinowitz, 2007), and post-traumatic stress disorder (PTSD; Rosenman, 2002; Schnurr, Lunney, & Sengupta, 2004), scientists developed theories to explain how SEP gets “under the skin”. One explanatory model, the social causation theory, suggests poor economic situations induces psychopathology because they place an intolerable amount of stress on the individual (Hollingshead and Redlich, 1958; Murali and Oyeboode, 2004; Shallcross et al., 2016). Poor economic situations are often - but not always - linked to neighborhood socioeconomic disadvantage. Conversely, the social selection theory proposes that individuals with poorer mental health are driven into lower SEPs and therefore more deprived neighborhoods by societal forces (Dohrenwend, 2000; Shallcross et al., 2016). However, findings from a study in which a subset of the

population received financial supplements better aligned with the social causation theory: the increase in income correlated to a decrease in mental health symptoms (Costello, Compton, Keeler, & Angold, 2003). Mechanisms supporting the social causation theory were assembled with knowledge about psychosocial functioning and neurobiology. One such mechanism is described by the allostatic load theory: individuals in a lower SEP have greater adversity, which ultimately results in persistent and heightened neuroendocrine and neural stress system responding (Seyle, 1956; see also reviews by Carlson and Chamberlain, 2005, and McEwen, 2005).

The allostatic load theory is supported by work on the hypothalamic-pituitary-adrenal axis (HPA axis), one of the body's primary stress response pathways (see review by Stephens and Wand, 2012). In brief, neurons in the paraventricular nucleus of the hypothalamus release corticotropin-releasing factor (CRF) and arginine vasopressin (AVP; Pariante and Lightman, 2008). These neurohormones stimulate the anterior pituitary gland which in turn produces adrenocorticotrophic hormones (ACTH; Pariante and Lightman, 2008). Finally, synthesis and secretion of glucocorticoids, including cortisol, is promoted by ACTH (Carroll, Ritchie, Rogers, & Kim, 2019). Negative feedback loops modulate the HPA axis by attempting to maintain the production of CRF, AVP, and ACTH, at predetermined set-points (Stephens and Wand, 2012; Carroll, Ritchie, Rogers, & Kim, 2019). The maintenance of homeostasis is vital to the overall health of the individual: an overproduction or underproduction of glucocorticoids can be detrimental (Stephens and Wand, 2012). Individuals in lower SEPs have higher levels of cortisol, widely-considered a biomarker of stress (Cohen et al., 2006; Viegenthart et al., 2016; Lupien, King, Meaney, & McEwen, 2001; Lupien, King, Meaney, & McEwen,

2000). Merely living in disadvantaged neighborhoods can also result in higher cortisol levels (Chen and Paterson, 2006; Karb, Elliott, Dowd, & Morenoff, 2012; Gidlow, Randall, Gillman, Smith, & Jones, 2016). Indeed, neighborhood disadvantage explains variability in cortisol levels over and above individual SEP (Karb, Elliott, Dowd, & Morenoff, 2012).

The proposed project builds upon research examining the impact of neighborhood disadvantage on stress response systems and work identifying the neural impact of low SEP and childhood trauma. The allostatic load theory is supported by research on the HPA axis and significant work has been conducted identifying brain regions that are particularly vulnerable to stress. Still, little is known about how brain structures are impacted by neighborhood disadvantage (Stephens and Wand, 2012; Carroll, Ritchie, Rogers, & Kim, 2019; Hackman, Farah, & Meaney, 2010). This study is unique as it investigates whether area-level SEP, in addition to childhood trauma and individual SEP, is associated with differences in brain morphology.

Defining Individual and Neighborhood SEP: Composite or Component?

As research on the neural correlates of SEP has grown, it has become increasingly apparent that how society and research operationally defines SEP is crucial to understanding its effects. Although individual SEP frequently appears in neuroscience literature, the variable itself is poorly defined (Farah, 2017; Ross and Mirowsky, 2008). SEP is often objectively conceptualized as a combination of an individual's household income, education, resources (e.g. financial, material), and occupation. Individual characteristics, namely education and income, are commonly used as proxies for SEP (Farah, 2017). Often only one metric is incorporated in the study design; however, the

nuances of selecting which measure to include may be less rooted in theoretical considerations and more based on practical concerns. In the current study, both education and income were collected and will be analyzed. Although income and education are correlated, they likely capture different aspects of SEP and thus may have differential effects on brain morphology. On the casual pathway, educational attainment is often considered as preceding income (Muller, 2002).

While income and education are undeniably components of SEP, the variables may not fully capture the theoretical “essence” of individual SEP. Initially SEP was calculated in part by looking at occupational “status” or “prestige”. An epidemiological study in 1999 investigated mortality rates across social status, using a “prestige” and a “socioeconomic component” (Johnson, Sorlie, & Bucklund, 1999). The authors discovered that differences in mortality rates were almost entirely attributable to variability in income and education (Johnson, Sorlie, & Buckland, 1999) suggesting education and income are both theoretically and empirically ideal proxies for individual SEP.

Neighborhood and family characteristics are also frequently included to provide a better picture of related environmental factors, such as self-reported measures of exposure to violence, overall “richness” of the environment, neighborhood walkability, and access to healthcare (Hackman, Farah, Meaney, 2010). In the proposed study, we conceptually disentangle neighborhood characteristics from individual-level measures. We will calculate Area Deprivation Index rankings for each participant (ADI; Singh, 2003; Kind and Buckingham, 2018). The index, redeveloped and maintained by Dr. Amy Kind and colleagues at University of Wisconsin-Madison, is a measure of a

neighborhood's disadvantage that encompasses factors related to housing quality, employment, and the SEP of individuals living in the community (Kind and Buckingham, 2018).

Individual SEP and area-level disadvantage are intercorrelated with each other (Farah, 2017). A single measure or even a composite score, such as ADI, may implicitly represent various types of stressors, such as financial stressors, exposure to pollution and lack of environmental infrastructure (e.g. green spaces) (Farah, 2017). Although the current study will not collect information on many of these variables, we will probe this phenomenon further by deriving neighborhood crime rates. ADI does not incorporate any measure of neighborhood crime, which may have a unique influence on brain structure. For this reason, the proposed project also will examine the relationship between neighborhood crime rates and structural volumes.

Critically, individual SEP and neighborhood disadvantage can be highly intercorrelated with other demographic variables, namely race and ethnicity (Farah, 2017). Race was created as a method of human categorization that promoted hierarchal division between groups of people (Smedley and Smedley, 2005). The "categories" of race today are not reflective of a biological difference between people (Krieger, 2000), rather they represent systemic efforts by White people to continually exert power over groups of individuals for political, economic, and social gain (Smedley, 2002). In the United States, health disparities by race and ethnicity and SEP, remain prominent (Kawachi, Daniels, & Robinson, 2005; LaVeist, 2005). Although race and ethnicity will not be directly examined in this study, the breakdown of individual ADI by self-reported race and ethnicity, as well as gender, will be discussed.

A Neuroscientific Approach to Health Disparities

Brain structure and function are shaped by factors related to low SEP (Hackman and Farah, 2009). Rightfully, research in this area should be utilized to develop interventions, improve existing programs, and inform policies, with the ultimate goal of eliminating the political, economic, and social structures fueling inequities. In the meantime, by determining which regions are most susceptible to stress, researchers may identify promising targeted interventions that counter the consequences of low individual- and area-level SEP. For example, Pavlakis and colleagues (2015) assessed whether electrophysiology (e.g. electroencephalogram) and neuroimaging (e.g. fMRI) may be able to identify biomarkers of educational interventions targeting the effects of low SEP.

Together animal and human neuroscience offers a unique approach to the study of health disparities. Health disparities can be characterized as avoidable, unfair, and unjust differences in health outcomes (Braveman, 2006). Although identifying these inequities has been undertaken across disciplines, historical attempts to understand how SEP “gets under the skin” have fallen short of offering significant evidence of casual mechanisms (Gianaros and Hackman, 2013). The study of health disparities could benefit from integrating neuroscience approaches (Gianaros and Hackman, 2013). Moreover, human neuroscience, which often seeks to explain individual differences in behavior or mental health outcomes would benefit substantially from considering individual- and area-level SEP (Gianaros and Hackman, 2013).

Impact of Individual- and Area-Level Variables on Brain Structure and Function

As portrayed in the allostatic load theory, the interaction between individual SEP on mental health and cognitive function is mediated by the increased stress associated with low SEP (Evans and English, 2002; Farah, 2017). Children growing up in a lower SEP as well as adults living in a lower SEP display impairment in emotional processing and executive functioning (Hackman, Farah, & Meaney, 2010). Structural and functional imaging studies have demonstrated changes in regions supporting these critical domains (Farah, 2017; Hackman, Farah, & Meaney, 2010). Although wide-spread disruption of brain circuitry is presumably responsible for functional impairments, human and animal research suggest the amygdala, prefrontal cortex, and hippocampus are particularly vulnerable to stress (Hackman, Farah, Meaney, 2010; Lawson et al., 2013; Johnson, Riis, & Noble, 2016). Despite evidence from animal research that environmental deprivation can detrimentally affect underlying neurobiology, the impact of area-deprivation in human studies has been widely understudied.

Emotion regulation and processing facilitates an individual's overall stability (McRae and Gross, 2020). Adaptive neural mechanisms assist in "coping" when stressful events occur (McRae and Gross, 2020). Although there is not a clear definition of "emotion" brain regions, the consistent activation of certain structures during affective tasks suggests the amygdala and areas of the prefrontal cortex (e.g. ventromedial prefrontal cortex; vmPFC) assist in this domain (Pechtel and Pizzagalli, 2011; Motzkin et al., 2015; Blair, 2008; Banks et al., 2007; Morawtz, Bode, Baudewig, & Heekeren, 2017). While the amygdala is involved in processing information and initiating responses to salient and threatening stimuli (LeDoux, 2000; Morris, Buchel, & Dolan,

2001; Sangha, Diehl, Bergstrom, & Drew, 2019), the vmPFC exhibits top-down control over sub-cortical structures to suppress stress-related behaviors and broadly regulate responses to negative situations (Ochsner, Silvers, & Buhle, 2012; Morawetz, Bode, Baudewig, & Heekeren, 2017; Sangha, Diehl, Bergstrom, & Drew, 2019).

The vmPFC directly projects to the periaqueductal gray and hypothalamus, which generate behavioral responses to both physical and psychological stressors (Koenigs and Grafman, 2009). Notably, individuals with depression (e.g. Luking et al., 2011; Koenigs & Grafman, 2009), PTSD (e.g. Depue et al., 2014; Milad et al., 2005), and schizophrenia (e.g. Niu et al., 2004; Hooker et al., 2011), show aberrations in the amygdala and vmPFC structure and function. Both the amygdala and vmPFC are implicated in stress-related disorders (Pacak and Palkovits, 2001; Bremner, 2007; Mahan and Kessler, 2012) and low SEP may bestow additional vulnerability of developing disorders or perpetuating mental health symptoms by modifying these regions.

Indeed, the structure and function of the amygdala are highly susceptible to low SEP (Javanbakht et al., 2015; Muscatell et al., 2012; Noble, Houston, Kan, & Sowell, 2012). In children, smaller amygdala volume is significantly correlated with fewer years of parental education (Noble, Houston, Kan, & Sowell, 2012). In an undergraduate sample, Gianaros and colleagues (2008) found that lower perceived parental social standing was associated with increased amygdala reactivity to threatening stimuli even after controlling for various individual factors, such as race/ethnicity, self-perceived social standing, and dispositional emotionality. Additional research with children replicated the finding with an objective measure of SEP: amygdala activity to

threatening faces is increased in individuals with lower childhood family income-to-need ratio (Javanbakht et al., 2015) and household income (Muscatell et al., 2012).

Childhood poverty is also associated with weaker functional connectivity between the amygdala and ventromedial prefrontal cortex (Javanbakht et al., 2015; Hanson et al., 2019). Critically, amygdala-vmPFC coupling during adolescence is predictive of future mental health outcomes (Hanson et al. 2019).

In addition to being vulnerable to low individual SEP, the amygdala is unsurprisingly altered by childhood trauma. Lower individual SEP is notably associated with greater adverse childhood experiences (Mock and Arai, 2011) and a higher number of adverse experiences in adolescents is predictive of smaller amygdala volume (Woon and Hedges, 2015; Marusak et al., 2015). In general, childhood trauma predisposes individuals to poorer mental health outcomes (Nemeroff, 2001). For example, childhood trauma exposure increases the risk of developing PTSD in adulthood (Yehuda, Halligan, Grossman, 2001; Nemeroff, 2004). Considering the prefrontal cortex is one of the last areas of the brain to fully develop, it is unsurprising that the region is sensitive to childhood experiences (Avants et al., 2015; Moriguchi and Shinohara, 2019; Lawson et al., 2014). The richness of the childhood home environment (i.e. environmental stimulation) predicts cortical thickness in frontal and temporal cortices (Avants et al., 2015); however, environmental deprivation is related to thinner prefrontal cortices (Hodel et al., 2015).

Although the majority of the brain is likely responsible for some aspect of memory, the hippocampus is crucial for both working and long-term memory (Battaglia et al., 2011). High levels of cortisol are predictive of smaller hippocampal volume in

aging adults (Lupien et al., 1998) suggesting increased HPA axis activity because of stress causes structural reductions. In children, hippocampal volume is also negatively associated with lower parental income (Hanson, Chandra, Wolfe, & Pollak, 2011) and childhood SEP predicts adult hippocampal volume (Staff et al., 2012; Noble et al., 2012). In adults, larger hippocampal volume as well as fewer microstructural changes (i.e. mean diffusivity, a proxy for cellular death) in the hippocampus are significantly associated with higher education (Piras, Cherubini, Caltagirone, & Spalletta, 2011; Noble et al., 2012). Higher levels of self-reported stress in late adulthood predicts a reduction of hippocampal volume twenty-years later (Gianaros et al., 2007). Thus, the hippocampus appears vulnerable to both early-life stressors and adulthood SEP (Gianaros et al., 2007; Noble et al., 2012).

Collectively, research on the impact of low SEP has largely ignored objective measures of area-level SEP, such as neighborhood crime or ADI. Recent international research suggests area-level variables are critical to include. One study demonstrated adult cortical morphology including cortical thickness, volume, and surface area, was significantly associated with neighborhood disadvantage (Krishnadas et al., 2013). Individuals who lived in the most deprived neighborhoods of Scotland had significantly thinner Wernicke's area, a region crucial for language as well as smaller fusiform cortex and posterior parietal cortex surface area (Krishnadas et al., 2013). A longitudinal study in Australia found neighborhood disadvantage predicted abnormal development of the amygdala as well as the temporal and prefrontal cortices (Whittle et al., 2017). A 2020 U.S.-based study examined the effects of ADI on older adults. Neighborhood disadvantage was related to smaller hippocampal and total brain volume even after

controlling for individual education, age, and sex (Hunt et al., 2020). Another American study found a significant association between community disadvantage and cortical morphology, including the lateral orbital frontal cortex, rostral middle frontal gyrus, and superior frontal gyrus, but not subcortical morphology (amygdala and hippocampus; Gianaros et al., 2017). The results were significant even after controlling for individual SEP measures (Gianaros et al., 2017). Neuroscience research on the effects of area-level variables is relatively novel. As methods are refined and research questions are expanded the inclusion of area-level factors alongside individual variables will likely become standard practice in the field of cognitive neuroscience.

The Current Study

We will first determine whether individual SEP and childhood trauma exposure are associated with brain volume in the amygdala, hippocampus, and vmPFC. As reviewed above, these three regions of interest (ROIs) appear particularly susceptible to low individual SEP and childhood trauma exposure. Using a hierarchical linear regression approach, in which groups of regressors can be added in a step-wise fashion, we will examine whether area-level variables predict over and above the individual factors. In line with previous research, we predict all the individual variables (childhood trauma exposure, education, and income) in the reduced model of the regression will significantly predict cortical volume in all three regions. We will then determine if area-level factors (full model) can explain additional variability in cortical volumes.

We hypothesize neighborhood disadvantage, as measured using the Area Deprivation Index (ADI), but not neighborhood homicide rate, will be significantly associated with *smaller* amygdala, hippocampus, and vmPFC volume. As the homicide

rate is a specific measure of neighborhood exposure to crime/violence, we do not expect that it will explain any variability in cortical volume over and above ADI. If the proposed project examined task-based data or resting-state functional connectivity, we would hypothesize neighborhood homicide rates may be associated with differences between individuals. However, in this structural analysis, we predict a broader measure of neighborhood disadvantage will better address structural variability. In the full model, we hypothesize only ADI and income will be the significant regressors.

Previous epidemiological research suggests contextual-level variables have a smaller effect size than individual-level factors. Several studies do find area-level variables carry additional utility in explaining variability (Karb, Elliott, Dowd, & Morenoff, 2012; Whittle et al., 2017; Hunt et al., 2020; Krishnadas et al., 2013). Still others demonstrate individual SEP variables carry all the variance (Karb, Elliott, Dowd, & Morenoff, 2012; Whittle et al., 2017; Hunt et al., 2020; Krishnadas et al., 2013). Importantly, preclinical research examining the role of chronic exposure to deprived environments, suggest there is a unique impact of deprivation on the brain (Kentner et al., 2018). Individuals with lower SEP often (but not exclusively) live in more deprived neighborhoods whereas individuals with higher SEP typically live in more advantaged areas (Chen and Paterson, 2006). Previous research has suggested the correlation between neighborhood SEP measures and family SEP measures varies between $r = .28$ to $.60$ (Chen and Paterson, 2006). A significant correlation between the individual and area-level factors in this study may influence the results and multicollinearity can make some regressors insignificant when in fact they should be significant (Daoud, 2017).

Methods

Participants.

Between 2017 and 2019, 215 participants were recruited and enrolled in this study. Nine hundred and sixty-nine traumatically injured individuals were recruited from an Emergency Department (ED) in southeastern Wisconsin. Participants were screened for eligibility in the ED. Inclusion criteria required the participant to be English-speaking, between 18-60 years old, and able to schedule a research visit within 30 days of the trauma. Participants were deemed eligible if they experienced a traumatic event which met Criterion A of a PTSD diagnosis (as defined in the Diagnostic and Statistical Manual- 5th edition; American Psychiatric Association, 2013), scored a minimum of a 3 on the Predicting PTSD Questionnaire (Rothbaum et al., 2014) or endorsed that the event was a near-death experience. Notably, this procedure oversampled individuals at risk-of PTSD. Participants were excluded if they scored 13 or higher on the Glasgow Coma Scale (Teasdale, Jennett, Murray, & Murray, 1983), had a spinal cord injury with neurological deficits, or were diagnosed with any neurological condition affecting brain structure or function. Additional exclusion criteria included: a self-inflicted traumatic injury, severe vision or hearing impairments, history of psychotic or manic symptoms, current antipsychotic medication use, substance abuse, on a police hold to be released to jail, and/or any contraindications for MRI scanning including metal objects or fragments in the body, claustrophobia, and pregnancy or planned pregnancy within the next 6 months.

Of the 215 participants enrolled, 208 completed some of the study's neuroimaging portion. Of those, 112 (53.85%) were female. The mean age of the

sample was 33.1 years old (SD = 10.88). Approximately 27.40% of the sample self-identified as White, 58.17% self-identified as African American and/or Black, 1.92% self-identified as Asian or Pacific Islander, and 6.73% self-identified as more than one race. The remaining 5.78% of participants selected “unknown” or chose not to respond. A minority (8.17%) of participants did not graduate from high school or obtain a high school equivalency certificate. 31.73% completed high school or obtained a high school equivalency certificate and 55.77% of participants self-reported higher than high school education. Approximately 4% of participants chose not to disclose their education level. The distribution of participants self-reported annual household income comprised of 33.17% between \$0-\$20,000, 24.04% between \$20,000-40,000, 15.87% between \$40,000-60,000, 11.54% between 60,000-80,000, and roughly 1% reporting above \$80,000. Approximately 4% of participants selected “unknown” or chose not to report their household’s annual income.

Procedure.

Briefly, participants were screened in the ED and provided written informed consent prior to participating in research activities. This analysis uses a subset of data collected as part of a larger longitudinal study examining PTSD risk and resilience following a traumatic injury. Participants underwent structural and functional imaging scans acutely post-trauma (two-weeks post trauma) as well as six-months post trauma. Only the first structural scan, acquired two-weeks post-trauma, will be examined in the proposed project. At these visits, participants also completed questionnaires and neurocognitive assessments. The study’s protocol was approved by the Institutional Review Board of the Medical College of Wisconsin.

Self-Report Measures.

Demographic data was entirely self-reported. Participants provided information on their gender, age, and race/ethnicity. Gender was represented as a dichotomous variable that equals 0 for males and 1 for females. Annual house-hold income was provided on a semi-continuous scale (1-11) where 1 reflected a \$0-10,000 income bracket 11 represented an income of \$100,000 and/or above. Educational level was also reported on a semi-continuous scale and reflected the number of years of education completed. A score of 12 or 13 reflected a high school diploma or equivalency certificate. Participants provided contact information, including their current address.

A subset of questionnaires completed on the first day of scanning will be used in this analysis. The Childhood Trauma Questionnaires (CTQ) is a validated measure for self-reported, retrospective childhood trauma history (Bernstein et al., 2003). The CTQ consists of 28 items evaluating childhood physical abuse (PA), emotional abuse (EA), sexual abuse (SA), emotional neglect (EN), and physical neglect (PN). A score for each of the trauma types can be derived by summing the sub-scale specific questions and a total score can be created by summing all the items (Bernstein et al., 2003).

Area-Level Derived Measures.

Area Deprivation Index (ADI), a measure of neighborhood disadvantage was calculated for each participant. ADI had been used to analyze the association between area deprivation and numerous health outcomes, such as cancer, childhood mortality, and hospital readmission (Kind et al., 2014; Ludwig et al., 2011). The 2015 version of ADI utilizes data from the 2011-2015 American Community Survey (ACS; a survey of the U.S. Census Bureau). The smallest ACS geographic area is a block-group, which has a

maximum of 3,000 people or 1,200 housing units (U.S. Census Bureau, 2020). The block-group factor-based index represents 17 variables from the US Census including measurements of poverty, education, housing, and employment. A dataset including all Wisconsin block-level ADI scores was downloaded from <https://www.neighborhoodatlas.medicine.wisc.edu/>.

Block-group IDs for each participant were hand derived using the Census website: <https://geocoding.geo.census.gov/geocoder/geographies/address?form>. Participants were excluded if they designated a post office box as their residence or if their address is not associated with a block-group ID. The first address provided by the participant was used to derive their block-group ID, thus participants were not excluded if they relocated during the study.

The database provides ADI values that have been ranked into percentiles by increasing neighborhood disadvantage. National rankings and state rankings are provided. State rankings are on a scale of 1-10, where 10 is the most deprived neighborhood and 1 is a neighborhood with the highest advantage. National rankings are on a scale of 1-100, where 100 is the most disadvantaged. The benefit of employing ADI, a relative measure of neighborhood disadvantage rather than an absolute measure is that ADI is meaningful across time and space. In the state ranking, any block-group's deprivation is measured relative to all other block-groups in the same time span. This is advantageous as health disparities are directly concerned with health outcomes of a group relative to another group. As such using a relative measure of neighborhood disadvantage that can be adjusted throughout time is a powerful tool.

Although ADI provides a proxy for neighborhood disadvantage, it may not capture all relevant elements of stressful and deprived environments. For this reason, crime rates associated with each participants block-group ID were derived from the Applied Geographic Solutions (AGS) crime data. Previous studies have been limited by the often unreliable and/or missing geo-coded publicly accessible crime data (Nau et al., 2020). Several studies have examined the reliability of for-purchase crime data sets, most commonly the AGS CrimeRisk© indices (Nau et al., 2020; Applied Geographic Solutions, 2016). An important limitation of the AGS dataset is it utilizes data from the Federal Bureau of Investigation's Uniform Crime Report which does not provide block-group data. For this reason, AGS must use predictive modeling to approximate crime rates at the block-group (Nau et al., 2020).

Homicide, rape, robbery, assault, burglary, larceny, and motor vehicle theft are used to calculate rates of total, personal, and property crime. In theory, the AGS crime rates should match local police departments reports; however, a recent reliability study suggested only some rates (robbery, homicide, assault, motor-vehicle theft, and personal crime) are accurate when compared to local police department databases. For this reason, instead of using a composite score such as total crime, the analyses included homicide rates (noted to have high reliability in Nau et al., 2020). Although the most deprived neighborhoods may not always have the highest rates of crime, a relationship between violent crime and neighborhood economic disadvantage has been established (Masi et al., 2007; Hannon and Knapp, 2003).

Imaging Acquisition.

Brain images were collected on a 3.0 Tesla short bore GE Signa Excite system. High resolution spoiled gradient recalled (SPGR) anatomical images were acquired in a sagittal orientation (TR=8.2 ms; TE=3.2 ms; FOV=24 cm; flip angle=12°; voxel size=1 x 0.9375 x 0.9375mm).

Image Analysis.

FreeSurfer is an automated software tool used to perform volumetric quantification of brain structures (v5.30; <http://surfer.nmr.mgh.harvard.edu/>; Fischl, 2012). The program performs skull-stripping and smoothing, among other preprocessing steps. The proposed project uses the standard FreeSurfer pipeline which performs structural segmentation based on a-priori knowledge. In brief, FreeSurfer estimates probability measures to assign any given voxel to a specific structure. Prior to extracting statistical output, each participant's image will be visually inspected to ensure 1) the skull was properly stripped, 2) white matter and pial boundaries are correctly defined, and 3) the structural segmentations are reasonable. Manual edits will be performed as needed. I performed segmentation of the whole brain and extract cortical volume measures (mm³) for the amygdala, hippocampus, and vmPFC. Because the vmPFC is not a default region in FreeSurfer, we used a protocol previously described (Desikan et al., 2006; Morey et al., 2016) in which the volumes from the medial orbital frontal and lateral orbital frontal (defined by default in FreeSurfer) are summed.

Statistical Analysis: Hierarchical Multiple Linear Regressions

All analyses were conducted in R (R Core Team, 2013). The primary goal was to determine if ADI is associated with volume (mm³) of the amygdala, hippocampus, and

vmPFC. Prior to analysis, study measures were mean-centered and ROI volumes and crime data were standardized. First, Pearson correlations between age, ADI, neighborhood homicide rate, individual education, individual income, CTQ sub-scales, and brain volumes for each region of interest will be calculated. Biserial correlations were also conducted between gender and study measures. Age and gender have been noted to impact cortical volumes (Lemaitre et al., 2012; Luders et al., 2005), therefore the two variables will be included as covariates for all analyses.

Multi-collinearity was assessed by evaluating variance inflation factors (VIF). To examine the unique contribution of neighborhood context in the explanation of ROI volume, we performed hierarchical multiple linear regressions analyses. In three separate hierarchical linear regression analyses, we examined the contribution of individual factors (education, income, CTQ subscales, gender, and age) on brain volumes (Step 1; reduced model). In a final step, area-level variables will be entered into the model (Step 2; full model). We predicted that ADI would be associated with *smaller* amygdala, hippocampus, and vmPFC volumes. We hypothesized neighborhood homicide rate would not be associated with brain morphology.

Exploratory Structural Equation Modeling

In an exploratory aim, we used structural equation modeling (SEM) to examine the relationship between these variables using another technique. Structural equation modeling allows a researcher to define a latent construct (e.g. individual SEP) with observed variables (e.g. education and income; Kline, 2005). This method is similar to a path analysis or multiple regression however it offers additional flexibility as it allows for verification of interdependences between constructs. While two observed variables are

sufficient for constructing a latent variable, at least three observed measures are preferred (Kline, 2005). For this reason, another crime variable, Robbery rate, which has been shown to have good reliability with police statistics (Nau et al., 2020) was selected. In the context of this project, SEM verifies whether childhood trauma exposure (measured by the six sub-scales), neighborhood context (ADI, Robbery, and Homicide), and individual SEP (as observed using education and income) significantly and interdependently influence brain volume.

We evaluated the fit of the model using four fit indices: Chi-Square test of model fit, Root Mean Square Error of Approximation (RMSEA), Comparative Fit Index (CFI), and the Standardized Root Mean Residual (SRMR; Hooper et al., 2008; Kline, 2005). Chi-squared statistics are also often considered ($p < .05$ indicative of a poor fit) however the test is highly sensitive to sample size (Kline, 2005). Adequate fit was considered achieved if the RMSEA was below 0.08, CFI was greater than 0.90, and the SRMR values were below 0.10 (Hooper et al., 2008; Kline, 2005).

Results

Of the 208 participants who underwent structural scanning, 192 had useable scans after manual edits were performed. Eleven individuals were removed because they could not be successfully geocoded, and nine participants were excluded from analysis because they were missing demographic data (final sample characteristics are presented in Table 1). The distribution of ADI scores is provided in Figure 1. Twelve participants did not complete the CTQ, therefore sub-scale scores were mean imputed. Univariate outliers were defined as being three standard deviations above or below the mean and three participants were excluded because their cortical volumes were above the cut-off.

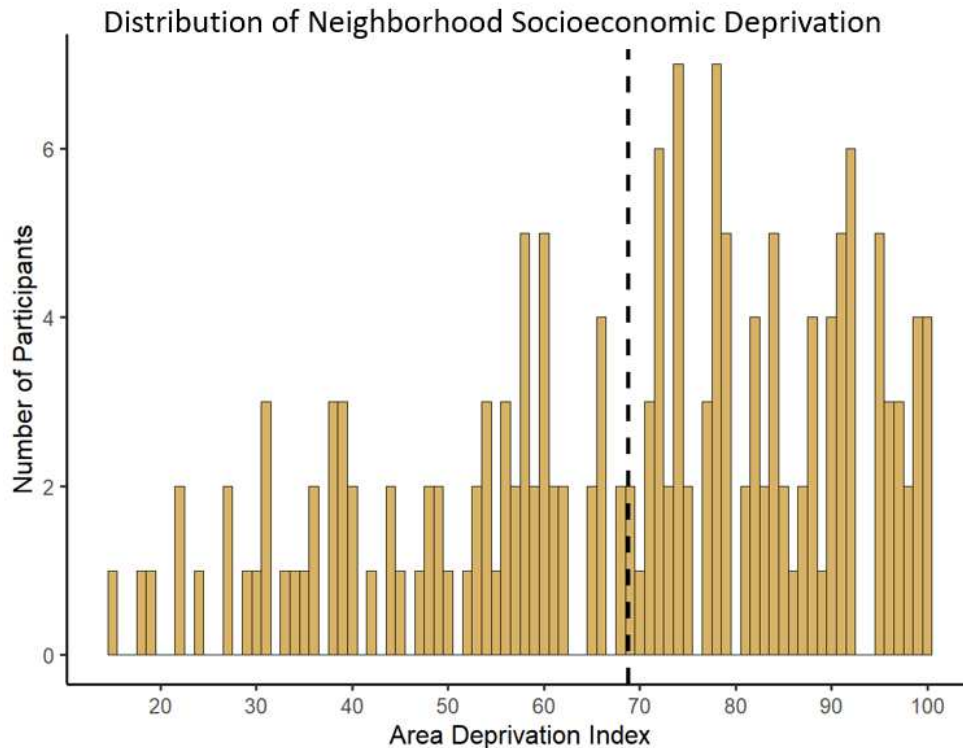


Figure 1. Distribution of Area Deprivation Index rankings shows the majority of participants are from more disadvantaged neighborhoods (N = 169, Mean = 68.74, Standard Deviation = 21.74).

Although the primary analyses were not stratified by race and ethnicity or gender, two independent t-tests were conducted to examine whether there was a significant difference in ADI rankings between genders and racial groups (Figure 2). Men (M = 71.24, SD = 20.95) and women (M = 66.74, SD = 22.25) did not differ in ADI, $t(167) = 1.34$, $p = .182$. Black participants (N = 101, M = 77.83, SD = 15.46) lived in significantly more disadvantaged neighborhoods than White participants (N = 43, M = 51.19, SD = 23.29; $t(142) = 8.07$, $p < .001$). Due to small group sizes amongst the other reported racial and ethnic groups, no other tests were conducted.

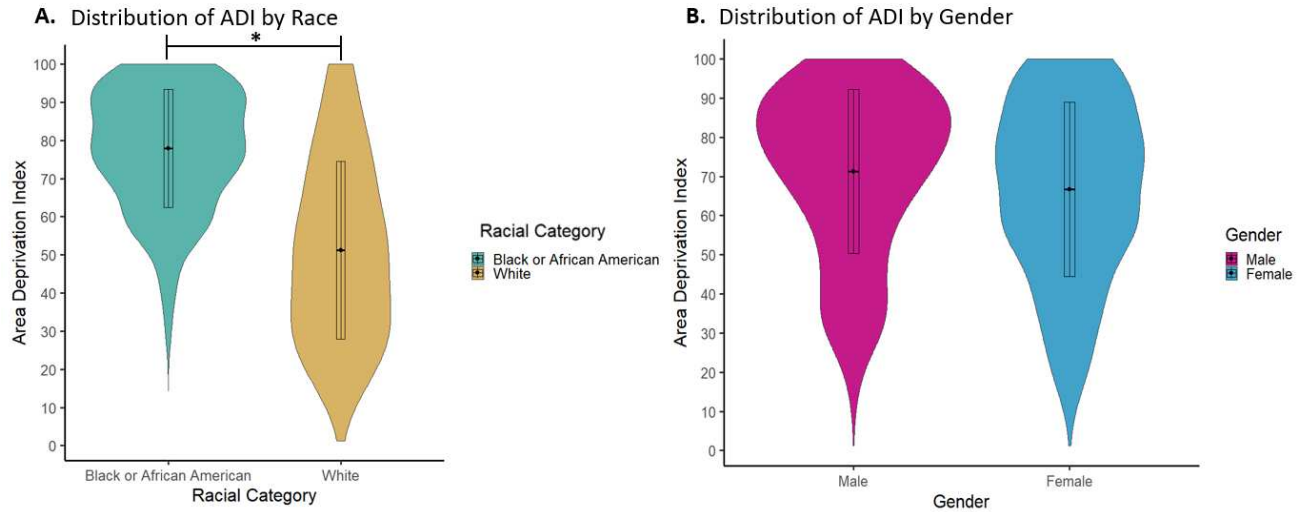


Figure 2. Area Deprivation Index Rankings by Racial Group (A) and Sex (B).

Unfortunately, crime statistics could not be derived for all participants: 21 subjects lived outside of the county and crime data could not be obtained. We hypothesized that homicide rate would not be significantly correlated with brain structure; indeed, there was not a significant relationship between homicide rates and ROI volumes. With the intention of retaining as many participants as possible for the main analyses, homicide rate was dropped as a variable of interest. However, crime data (robbery and homicide block-level statistics) was included in the exploratory analysis using SEM. The final sample size for the main aim was 169 participants.

Table 1 Sample Characteristics

<i>Variable</i>	<i>Percent (%)</i>	<i>Mean</i>	<i>SD</i>
Age (years)		32.60	10.90
Sex			
Female	55.6		
Race and Ethnicity			
African American/Black	59.8		
White	25.4		
More than one race	7.7		
Other	<5		
Unknown/Not reported	5.9		
Education			
Less than high school/GED	10.1		
High school/GED or below	33.1		
Some post-secondary education/college	26.6		
Associate degree	13.6		
Bachelor's degree or beyond	16.6		
Annual Household Income			
\$0-10,000	21.3		
\$10-20,000	14.8		
\$20-30,000	17.2		
\$30-40,000	8.3		
\$40-50,000	7.7		
\$50-60,000	5.9		
\$60-70,000	5.3		
\$70-80,000	7.1		
\$80-90,000	<5		
\$90-100,000	<5		
\$100,000 or higher	5.9		
Area Deprivation Index (ADI)		68.74	21.73
Childhood Trauma Questionnaire		43.17	10.90
Emotional Abuse (EA)		8.87	4.59
Physical Abuse (PA)		8.04	4.12
Sexual Abuse (SA)		7.64	5.45
Physical Neglect		8.30	3.59
Emotional Neglect		10.51	5.16

Note: N = 169.

Relationships Between Study Measures

Correlation coefficients between all study measures can be found in Table 2.

Correlations with Crime Statistics.

As aforementioned, homicide rate was not significantly associated with amygdala ($r_{(146)} = -.07, p = .381$), hippocampus ($r_{(146)} = -.13, p = .114$), or vmPFC volume, $r_{(146)} = -.05, p = .579$. As hypothesized, homicide rate was significantly associated with ADI scores ($r_{(146)} = .70, p < .001$), income ($r_{(146)} = -.37, p < .001$), and education, $r_{(146)} = -.28, p = .001$. Homicide rate ($r_{(146)} = -.18, p = .025$) was significantly associated with EA, but none of the other CTQ sub-scales (EN: $r_{(167)} = .05, p = .574$; PN: $r_{(167)} = .09, p = .289$; PA: $r_{(167)} = -.01, p = .909$; SA: $r_{(167)} = .01, p = .865$).

Area and Individual-Level SEP Associations with ROI Volumes.

ADI scores were significantly associated with hippocampus ($r_{(167)} = -.18, p = .019$) and vmPFC ($r_{(167)} = -.17, p = .032$), but not amygdala ($r_{(167)} = -.11, p = .114$) volumes. Gender was significantly associated with all three volumes (hippocampus: $r_{(167)} = -.29, p < .001$; amygdala: $r_{(167)} = -.42, p < .001$; vmPFC: $r_{(167)} = -.38, p < .001$) whereas age was negatively associated with amygdala and vmPFC volume, ($r_{(167)} = -.17, p = .027$ and $r_{(167)} = -.40, p < .001$, respectively), but not hippocampal volume $r_{(167)} = -.08, p = .315$. Education was not significantly associated with any of the ROI volumes (hippocampus: $r_{(167)} = -.06, p = .44$; amygdala: $r_{(167)} = -.02, p = .757$; vmPFC: $r_{(167)} = -.03, p = .663$); however income was significantly related to amygdala ($r_{(167)} = .16, p = .040$) and vmPFC volume ($r_{(167)} = .23, p = .002$), but not hippocampal volume, $r_{(167)} = -.12, p = .130$.

Area and Individual-Level SEP Associations with CTQ.

Both gender and age were significantly related to education (gender: $r_{(167)} = .16, p = .042$; age: $r_{(167)} = .18, p = .020$), but not income (gender: $r_{(167)} = -.07, p = .397$; age: $r_{(167)} = .03, p = .712$). Age was not significantly related to any of the CTQ subscales (EN: $r_{(167)} = -.02, p = .833$; PN: $r_{(167)} = -.05, p = .529$; EA: $r_{(167)} = .03, p = .703$; PA: $r_{(167)} = .14, p = .072$; SA: $r_{(167)} = .11, p = .147$). However, female gender was significantly associated with emotional and sexual abuse (EN: $r_{(167)} = -.04, p = .639$; PN: $r_{(167)} = -.09, p = .233$; EA: $r_{(167)} = .16, p = .038$; PA: $r_{(167)} = .100, p = .196$; SA: $r_{(167)} = .30, p < .001$). Income was significantly associated with EN ($r_{(167)} = -.25, p < .001$) and PN ($r_{(167)} = -.32, p < .001$), but not EA ($r_{(167)} = -.13, p = .098$) or PA ($r_{(167)} = -.12, p = .122$). The relationship between income and SA trended towards significance, $r_{(167)} = -.15, p = .052$.

Educational attainment was also significantly associated with EN ($r_{(167)} = -.24, p = .002$) and PN ($r_{(167)} = -.27, p < .001$), but none of the other CTQ sub-scales (EA: $r_{(167)} = .07, p = .369$; PA: $r_{(167)} = .01, p = .857$; SA: $r_{(167)} < .01, p = .965$). ADI scores were not associated with any of the CTQ sub-scales (EN: $r_{(167)} = .04, p = .595$; PN: $r_{(167)} = -.01, p = .943$; EA: $r_{(167)} = -.07, p = .394$; PA: $r_{(167)} = .01, p = .900$; SA: $r_{(167)} = .12, p = .130$).

CTQ Associations with ROI Volumes.

Childhood sexual abuse was significantly associated with smaller volumes for all three ROIs (hippocampus: $r_{(167)} = -.15, p = .049$; amygdala: $r_{(167)} = -.19, p = .015$; vmPFC: $r_{(167)} = -.17, p = .030$). None of the other sub-scales predicted amygdala (EN: $r_{(167)} = -.01, p = .939$; PN: $r_{(167)} = .06, p = .460$; EA: $r_{(167)} = -.02, p = .836$; PA: $r_{(167)} = -.06, p = .430$), hippocampus (EN: $r_{(167)} = .09, p = .269$; PN: $r_{(167)} = -.07, p = .354$; EA: $r_{(167)} = -.01, p = .887$; PA: $r_{(167)} = -.12, p = .119$), or vmPFC (EN: $r_{(167)} = -.06, p = .451$; PN: $r_{(167)} = .07, p = .378$; EA: $r_{(167)} = -.03, p = .717$; PA: $r_{(167)} = -.14, p = .060$) volumes.

Intercorrelations between Study Measures.

As anticipated, ADI was significantly correlated with both income ($r_{(167)} = -.43, p < .001$) and education ($r_{(167)} = -.33, p < .001$). There was not significant correlation between ADI and gender ($r_{(167)} = -.10, p = .182$) or age, $r_{(167)} = .03, p = .661$. CTQ sub-scales were also significantly intercorrelated (EN-PN: $r_{(167)} = .66, p < .001$; EN-EA: $r_{(167)} = .49, p < .001$; EN-SA: $r_{(167)} = .24, p = .002$; EN-PA: $r_{(167)} = .36, p < .001$; PN-EA: $r_{(167)} = .47, p < .001$; PN-PA: $r_{(167)} = .45, p < .001$; PN-SA: $r_{(167)} = .45, p < .001$; EA-SA: $r_{(167)} = .50, p < .001$; EA-PA: $r_{(167)} = .62, p < .001$; SA-PA: $r_{(167)} = .46, p < .001$). The three ROI volumes were also significantly related to each other (hippocampus-amygdala: $r_{(167)} = .44, p < .001$; amygdala-vmPFC: $r_{(167)} = .40, p < .001$; vmPFC-hippocampus: $r_{(167)} = .39, p < .001$).

Table 2 Correlation Coefficients Between Study Variables

<i>Study Measure</i>	1	2	3	4	5	6	7	8	9	10	12	13	14	15
1. Age	-													
2. Gender	.10	-												
3. ADI	-.03	-.10	-											
4. Income	.03	-.07	-.43**	-										
5. Education	.18*	.16*	-.33**	.48**	-									
6. CTQ EN	-.02	-.04	.04	-.25**	-.24*	-								
7. CTQ PN	-.05	-.09	-.01	-.32**	-.27**	.66**	-							
8. CTQ EA	.03	.16*	-.07	-.13	.07	.49*	.47**	-						
9. CTQ PA	.14	.10	.01	-.12	.01	.36**	.45**	.62**	-					
10. CTQ SA	.11	.30**	.12	-.15 ⁺	<.01	.24**	.24**	.51**	.47**	-				
11. Hippocampal Volume	-.08	-.29**	-.18*	.12	-.06	.09	.07	-.01	-.12	-.15*	-			
12. Amygdala Volume	-.17*	-.42**	-.13	.16*	-.02	<.01	.06	-.02	-.06	-.19*	.44**	-		
13. vmPFC Volume	-.40**	-.38**	-.17*	.23**	-.03	.06	.07	-.03	-.15 ⁺	-.17*	.39**	.40**	-	
14. Homicide Rate	.02	-.13	.70**	-.37**	-.28*	.05	.09	-.18*	.01	-.01	-.13	-.07	-.05	-

Note: N = 169; for correlations with homicide rate: N = 148; ⁺ p < .06, * p < .05, ** p < .001.

Unique Contribution of ADI in the Explanation of ROI Volumes

As previously discussed, homicide rates were not included in the following analyses. In the first step of the regression model, gender, age, income, education, CTQ EA sub-scale score, CTQ EN sub-scale score, CTQ PA sub-scale score, CTQ PN sub-scale score, and CTQ SA sub-scale score were entered as the independent variables. In Step 2, ADI score was entered with the individual variables. Residuals were evaluated and the data did not violate assumptions of independence or homoscedasticity. Critically, multicollinearity assumption was not violated; VIFs did not exceed the standard cut-off of 2.5 (Johnston, Jones, & Manley, 2018).

Factors Impacting Hippocampal Volume.

Approximately 14% of the variation in hippocampal volume was explained by the nine individual-level variables (adjusted $R^2 = .137$, $F_{(9, 159)} = 2.80$, $p = .004$). Gender significantly predicted hippocampal volume, $\beta = -0.49$, $t_{(159)} = -3.03$, $p = .003$). However both Income and PA trended towards significance, $\beta = 0.05$, $t_{(159)} = 1.80$, $p = .072$ and $\beta = 0.05$, $t_{(159)} = -1.81$, $p = .072$, respectively. ADI uniquely accounted for an additional 2.8% of hippocampal volume variance, which significantly improved the model, $\Delta R^2 = .028$, $F_{(1, 158)} = 5.36$, $p = .022$. The intercept and the standardized regression coefficients (β) for the full model are reported in Table 3. In the full model, only gender ($\beta = -0.55$, $t_{(159)} = -3.43$, $p < .001$) and ADI ($\beta = -0.80$, $t_{(159)} = -2.32$, $p < .001$) were significant regressors.

Table 3 Hierarchical Linear Regression of Hippocampal Volume

<i>Variable</i>	<i>B</i>	<i>t</i> ₍₁₅₈₎	<i>P</i>
Intercept	0.92	3.00	.003
Education	-0.04	-1.10	.281
Income	0.03	0.84	.401
EA	0.02	1.02	.311
PA	-.04	-1.70	.090
SA	-0.01	-0.40	.690
PN	0.01	0.23	.815
EN	0.02	0.44	.443
Gender	-0.55	-3.43	.008*
Age	<-.01	-0.19	.853
ADI	-0.01	-2.32	.022*

* $p < .05$; EA: emotional abuse; PA: physical abuse; SA: sexual abuse; PN: physical neglect; EN: emotional neglect; ADI: Area Deprivation Index.

Factors Impacting Amygdala Volume.

The results of step 1 indicated that approximately 23% of the variation in amygdala volume could be accounted for by the first nine independent variables, adjusted $R^2 = .229$, $F_{(9, 159)} = 5.26$, $p < .001$. Gender was the only statistically significant independent variable in this model ($\beta = -0.77$, $p < .001$), although income approached significance, $\beta = 0.05$, $p = .067$. Adding ADI into the model during Step 2 did not significantly improve the model, $\Delta R^2 = .008$, $F_{(1, 158)} = 1.58$, $p = .210$. The intercept, standardized regression coefficients (β), t-statistic, and significance values for the full model are reported in Table 4. In the full model, only gender contributed to amygdala volume, $\beta = -0.80$, $p < .001$.

Table 4 Hierarchical Linear Regression of Amygdala Volume

<i>Variable</i>	<i>B</i>	<i>t</i> ₍₁₅₈₎	<i>P</i>
Intercept	0.45	4.04	>.001
Education	-0.02	-0.44	0.663
Income	0.04	1.25	0.213
EA	0.03	1.23	0.220
PA	-0.01	-0.39	0.695
SA	-0.01	-0.82	0.412
PN	0.02	0.58	0.561
EN	-0.01	-0.73	0.469
Gender	-0.80	-5.22	<.001*
Age	-0.01	-1.63	0.106
ADI	<-.01	-1.26	0.210

* $p < .05$; EA: emotional abuse; PA: physical abuse; SA: sexual abuse; PN: physical neglect; EN: emotional neglect; ADI: Area Deprivation Index.

Factors Impacting vmPFC Volume.

Approximately 35% of the variation in vmPFC volume was explained in Step 1 (adjusted $R^2 = .348$, $F_{(9, 159)} = 9.41$, $p < .001$). Gender ($\beta = -0.61$, $t_{(159)} = -4.38$, $p < .001$), income ($\beta = 0.09$, $t_{(159)} = 3.53$, $p < .001$), and age ($\beta = -0.03$, $t_{(159)} = -5.22$, $p < .001$) significantly predicted vmPFC volume. The addition of ADI in Step 2, did not significantly improve the model, $\Delta R^2 = .018$, $F_{(1, 158)} = 2.90$, $p = .091$. Results of the full model are reported in Table 5. In the full model, only gender ($\beta = -0.65$, $t_{(159)} = -4.64$, $p < .001$) age ($\beta = -0.03$, $t_{(159)} = -5.27$, $p < .001$), and income ($\beta = -.07$, $t_{(159)} = 2.67$, $p = .008$) were significantly associated with vmPFC volume.

Table 5 Hierarchical Linear Regression of vmPFC Volume

<i>Variable</i>	<i>B</i>	<i>t</i> ₍₁₅₈₎	<i>P</i>
Intercept	0.36	3.53	<.001
Education	-0.02	-0.51	.611
Income	0.07	2.67	.008
EA	0.02	0.84	.404
PA	-0.03	-1.61	.109
SA	<.01	0.14	.892
PN	0.02	0.68	.498
EN	0.01	0.65	.517
Gender	-0.65	-4.64	<.001
Age	-0.03	-5.27	<.001
ADI	-0.01	-1.70	0.091

* **p < .05**; EA: emotional abuse; PA: physical abuse; SA: sexual abuse; PN: physical neglect; EN: emotional neglect; ADI: Area Deprivation Index.

Exploratory Aim: Structural Equation Modeling

Prior to SEM, a factor analysis was conducted to determine that three factors (i.e. Trauma, Individual SEP, and Neighborhood) would be sufficient; in other words, the purpose of the factor analysis was to ensure the observed measures loaded on three factors that would be theoretically relevant. We hypothesized one latent variable representing Individual SEP would have two indicators: education and income (mean-centered). A second latent variable, Trauma, would load all five CTQ sub-scales (mean-centered) and the final latent construct, Neighborhood, would be represented with ADI (mean-centered), Homicide and Robbery rates (standardized rates).

A maximum likelihood factor analysis, with a varimax rotation, demonstrated that the three factors was not sufficient, $\chi^2 (18, N = 148) = 47.08, p < .001$. The observed variables did load sufficiently onto four variables, $\chi^2 (11, N = 148) = 5.74, p = .890$. Instead of a single trauma construct, the sub-scales were better divided into two latent

variables: a neglect factor (PN and EN) and an abuse factor (EA, PA, and SA).

However, given the original theoretical framework, that suggests childhood trauma, regardless of type, impacts brain morphology as well as the consideration that a small sample size and a higher number of variables can result in the model not converging, the following analyses proceeded with only three latent variables: Trauma, Neighborhood, and Individual SEP.

Three separate SEM analyses (N = 148) were conducted for the three volumes using the Maximum Likelihood method of estimation (default in the R package Lavaan; Rosseel, 2012). Initial models exceed CFI, RMSEA, and SRMR cut-offs, which demonstrated poor fit, therefore modification indices were consulted. Modification indices describe relationships/parameters that, if included in the model, would improve the overall fit. Based on these indices, residual correlations/covariances between Income and ADI were included in all the final models. Figure 3, Figure 4, and Figure 5 provide a path diagram with coefficients depicting the models evaluating the amygdala, hippocampus, and vmPFC volume, respectively. For each latent factor, one observed variable was fixed to set the scale for the constructs; EA was fixed for the trauma construct, education was fixed for the individual SEP factor, and ADI was fixed for the neighborhood variable.

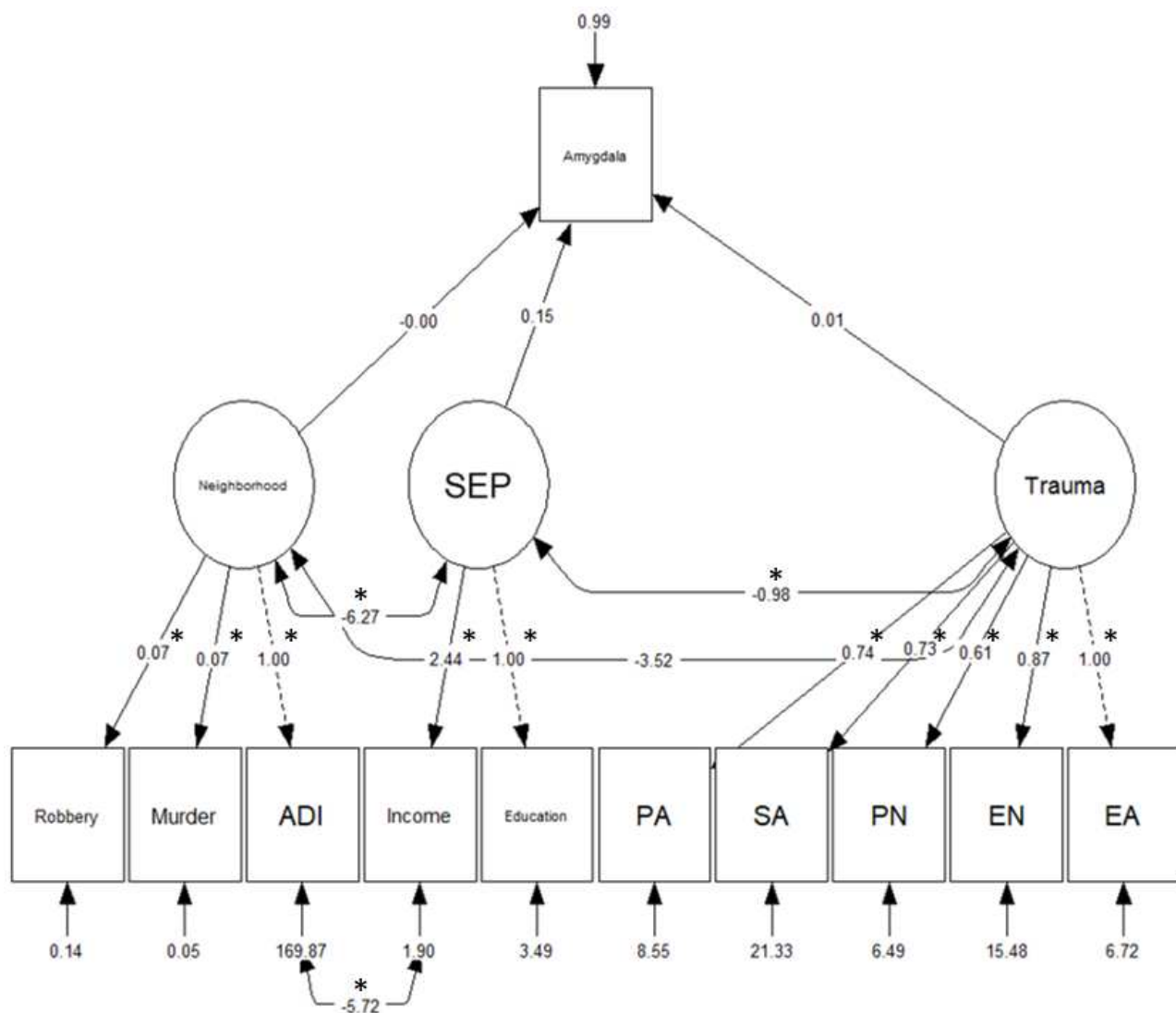


Figure 3. Schematic representation of the structural equation model with path coefficients showing the direct effect of the latent variables of Neighborhood SEP (Neighborhood), Individual SEP (SEP), and Childhood Trauma Exposure (Trauma) on Amygdala volume (Amygdala). *Note:* * $p < .05$. EA: emotional abuse; PA: physical abuse; SA: sexual abuse; PN: physical neglect; EN: emotional neglect; ADI: Area Deprivation Index.

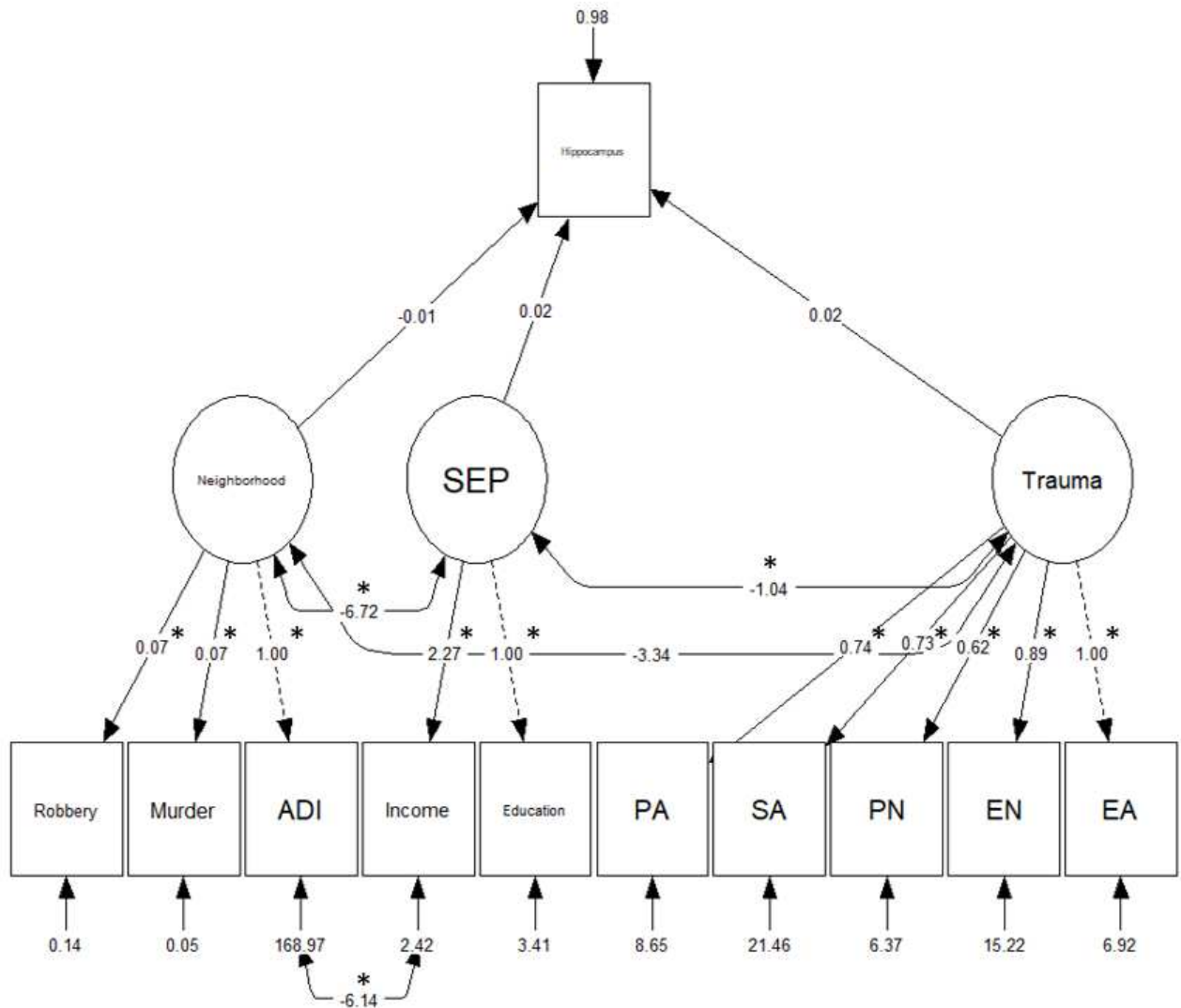


Figure 4. Schematic representation of the structural equation model with path coefficients showing the direct effect of the latent variables of Neighborhood SEP (Neighborhood), Individual SEP (SEP), and Childhood Trauma Exposure (Trauma) on Hippocampus volume (Hippocampus). *Note:* * $p < .05$; EA: emotional abuse; PA: physical abuse; SA: sexual abuse; PN: physical neglect; EN: emotional neglect; ADI: Area Deprivation Index.

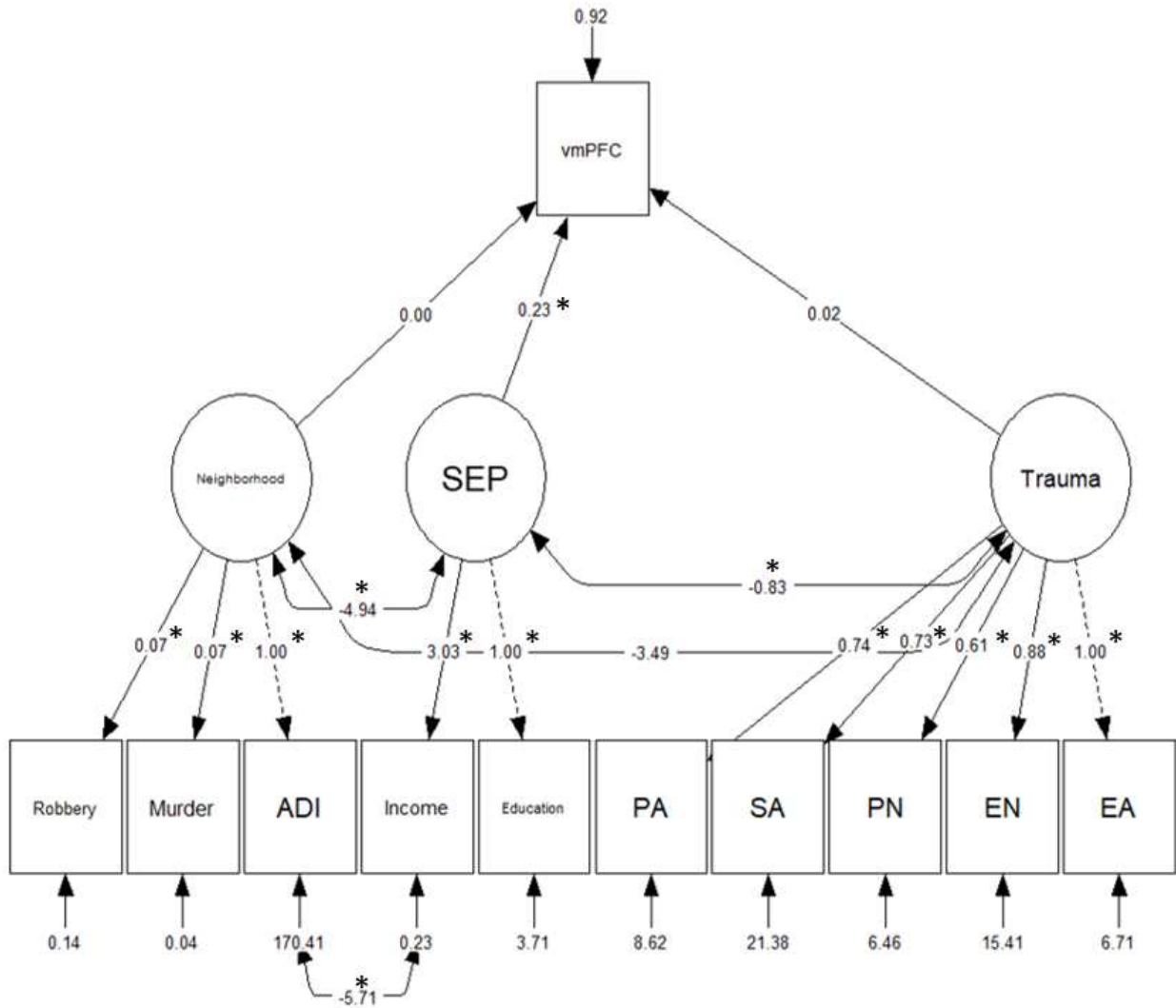


Figure 5. Schematic representation of the structural equation model with path coefficients showing the direct effect of the latent variables of Neighborhood SEP (Neighborhood), Individual SEP (SEP), and Childhood Trauma Exposure (Trauma) on ventromedial prefrontal cortex volume (vmPFC). *Note:* * $p < .05$; EA: emotional abuse; PA: physical abuse; SA: sexual abuse; PN: physical neglect; EN: emotional neglect; ADI: Area Deprivation Index.

A summary of fit indices for all models can be found in Table 6. All three models had values close to the CFI cut-off of 0.9 and SRMR values below 0.1 (amygdala: CFI =

.875, SRMR = .086 hippocampus: CFI = .877, SRMR = .087; vmPFC: CFI = .871, SRMR = .091). In general, the models had poor fit when consulting the RMSEA index (adequate fit if less than 0.08) and the chi-squared statistic (amygdala: RMSEA = .124, 90% confidence interval(CI)[0.100, 0.149] , χ^2 (38, N = 148) = 124.88, $p < .001$; hippocampus: RMSEA = .087, 90% CI[0.100, 0.148], χ^2 (38, N = 148) = 123.72, $p < .001$; vmPFC: RMSEA = .127, 90% CI[0.103, 0.151], χ^2 (38, N = 148) = 128.33, $p < .001$).

All items loaded statistically significantly ($p < .05$) on the theorized latent variables. The regression coefficients for the three latent constructs were non-significant for the amygdala or hippocampus model. However, individual SEP was a significant regressor in the model fitting vmPFC variance ($\beta = 0.23$, $p = .028$).

Table 6 Fit Indices for Exploratory Structural Equation Models

<i>Dependent Variable</i>	<i>Index/Test</i>			
	<i>CFI</i>	<i>RMSEA</i>	<i>SRMR</i>	<i>Chi-Square Test</i> χ^2 (38, N = 148) =
Amygdala	.875	.124	.086	124.88, $p < .001$
Hippocampus	.877	.087	.087	123.72, $p < .001$
vmPFC	.871	.127	.091	128.33, $p < .001$

Note: CFI: Comparative Fit Index; RMSEA: Root Mean Square Error of Approximation; SRMR: Standardized Root Mean Square Residual.

Discussion

In the current study, we explored the relationship between brain morphology and individual SEP, neighborhood disadvantage, and childhood trauma. We probed the effect of these variables on the volumes of the three brain regions which are noted as

highly susceptible to stress: the amygdala, hippocampus, and vmPFC. Based on previous literature, we anticipated individual factors (e.g. individual SEP and trauma) would be associated with significantly smaller ROI volumes (Noble, Houston, Kan, & Sowell, 2012; Woon and Hedges, 2015; Marusak et al., 2015; Staff et al., 2012; Noble et al., 2012; Avants et al., 2015; Moriguchi and Shinohara, 2019; Lawson et al., 2014) however, we also hypothesized neighborhood socioeconomic disadvantage would uniquely contribute to brain morphology.

Unsurprisingly, we demonstrated income and education are negatively correlated with neighborhood disadvantage. Participants who reported lower years in school/training and lower annual household income tended to live in more disadvantaged neighborhoods. Interestingly, female gender was associated with greater educational attainment, but not income. In the United States, although the majority of college graduates are women (U.S. Department of Education, 2019), women are paid approximately 80 cents per every dollar their male counterparts earn (U.S. Census Bureau, 2018). There was a non-significant relationship between education and income. For many groups of people, such as for women and for racial and ethnic minorities, number of years in school does not directly translate into future employment or income (Nuru-Jeter et al., 2018; U.S. Census Bureau, 2018).

Childhood trauma exposure has been linked to lower childhood SEP (Mock and Arai, 2011; Walsh, McCartney, Smith, & Armour, 2019). We extend these results by showing lower income and less education in adulthood is significantly related to higher rates of childhood emotional and physical neglect. The association between low income and sexual abuse trended towards significance in our sample. Previous work has

suggested that while childhood sexual abuse may occur to children across socioeconomic positions (Yahaya, de Leon, Uthman, Soares, & Macassa, 2014), the exposure may adversely influence socioeconomic outcomes in adulthood (Fergusson, McLeod, & Horwood, 2013). Notably, neighborhood socioeconomic disadvantage was not associated with any of the CTQ sub-scales. This contradicts reports from adolescents suggesting neighborhood poverty is associated with childhood adversity and abuse, even after adjusting for parental income (Baglivio, Wolff, Epps, & Nelson, 2017; Maguire-Jack, & Font, 2017). In our adult sample, neighborhood disadvantage was defined in adulthood, with childhood trauma exposure measured retrospectively.

A recent study in women found adverse childhood experiences impact amygdala and hippocampus volumes, but these effects fluctuate depending on timing and severity of exposure (Herzog et al., 2020). In the current study only childhood sexual abuse significantly predicted smaller ROI volumes. Childhood sexual abuse has been noted to evoke wide-spread alterations to brain structure and function, which can have a lasting impact on future mental health outcomes (Andersen, et al., 2008; Edwards, 2018). Future work exploring the relationship between childhood adversity, socioeconomic variables, and brain structure should employ a longitudinal design, from adolescence to adulthood, which would offer an opportunity for more robust analyses and potentially greater insight into casual pathways.

Sex, gender, and age are strong predictors of brain morphology (Jernigan et al., 1991; Lüders, Steinmetz, & Jäncke, 2002; Perlaki et al., 2014; Sacher, Neumann, Okon-Singer, Gotowiec, & Villringer, 2013; Shalev, Admon, Berman, & Joel, 2020). In our sample, younger age was related to smaller amygdala and vmPFC volumes

whereas female gender was associated with smaller volumes in all three ROIs. Our bivariate results highlighted a potential for unique contributions from individual and neighborhood SEP: ADI was significantly associated with vmPFC and hippocampal volume whereas individual income was related to amygdala and vmPFC volume. Interestingly, we did not replicate previous findings linking hippocampal volume to years of school (O'Shea et al., 2018; Noble et al., 2012); however, this relationship may be more apparent in children and aging adults, with some cross-sectional studies showing null results (c.f. Hanson, Chandra, Wolfe, & Pollak, 2011; Staff et al., 2012). Indeed, age is an important consideration when studying SEP and the hippocampus; in older adults, educational attainment moderates the detrimental effects of aging on the hippocampus (Noble et al., 2012).

Results of the three separate hierarchical multiple regression analyses demonstrated individual and neighborhood factors make unique contributions to structural volumes. Surprisingly, only female gender was related to amygdala volume. Although women have smaller brains, even after controlling for relative intracranial volume, a smaller amygdala is evident in females (Goldstein et al., 2001). Developmental timing may play an important role in quantifying the relationship between amygdala volume and socioeconomic variables. Recently, Gard and colleagues (2020) found neighborhood disadvantage was associated with a larger amygdala as well as amygdala reactivity to faces in early childhood and young adulthood. Another study demonstrated the relationship between individual SEP and amygdala volume varied by age, showing no association between income and amygdala volume in early childhood (Merz, Tottenham, & Noble, 2017). These seemingly contradictory findings may be

indicative that the amygdala is differentially impacted by neighborhood and individual SEP *and* that these associations are dependent on age (and likely gender).

Several studies, namely in early childhood and adolescence, have demonstrated the prefrontal cortex structure and function is susceptible to the stress connected to low SEP and we replicated structural findings demonstrating lower SEP is associated with smaller prefrontal cortex volume, specifically vmPFC volume (Hanson et al., 2015; Kiwshyama, Boyce, Jimenez, Perry, & Knight, 2009; Noble et al., 2015). In the full model, younger age and female gender was associated with smaller vmPFC, while every \$10,000 increase in annual household income was related to an increase in vmPFC volume. Broadly, the results of the hierarchical multiple regression analyses confirmed our hypothesis that neighborhood SEP is distinctively associated with adult brain morphology. We replicated Hunt and colleagues' (2020) finding that ADI is related to hippocampus volume. The only two significant regressors in the analysis predicting hippocampal volume were gender and ADI. For an individual with the average income *and* education, living in a disadvantaged neighborhood was associated with smaller hippocampal volume.

This study has several noteworthy limitations. First, the participants enrolled were recruited from a traumatically-injured population. While the structural scans included in these analyses were acquired two-weeks post-trauma, likely before any significant structural changes took place, we cannot definitively claim there was no effect of trauma. Secondly, the adult participants reported childhood trauma exposure retrospectively, often many years after the endorsed trauma would have occurred. Retrospective reporting often carries inherent bias which may include measurement

bias, false-reporting, or mis-remembering (Hardt and Rutter, 2004; Newbury et al., 2018). In addition, questionnaires on traumatic experiences may be influenced by any recent trauma or ongoing/current mental health symptoms (Colman et al., 2016; Newbury et al., 2018). Finally, we examined a single metric of morphology, cortical volume. While cortical volume can be viewed as an ideal index of the brain's overall "health", it does not capture the full extent of structural changes that occur throughout the lifespan. Cortical volume is influenced by both surface area and cortical thickness, two additional measures that can be, at specific developmental periods, distinct (Noble et al., 2015; Raznahan et al., 2011)

Exploratory Structural Equation Modeling

As part of an exploratory aim, we applied SEM to explore the relationships between individual SEP, neighborhood context, and brain morphology. SEM was particularly well-positioned to address this research question because it allowed for the creation of latent factors from observed variables (Kline, 2005). Each latent factor represented a theoretical construct (e.g. individual SEP) that could not be directly measured. The model fit indices, even after consultation of the model modification suggestions, indicated a poor fit for all models. SEM requires fairly large sample sizes and performs best with three or more observed variables per latent factor (Kline, 2005). In the current study, there were only two measures of individual SEP, education and income, and three of neighborhood SEP, ADI, robbery and homicide rates. While theoretically the technique may be better suited for studies examining the effects of SEP, the sample size demands likely influenced the results. Still the model explaining vmPFC volume aligned with the hierarchical multiple regression results, in that individual SEP

significantly explained volume variance. Future work should consider SEM when working with socioeconomic variables that may not fully capture SEP-related constructs (e.g. wealth, status, position, prestige, etc.) and collect *at least* three measure to include per latent construct.

Conclusions

Future directions should explicitly probe the intersectionality between race, gender, and SEP. An individual's multi-faceted identity influences their life experiences, which impact brain development and functioning across the lifespan. In the United States, individuals identifying as a racial or ethnic minority disproportionately live in disadvantaged neighborhoods (Pager and Shepherd, 2008; Houston, Wu, Ong, & Winer, 2004). While our full sample had sufficient variability in ADI to address the research question, it also reflected this reality, and therefore stratifying participants by race, gender, individual SEP, and neighborhood disadvantage was impractical. In our sample, as in other studies (e.g. Kind et al., 2014), the participants with higher ADI scores were more likely to be Black whereas White participants were more apt to live in advantaged neighborhoods. Practices such as redlining (i.e., the denial of services such as mortgages based on onerous terms, namely an individual's race or ethnicity) have facilitated residential racial segregation in the United States (Squires and Woodruff, 2019), thereby confounding neighborhood disadvantage and race and ethnicity (Squires and O'Connor, 2001). As all the analyses were collapsed across racial and ethnic identities and the study was not designed to stratify race, gender, and/or SEP differences, we conducted correlational rather than comparative analyses.

We demonstrated neighborhood disadvantage uniquely influences hippocampal size, even after controlling for income whereas income, but not ADI, is associated with vmPFC volumes. Although the impact of a smaller hippocampus, amygdala or vmPFC, throughout the lifespan is not fully understood, volumetric reductions are associated with functional impairments (Porcu, Wintermark, Suri, & Saba, 2020; Qing and Gong, 2016). Each structure does not work in isolation (Genon, Reid, Langner, Amunts, & Eickhoff, 2018) and it is probable that compensatory processes alleviate deficits in functioning (Cirstea and Levin, 2000). Moreover, the brain's ability to adapt and even heal throughout the lifespan offers an optimistic outlook that any neural impairments or reductions may be reconciled. By studying the nexus between the brain, experiences, and the environment, we may better understand how societal structures work in unison with a person's underlying biology and characteristics to impact health status. This cross-disciplinary approach may assist in predicting an individual's health outcomes and may lead to the development of better disease treatments and early interventions.

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