Childhood Adversity and Perceived Social Standing: Negative Associations of Trauma and Absence of Effects of Perceived Childhood Socioeconomic Status on Resting-State Functional Connectivity within a Central Visceral Circuit

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Abstract

Adverse experiences in childhood can have long lasting effects on adulthood stress neural pathways. Literature suggests that there may be different dimensional influences of threat and deprivation within a central visceral neural circuit. This circuit is comprised of regions such as the: subgenual anterior cingulate cortex (sgACC), paraventricular nucleus of the hypothalamus (PVN), bed nucleus of the stria terminalis (BNST) and amygdala; Therefore, playing an important role in stress and emotional regulation. At present, there is not much known about effects of adversity on this central, visceral neural network. Given the incidence and influence of early effects on neural networks, the influence between childhood threat and childhood socioeconomic deprivation and perceived social standing on the resting-state functional connectivity was examined. Threat was measured by measures of childhood traumatic events and abuse including THQ and CTQ. Socioeconomic deprivation (SED) was determined by a measure of childhood socioeconomic status (parental education level) and perceived social standing was measured by the community and United States Macarthur ladder. In this sample, lower BNST-PVN, amygdala-sgACC and PVN-sgACC connectivity was determined. No significant relationships were found between SED and resting-state connectivity or between perceived social standing in community or United States and resting-state connectivity. It is possible that threat in childhood may contribute to neural alterations which may lead to dysregulation in these

regions which may contribute to the development of affective disorders, given the vital role that these ROI-to-ROI connections play in emotional regulation and associations to disorders.

Introduction

Adverse experiences within childhood have been linked to alterations in adulthood stress reactivity. Adverse early life experiences have been linked to different effects across the dimensions of threat and deprivation and can influence stressor-evoked activity within central visceral neural circuits. This central visceral neural circuit plays a role in the regulation of stress responses and includes the subgenual anterior cingulate cortex (sgACC), paraventricular nucleus of the hypothalamus (PVN), bed nucleus of the stria terminalis (BNST), and amygdala (Banihashemi et al, 2022). Currently, the relationship between childhood adversity (including deprivation) and the resting-state connectivity of this central visceral network remains unclear and few studies have explored the effects within this neural circuit. We examined the relationship between childhood threat and measures of socioeconomic deprivation, using perceived social standing, on resting-state connectivity between our regions of interest (ROIs). This analysis took place with participants who were males and females (n = 100; mean age = 27.28, SD = 3.99; 59 females), with a full distribution of maltreatment history and symptom severity across multiple affective disorders. Resting-state data were acquired using a 7.2-min functional magnetic resonance imaging (fMRI) sequence; noted ROIs were applied as masks to determine ROI-to-ROI connectivity. Threat was determined by reported trauma history. Perceived socioeconomic status was determined by reported perception of parental

socioeconomic standing (SES) compared to others living in the United States or those living within the same community as the participant. Covarying for age, race and sex, greater childhood threat was significantly associated with lower amygdala-sgACC and PVN-sgACC connectivity. No significant relationships were found between perceived social standing and resting-state connectivity. Alterations in the patterns of resting-state connectivity between these stress-related ROIs may result from experiencing early childhood threat. These alterations may lead to dysregulated neural responses to stress within this neural circuit and subsequently be implicated risk for affective disorders including depression, anxiety, and PTSD.

Introduction

Experiences which occur early in life can be important in influencing neural, psychological, and physiological development. Adversity in early life has been well documented in contributing to alterations in brain structure, volume, and function. Understanding these relationships is vital because of its associated risk in mental health disorders. In fact, it has been linked to one-third of psychiatric disorders (Mclaughlin, 2012). Adversity in childhood can encompass a range of experiences including trauma, abuse, and neglect, deprivation and has been linked to a variety of physical and psychological disorders in adulthood (Mclaughlin, 2012; Nelson, 2020). These disorders include mood, anxiety, and substance abuse disorders as well as high blood pressure- and obesity (Genc et al, 2022). Given the prevalence and the gravity of physiological and pathological affects, understanding potential adaptions and alterations could lead to important advancements in understanding risk, pathology, and treatment of a variety of psychological health conditions. To investigate early childhood adversity, an emerging framework has been influencing in shaping the methodological design of study. The Dimensional Model for Childhood Adversity and Psychopathology (DMAP) has become a useful tool to study the effects of childhood adversity because it considers the type and frequency of adverse childhood experiences. The types of adversity are defined as dimensions of threat or deprivation (McLaughlin, 2010). Threat is defined as exposure to threatening or harmful experiences or stimulation or an experience that may affect physical integrity of an individual. Deprivation has been defined as lack of associated resources. While both dimensions may co-occur and have physiological effects on an individual, there are some differences in affects.

Threat has been linked dysregulations in the areas of emotional processing, fear learning, and decision making. Evidence suggests that threat can influence the development of the hippocampus, amygdala, and ventromedial prefrontal cortex. Within the amygdala, threat is linked to overactivation particularly in non-threatening situations and dysregulation. Deprivation has been linked to problems with cognitive performance in adolescents and adults who have experienced this dimension of adversity in childhood. Prior literature has linked these adversities to associated changes in brain structures measured with volume and cortical thickness including the prefrontal cortex, cingulate cortex, limbic structures, and temporal lobe (Dannlowski, U. et al, 2012; Van Harmelen, A. L. et a, 2010; Gold, A. L. et al, 2016). Childhood adversity is associated with changes to neural stressor-evoked responses both in childhood and adulthood. There have been marked changes to cortical thickness, alterations to white matter pathways, as well as resting state connectivity.

Impact of Socioeconomic Status (SES) Effects

Adversity in childhood does include effects of socioeconomic status (SES). Given that approximately 90% of the children of the world live in abject poverty, understanding the implications of socioeconomic status is important, as it affects a significant population of children each year (Schmidt et al, 2021; Unicef, 2020). Understanding the implications of this type of adversity is important because socioeconomic status has been implicated in numerous health conditions. Within the brain, disparities have been strongly implicated in risk for multiple psychiatric disorders including depression and anxiety disorders (Merz et al,2015). Children who perceive themselves to be a lower social status than the rest of their peers are also at higher risk for being depressed or having suicidal thoughts (Zou et al, 2020). Physiologically, lower SES has been linked to reduced gray matter in the hippocampus and anterior cingulate cortex (ACC), which are involved in cognitive skills including episodic memory and executive function and associated with smaller amygdala volume in adolescence (Zou et al, 2020).

Investigation into how socioeconomic impact on an individual shows that income, employment, and education impact an individual, as does psychosocial variables including self-rated health and neighborhood satisfaction, and perceived social standing. Investigation into how these circumstances may affect physiology have been assisted by utilization of the MacArthur ladder. The MacArthur ladder is a measure which looks at subjective socioeconomic status, which has to do with how an individual might perceive their own family's socioeconomic status in childhood (Adler et al, 2000; Gianaros et al, 2007). Having a lower socioeconomic status which is defined by having fewer resources or holding a lesser social standing than others is linked to an increased risk of many medical disorders (Gianaros et al, 2007; Adler et al, 1993,1994, 1999). A recent study has found that subjective social status, in which an individual reports their perception of their own social status was linked to psychological distress, conduct problems, substance abuse, and mental health issues (Rivenbark et al, 2019).

Introduction to Resting State

There is a blooming field of neuroimaging research that examines brain activity obtained during the "resting state" (which is when participants rest in the scanner without concentrating on any task) which can shed light on brain network activity between or within several structures. Higher or lower connectivity between regions can shed light on how the brain is functioning. Childhood adversity has been demonstrated to affect the activity of various regions in the brain.

Threat experiences in childhood have been linked to alterations in resting state connectivity in or between many regions of the brain. In children who are exposed to threat due to trauma, there has been reported higher activity between the amygdala and other regions (amygdala-sgACC cortex, amygdala-hippocampus, amygdala-salience network) (Marusak et al, 2015; Thomason et al, 2015;Rakesh et al 2021). However, adults who experienced threat vis trauma in childhood have been reported to have lower resting-state connectivity between the amygdala and other regions (amygdala-sgACC, amygdala-ventromedial prefrontal cortex, amygdala-orbitofrontal cortex/insula/hippocampus, amygdala-cuneus/precuneus (Herrings et al;2013'voxel et al, 2022; Rabillino et al, 2018).

Resting state literature has also detected emerging relationships between SES and functional connectivity. Lower SES has been linked to hypoactivity within executive network regions and hyperactivity within reward-related regions (Yaple and Yew, 2021). Socioeconomic deprivation leads to altered resting state connectivity in many networks and between many networks. Those who grow up in lower SES homes have been found to have lower within- and between-network connectivity (between ventral tegmental area (VTA), nucleus accumbens (NAcc), anterior hippocampus (aHipp), rostral anterior cingulate cortex (rACC)) than those growing up in high-SES homes (Sripada et al, 2014; Gao et 2015; Dejoesph et al,2022). This finding persists into adolescence and early adulthood. Experiencing poverty in childhood has also been shown to predict lower connectivity in key networks in adulthood (Brody et al, 2019; Tooley et al, 2020; Sripada et al,2014; Park et al, 2021). Based on previous literature, there is a trend that correlates individuals with low SES with hypoactivity within executive network regions and hyperactivity within reward-related regions (Yaple and Yew, 2021).

Study Goal

For our analysis, our goal was to focus on regions that contribute to stress regulation and emotional processing (Banihashemi et al, 2022). The circuit formed consists of the subgenual anterior cingulate cortex (sgACC), paraventricular nucleus of the hypothalamus (PVN), bed nucleus of the stria terminalis (BNST) and amygdala which together form a stress responsive, limbic forebrain-hypothalamic network. These regions form a central, visceral circuit which can be used to study resting state functional connectivity. Within this central, visceral circuit, the amygdala has been well studied for emotional processing, fear-encoding, emotional processing, emotional regulation, and anxiety. On the other hand, The BNST is involved in prediction of threat. All three regions have been studied and implicated in affective disorders and pathologies like PTSD, anxiety disorders, OCD, and depression (Insert citations).

Our Recent Work

To the date, there is little that is known about how childhood adversity might affect adulthood resting-state connectivity of this central visceral network. However, recently published work using this sample discovered that threat is associated with lower resting-state-connectivity in the central visceral limbic forebrain network (Banihashemi, 2022). This negative association in connectivity was found in three ROI-to-ROI connections. The connections are between BNST-PVN, Amygdala-sgACC and PVN-sgACC (Banihashemi et al, 2022). In that analysis, trauma, as measured by THQ, was reported to have a significant, negative association with BNST-PVN, Amygdala-sgACC and PVN-sgACC (Banihashemi, 2022).

Current Goal

The present investigation has a few goals. The first is to determine the relationship that exists between perceived social standing in childhood and adulthood resting-state functional connectivity in this central visceral circuit. Based on this prior analysis, three three ROI-to-ROI regions were selected to investigate how resting state connectivity might be influenced by deprivation and perceived socioeconomic status experienced in childhood. The ROI-to-ROI regions chosen to examine were BNST-PVN, Amygdala-sgACC and PVN-sgACC. (Banihashemi et al, 2022).

The secondary aim of this investigation to also explore the relationship that may exist between deprivation and adulthood resting-state functional connectivity within these ROI-to-ROI regions. There is an abundance of information that suggests environment and socio-economic status may affect the physiology these central visceral regions that play an important role in emotional process and stress regulation. The goal of this analysis is to examine the effects of deprivation and perceived social standing on resting-state functional connectivity. A greater understanding of how types of experiences might lead alterations in these regions could be signficant to understanding how childhood adversity and socioeconomic status contribute to alternations, pathology, and affective disorders.

Materials And Methods

Participants

Participants for this study were recruited from Allegheny County, Pittsburgh, Pennsylvania for another study (Banihashemi et al, 2022) using various methods including referrals from other research studies, and online and bus advertisements. Of the 1,020 140 contacts made, 111 (18.5%) underwent informed consented and were enrolled in a study. Of those 141 consented, 100 (90%) participants completed study procedures.

The total number of participants is n=100. Of those participants, 59 were female and 41 were male. Age of participants is mean of 27.28 years and standard deviation, SD, is 3.99. Demographically, of 100 participants that completed the study the breakdown is 45% White, 36% as Black or African American, 13% Asian, 4% multiracial, and 2% biracial. Hispanic or Latin American descent was reported by a total of 7 individuals.

Data was collected All participants provided informed consent after receiving an explanation of study protocols and were examined with the approval of the University of Pittsburgh Institutional Review Board. The exclusion criteria were: Magnetic resonance imaging (MRI) contraindications (e.g., claustrophobia, metal in the body, severe visual or auditory impairment), pregnancy, left-handedness, cardiovascular disease and diabetes, neurological disorders (including seizure disorders, migraine disorder, traumatic brain injury, or neurodegenerative disorders), psychotropic medications or any medications affecting cardiovascular or neural function, suicidality or marked functional impairment, and current psychiatric disorders (bipolar, psychotic disorders, substance abuse or dependence) except for depression, anxiety or trauma.

Childhood Adversity Measures

Experiences of threat in childhood were assessed using two questionnaires: the Childhood Trauma Questionnaire (CTQ) and the Trauma History Questionnaire (THQ). The CTQ is a 28-item Likert-type scale that examines five subscales of maltreatment: physical, emotional, and sexual abuse, and physical and emotional neglect. The THQ is a 24-item questionnaire that assesses the occurrence of traumatic events throughout the life course. For this study, an adapted version of the THQ was used in which participants responded yes or no to indicate whether a particular event occurred and then selected the relevant age range(s): age 0–11, age 12–17, and age > 18. Traumatic events included experiences with crime, environmental disasters, injury, or death, as well as physical or sexual abuse.

Socioeconomic Status in Adulthood

Participant's socioeconomic status was measured by self-reporting of their respective adulthood income in their household.

MacArthur ladder

Respondents view a drawing of a ladder with 10 rungs (right) and are instructed the following, "At the top of the ladder are the people who are the best off, those who have the most money, most education, and best jobs. At the bottom are the people who are the worst off, those who have the least money, least education, worst jobs, or no job. Please place an 'X' on the rung that best represents where you think your [parent] stands on the ladder." Participants were asked to compare their perception of their parent's socioeconomic standing to those in the community, or to others in the United States.

Figure 1. *The figure above shows the ten rung Macarthur ladder, with directions as it would be presented to participants (Adler,2000).*

The MacArthur ladder (Figure 1) is a measure which looks at subjective socioeconomic status, which has to do with how an individual might perceive the socioeconomic status of their family in childhood (Adler et al, 2000; Gianaros et al, 2007). Having a lower socioeconomic status which is defined by having fewer resources or holding a lesser social standing than others is linked to an increased risk of many medical disorders (Gianaros et al, 2007; Adler et al, 1993,

The MacArthur Scale of Subjective Social Status shows a ladder-like image with 10 points on the scale where participants are asked to put an X nearest the rung corresponding to their standing or ranking in relation to other individuals in the United States based on income, education, and occupational prestige. There are community and United States social ladders. The Community ladder asks participants to rate their perception of socio-economic status based on their surrounding community, while the United States ladder asks participants to rate their perception of their socioeconomic status compared to others in the United States.

Childhood Socioeconomic Deprivation

A sociodemographic inventory was used to assess childhood and adulthood SES. Maximum parental education level was used to determine childhood SES; the participants' own educational level determined adulthood SES. Both were presented as a 9-point education level scale (0 - No high school diploma, 1 – GED, 2 – High school diploma, 3 – Technical training, 4 – Some college, no degree, 5 – Associate degree, 6 – Bachelor's degree, 7 – Master's degree, 8 – MD/PhD/JD/PharmD). The Childhood Deprivation construct encompasses low SES, socioeconomic disadvantage or neighborhood deprivation (McLaughlin et al., 2014; Webb et al., 2017; Berti and Pivetti, 2019; Morris et al., 2019). Further, education level is often used as a measure of SES and is associated with mental health inequalities (Reiss, 2013), physiological stress (Ursache et al., 2017) and physical health, especially cardiovascular disease risk

(Winkleby et al., 1992). Thus, we used maximum parental education level (reverse coded) as our primary measure of childhood socioeconomic deprivation (SED). Adulthood SES was used as a covariate.

Negative Life Events

The 24-item Life Events List assesses significant life events experienced by the participant within the past 12 months (e.g., unemployment, separation or divorce, serious illness, death of someone close) (Cohen et al., 1991). Participants indicate whether or not they have experienced an event in the past year with follow up questions assessing valence and/or details if endorsed. This inventory was used to assess the total number of negative life events, which was used as a covariate.

Resting State fMRI Preprocessing and Analysis

Resting-state fMRI Preprocessing and Analysis Resting state fMRI data were preprocessed using Statistical Parametric Mapping software (SPM12, 249 http://www.fil.ion.ucl.ac.uk/spm/). Motion correction was applied through realignment of each 250 blood-oxygen-level dependent (BOLD) image to the mean reference image. The structural image was then coregistered to the mean functional image. Segmentation was performed on the structural image 252 using probability maps for six tissue classes, generating a deformation field that was then applied to 253 the functional images during normalization of all images to standard Montreal Neurological Institute 254 (MNI) space (2mm isotropic resolution). Smoothing was applied to functional images using a 4 mm 255 full-width-at-half-maximum Gaussian kernel. 256 Resting-state connectivity analyses were performed using standard SPM-based functions (in257 house MATLAB code was used to wrap these functions). Translation (mm) and rotation (deg) was assessed for each participant; motion was low across the sample of 100 participants (Translation: mean = 1.13mm, SD = 0.37; Rotation: mean = 0.86 degrees, SD = 0.73). Our threshold for maximum translation was 3mm of motion and none exceeded this. Motion artifact reduction was applied to smoothed functional images using the SPM BrainWavelet Toolbox wavelet despiking methods to identify and filter spike artifacts. A principal component analysis was performed by extracting five invariants of the BOLD signal principal time series from the white matter and cerebrospinal fluid simultaneously using singular value decomposition. Using multiple linear regression, the time series at each voxel was adjusted by applying these tissue components and the raw values of the six motion parameters (not their derivatives) from preprocessing as covariates. The residual time series was extracted from each voxel and we used a series of cosines to model the band pass Butterworth filter (0.008-0.15 Hz), which was applied on the residuals.

Data Analysis

The goal was to examine childhood deprivation and perceived social standing's effect on and resting state connectivity between our ROIs in three ROI-to-ROI connections (Amygdala-sgACC, BNST-PVN, PVN-sgACC). The hierarchical regression model covaried for age, race, and sex in Step 1. Step 2 involved examining perceived social standing via both community and United States standards using the MacArthur Ladder. These results were examined separately to determine if one had a more significant relationship than the other. Step 3 of the model entailed examining parental education level, CTQ, and measures of physical neglect. Step 4 involved THQ or CTQ, Step 5 of the model involved looking adulthood THQ, educational level, negative life events within the past year.

RESULTS

Trauma (Trauma History Questionnaire)

The current analysis upheld some findings determined previously in this sample. There is resting-state functional connectivity with Amygdala-sgACC (ß = −0.312; p = 0.003. Threat as measured by THQ had a significant, negative relationship between the Amygdala and subgenul anterior cingulate cortex (ß = -.390; p =.002, Table 1). This finding did remain significant with the introduction of additional covariates (adulthood trauma, adulthood negative life events, adulthood SES). In this analysis with the introduction of perceived social standing in community (Table 1) or in the United States (Table 2), there was no significant relationship with the other two ROI-to-ROI connections that were analyzed.

Perceived Social Standing (Community and US Macarthur Ladders)

One of the primary goals of this analysis was to examine closely the implications of perception of childhood socioeconomic standing, or perceived social standing, would affect connectivity within this central, visceral circuit. To examine perceived social status, participants were asked to rank their perceived social status using the MacArthur ladders for community and for united states. Upon investigation, it was determined that there is no significant relationship between perceived social standing either in the community or in the United States (Table 1 and Table 2).

Table 1. *Average Perceived Social Standing compared to Community*

Variable	Amygdala-sgACC	BNST-PVN	PVN-sgACC

Step		St. Beta	t	*p.*	St. Beta	t	*p.*	St. Beta	t	*p.*
1	**Age**	-.036	-.358	.721	-.107	-1.050	.296	.113	1.166	.247
	Race	-.177	-1.750	.083	.092	.910	.365	-.038	-.388	.699
	Sex	.007	.068	.946	.096	.943	.348	.301	3.111	.002
2	**Age**	-.038	-.375	.708	-.109	-1.063	.291	.110	1.134	.260
	Race	-.179	-1.765	.081	.090	.881	.380	-.041	-.421	.675
	Sex	.007	.068	.946	.096	.939	.350	**.301**	**3.101**	**.003**
	Perceived Social Standing (Community)	.044	.440	.661	.042	.411	.682	.059	.614	.541
3	**Age**	-.025	-.236	.814	-.816	2.239	.417	.110	1.134	.260
	Race	-.181	-1.770	.080	.856	-.816	.394	.149	1.478	.143
	Sex	-.003	-.031	.976	.755	.856	.452	-.045	-.466	.642
	Perceived Social Standing (Community)	.062	.569	.571	.648	.755	.519	.271	2.732	.008
	Physical Neglect	-.050	-.432	.667	-.708	.648	.481	.113	1.088	.280
4	**Age**	.000	-.002	.998	-.071	-.670	.504	.168	1.699	.093
	Race	-.119	-1.195	.235	.129	1.255	.213	.001	.008	.994
	Sex	.014	.142	.888	.090	.878	.382	**.283**	**2.931**	**.004**
	Perceived Social Standing (Community)	.059	.561	.576	.069	.636	.527	.110	1.088	.279
	Physical Neglect	.120	.977	.331	.031	.241	.810	-.024	-.202	.841
	THQ 0 to11	**-.359**	**-3.199**	**.002***	-.238	-2.057	.043	**-.265**	**-2.443**	**.016**
5	**Age**	1.551	.124	.959	.008	.070	.945	.178	1.551	.124
	Race	-.100	.920	.182	.118	1.147	.254	-.010	-.100	.920
	Sex	2.485	.015	.462	.050	.447	.656	**.264**	**2.485**	**.015**
	Average Perceived Social Standing (US)	1.135	.260	.454	.052	.477	.634	.117	1.135	.260
	Physical Neglect	-.030	.976	.242	.016	.122	.903	-.004	-.030	.976
	THQ 0-11	**-2.131**	**.036**	**.002***	-.163	-1.309	.194	**-.253**	**-2.131**	**.036**
	THQ > 18	.484	.630	.577	-.178	-1.358	.178	.060	.484	.630
	Parental Education	-.436	.664	.807	-.150	-1.456	.149	-.043	-.436	.664
	Negative Life Events	-.825	.412	.351	-.083	-.635	.527	-.102	-.825	.412
	Total Income	**.738**	**.462**	**.012***	-.101	-.886	.378	.080	.738	.462

TABLE 1*. Hierarchical linear regression results are listed above. Threat in childhood (trauma from ages 0-11) and central visceral network connectivity is reported here Also reported is the relationship between perceived community social standing and central visceral connectivity in three ROI-to-ROI regions.* ***Please note*** *bolded values are indicative of statistical significance of p < .05.*

Table 2. Average Perceived Social Standing compared to others in the United States

Step	Variable	Amygdala-sgACC			BNST-PVN			PVN-sgACC		
		St. Beta	t	*p.*	St. Beta	t	*p*	St. Beta	t	*p.*
1	**Age**	-.036	-.358	.721	-.107	-1.050	.296	.113	1.166	.247
	Race	-.177	-1.750	.083	.092	.910	.365	-.038	-.388	.699
	Sex	.007	.068	.946	.096	.943	.348	**.301**	**3.111**	**.002***
2	**Age**	.003	.028	.978	-.067	-.635	.527	.155	1.536	.128
	Race	-.175	-1.732	.086	.094	.936	.352	-.035	-.365	.716
	Sex	-.002	-.021	.984	.087	.855	.395	**.291**	**3.020**	**.003***
	Perceived Social Standing (US)	-.133	-1.267	.208	-.133	-1.271	.207	-.142	-1.419	.159
3	**Age**	.002	.016	.987	-.062	-.571	.569	.171	1.651	.102
	Race	-.175	-1.723	.088	.094	.928	.356	-.036	-.372	.711
	Sex	-.001	-.010	.992	.082	.790	.431	**.277**	**2.810**	**.006**
	Perceived Social Standing (US)	-.134	-1.239	.218	-.128	-1.181	.240	-.125	-1.214	.228
	Physical Neglect	.006	.052	.958	-.057	-.529	.598	-.075	-.725	.470
4	**Age**	.010	.096	.924	.131	1.283	.203	.177	1.745	.084
	Race	-.117	-1.175	.243	.093	.910	.365	.006	.063	.950
	Sex	.017	.169	.866	-.084	-.771	.443	**.290**	**2.997**	**.003***
	Perceived Social Standing (US)	-.066	-.616	.539	.069	.576	.566	-.076	-.732	.466
	Physical Neglect	.152	1.310	.193	-.084	-.771	.443	.030	.267	.790
	THQ 0-11	**-.345**	**-2.999**	**.003***	.069	.576	.566	-.249	-2.232	.028
5	**Age**	-.007	-.058	.954	.012	.102	.919	.173	1.501	.137
	Race	-.129	-1.305	.195	.120	1.173	.244	-.003	-.035	.972
	Sex	.087	.809	.420	.056	.504	.615	**.274**	**2.572**	**.012**
	Average Perceived Social Standing (US)	-.048	-.434	.665	-.071	-.619	.538	-.046	-.417	.678
	Physical Neglect	.177	1.514	.134	.040	.325	.746	.043	.370	.712
	THQ 0-11	**-.385**	**-3.183**	**.002***	-.154	-1.227	.223	**-.249**	**-2.063**	**.042**
	THQ > 18	.074	.585	.560	-.173	-1.315	.192	.064	.505	.615
	Parental Education	-.027	-.275	.784	-.150	-1.456	.149	-.049	-.493	.623
	Negative Life Events	.128	1.005	.318	-.066	-.499	.619	-.091	-.718	.475
	Total Income	**.269**	**2.446**	**.016***	-.114	-.996	.322	.064	.587	.559

TABLE 2. *Hierarchical linear regression results are listed above. Threat in childhood (trauma from ages 0-11) and central visceral network connectivity is reported here Also reported is the relationship between perceived community social standing and central visceral connectivity in three ROI-to-ROI regions.* ***Please note****: bolded values are indicative of statistical significance of p < .05.*

Exploratory Analyses

An exploratory analysis examined CTQ instead of THQ as a measure of threat, The results can be found in Table 3 and Table 4. The ROI-to-ROI region of Paraventricular Nucleus and subgenual anterior cingulate cortex was selected based on apriori analysis in which CTQ Threat had only a significant, negative association between PVN-sgACC (Banihashemi, 2022). This finding did not remain significant with the introduction of additional adulthood covariates and perceived social standing either in community or the United States. Hierarchical regression analysis found that there is no significant relationship between Perceived Social Standing in Community or the United States or CTQ threat on the resting connectivity of PVN-sgACC.

Table 3. *Exploratory Analysis of CTQ (threat) and Perceived Social Standing in Community*

Step	Variable	PVN-sgACC		
		St. Beta	t	*p.*
1	**Age**	.113	1.166	.247
	Race	-.038	-.388	.699
	Sex	**.301**	**3.111**	**.002***
2	**Age**	.155	1.536	.128
	Race	-.035	-.365	.716
	Sex	**.291**	**3.020**	**.003***
	Perceived Social Standing (Community)	-.142	-1.419	.159
3	**Age**	.171	1.651	.102
	Race	-.036	-.372	.711
	Sex	**.277**	**2.810**	**.006***
	Perceived Social Standing (Community)	-.125	-1.214	.228
	Physical Neglect	-.075	-.725	.470
4	**Age**	.178	1.735	.086
	Race	-.007	-.070	.944
	Sex	**.259**	**2.638**	**.010***
	Perceived Social Standing (Community)	-.069	-.637	.526
	Physical Neglect	.037	.300	.765
	CTQ Threat	-.214	-1.625	.108
5	**Age**	.206	1.783	.078
	Race	-.011	-.112	.911
	Sex	**.233**	**2.184**	**.032***
	Average Perceived Social Standing (Community)	-.010	-.088	.930
	Physical Neglect	.081	.616	.539
	CTQ Threat	-.236	-1.737	.086
	THQ > 18	.012	.097	.923
	Parental Education	-.062	-.623	.535
	Negative Life Events	-.123	-.969	.335
	Total Income	.089	.797	.428

TABLE 4. *Hierarchical linear regression results are listed above. The relationship between threat (CTQ) and ROI-to-ROI resting state functional connectivity between paraventricular nucleus and subgenual anterior cingulate cortex. . Perceived Social Standing in the United States and resting state functional connectivity between the paraventricular nucleus and subgenual anterior cingulate cortex Is measured in step 2 of the model. No statistical significance was reported.*

Table 4. *Exploratory Analysis of CTQ (threat) and Perceived Social Standing in Community between Paraventricular Nucleus and subgenual anterior cingulate cortex*

Step	Variable	PVN-sgACC		
		St. Beta	t	*p.*
1	**Age**	.113	1.166	.247
	Race	-.038	-.388	.699
	Sex	**.301**	**3.111**	**.002***
2	**Age**	.110	1.134	.260
	Race	-.041	-.421	.675
	Sex	**.301**	**3.101**	**.003****
	Perceived Social Standing (Community)	.059	.614	.541
3	**Age**	.149	1.478	.143
	Race	-.045	-.466	.642
	Sex	**.271**	**2.732**	**.008***
	Perceived Social Standing (Community)	.113	1.088	.280
	Physical Neglect	-.149	-1.362	.177
4	**Age**	.181	1.810	.074
	Race	-.008	-.080	.936
	Sex	**.241**	**2.460**	**.016***
	Perceived Social Standing (Community)	.169	1.617	.109
	Physical Neglect	-.002	-.018	.986
	CTQ Threat	**-.290**	**-2.280**	**.025***
5	**Age**	.221	1.947	.055
	Race	-.013	-.138	.890
	Sex	.217	2.060	.042
	Average Perceived Social Standing (Community)	.182	1.706	.092
	Physical Neglect	.047	.361	.719
	CTQ Threat	**-.297**	**-2.265**	**.026***
	THQ > 18	.020	.163	.871
	Parental Education	-.047	-.483	.630
	Negative Life Events	-.119	-.976	.332
	Total Income	**.115**	**1.043**	**.300***

TABLE 3. *Hierarchical linear regression results are listed above. The relationship between threat (CTQ) and ROI-to-ROI resting state functional connectivity is measured here. Perceived Social Standing in Community and resting state functional connectivity between the paraventricular nucleus and subgenual anterior cingulate cortex is measured as well. No statistical significance was reported.*

DISCUSSION

Dimensions of early life adversity have been studied on functional connectivity, gray matter, and white matter structural integrity. There is evidence that the dimensions of threat and deprivation may affect different neural correlated or that they might have divergent effects on the same pathways or mechanisms. Within the central, visceral network chosen for this analysis, few studies have examined how childhood adversity may affect the connectivity between or in these regions (amygdala, sgACC, BNST, pVN). Few studies how examined how perceived social standing would affect the connectivity within or between these regions. This analysis aimed to examine these regions to determine how childhood threat and perception of social standing might affect the resting state connectivity in this circuit. Originally, the hypothesis laid forth were that perceived social standing and threat would have effects within this central, visceral circuit. We hypothesized that threat and deprivation would have differential, potentially opposing effects on resting-state connectivity within this central visceral network. After analysis of data, it was discovered that threat (THQ, 0-11) was associated with lower connectivity within the ROI-to-ROI connection between the Amygdala-sgACC and PVN-BNST. However, an effect community or United States social standing was not found within any of the other ROI-to-ROI connections. Additionally, a signficant finding of adulthood socioeconomic status was found in the Amygdala-sgACC ROI.

Moderating Effects of Adulthood SES

During our analysis, a significant relationship was detected with higher connectivity between Amygdala-sgACC and adulthood SES, as measured by total household income earned in adulthood. This finding, examined in the greater context of adulthood SES literature, suggests that adulthood socioeconomic status could serve as a moderating or protective factor for lower SES status in childhood and adolescence. Lower childhood SES and higher adulthood SES predicted better health outcomes including less age-related decline and less adverse effects due to low childhood SES (Chan et al, 2017). Conversely, continued low SES into adulthood has been poorer cognitive function in adulthood and age-related cognitive decline (Chan et al, 2017). While few studies have examined the effect of adulthood socioeconomic status on resting state connectivity within this central visceral neural circuit, research into higher adulthood SES suggests that perhaps it may serve as a moderating or protective factor to age or deprivation-related decline (Chan et al,2017). Lower socioeconomic status in adulthood is linked to reduced resting state network organization and lower cortical gray matter thickness (MJ Farah, 2017; Chan et al, 2017). Some studies suggest that an individual's childhood SES cannot wholly account for the relationship between current SES and functional network organization (Chan et al, 2017).

THQ finding

The sgACC-amygdala connection has been implicated in mood disorders like anxiety and depression. The amygdala shares an indirect connection to the prefrontal cortices (PFC) via the subgenual anterior cingulate cortex, which serves an important role in both cognitive and emotional networks and can help modulate bottom-up emotional responses in the amygdala (Scharnowski et al, 2020). However, it remains unclear if positive-social emotion upregulation of the amygdala occurs directly through the dorsomedial PFC (dmPFC) or indirectly linking the bilateral amygdala with the dmPFC via the subgenual anterior cingulate cortex (sgACC), an area which typically serves as a gatekeeper between cognitive and emotion networks.

Sex-linked Differences and the Function of Bed Nucleus of Stria Terminalis-Paraventricular Nucleus Resting State Connectivity

We found a significant result of sex differences in the functional conenctivty between BNST-PVN. This finding replicates the one previously found within this sample (Banihashemi, 2022). The BNST works by mediating responses to distant, less predictable threats in future-oriented anxiety states. The BNST is interconnected with essential emotional processing regions, including prefrontal cortex, hippocampus, and amygdala. It is activated by stressor exposure and undergoes neurochemical and morphological alterations because of stressor exposure. Research suggests that there might be stronger BNST-hypothalamus structural connectivity in women, which could contribute to sex differences in substance abuse, namely alcohol abstinence risk for relapse (Flook et al, 2021). BNST is also heavily implicated in several other pathologies, including addiction, anxiety disorders, and PTSD (Lebow et al, 2016; Awasthi et al, 2020; Maeng et al, 2015). The SgACC-Amygdala ROI-to-ROI connection has been implicated in depression and anxiety disorders, as well (Connolly, 2013). Both the BNST and sgACC play an important role in emotional response and regulation. Sex linked differences in the connectivity of these regions is important as it is known that incidence of anxiety disorders and posttraumatic stress disorders (PTSD) is significantly higher in women than in men, almost two times higher (McLean et al, 2012). There are sex-linked differences in stress responsivity. Male stress involves relies on activity in the bed nucleus of the stria terminalis (BNST), whereas the female stress effect depends on mPFC activity (Bangasser, Santollo, & Shors, 2005; Bangasser & Shors, 2010; Maeng, Waddell, & Shors, 2010). The BNST appears to be involved in context fear expression in males, but not in females. The lateral amygdala was active in both sexes during context fear expression. Further, the reactivity of the HPA axis is different in males and females as females may have faster HPA reactivity and a increased release of stress hormones (Goel, Workman, Lee, Innala, & Viau, 2014). Further research into this area is ongoing and need to be done to determine what sex-related differences may contribute to subsequent pathologies.

Subjective Socioeconomic Status

The hypothesis was that there would be effects of perceived social standing within both the community and the United States on resting state functional connectivity within this central visceral circuit. However, this hypothesis was not supported. The Macarthur ladder has been well established to serve as a measure of perceived social standing in childhood. While little research exists on the resting state connectivity within the central, visceral neural circuit examined in this analysis, there is a multitude of data that examines influences of socioeconomic standing and SES on resting state functional connectivity. Research suggests that lower socioeconomic status is linked to neural alterations. Children from economically disadvantaged families may have an increased risk of mood disorders including depression (Hynek et al, 2022; Chen et al 2022; Dufford et al, 2019). Further, research suggests that a lower perceived social standing is linked to lower volume in the pACC (Gianaros, 2007). We found no signficant findings with relation to community or broader United States perceived social standing on our central, visceral neural network. Further research needs to be done to ascertain differential effects of deprivation and trauma on this central, visceral neural network.

Limitations

This study is not without its limitations. One limitation of the design of the study was the cross-sectional nature. The cross-sectional nature of this sample means that future work will need to be done to determine how dimensions affect the central visceral network as individuals develop. Literature has supported the theory that principals of neural connectivity at one point in life may be adaptive, while at another may confer risk (Tottenham, 2013). There are a range of sensitive periods during which adverse experiences may impact an individual. However, frequency and severity of childhood adversity have been demonstrated to have physiological effects. In this respect, the cross-sectional design of the study enables participants to be recruited who had experienced a range of physical abuse severity as well as socioeconomic statuses in childhood.

Additionally, a limitation in examining perceived social standing or SES might influence resting state functional connectivity of participants was the lack of recruitment for variety of SES backgrounds and environments. For this analysis, data was drawn from a prior study and were not selected on the basis income in childhood or adulthood (Banihashemi, 2022). Subsequently there was no matching or examination of higher versus lower income individuals. However, as discussed previously, there is some level of consistency of our findings with other human research. Additionally, there was a relatively even distribution of childhood SES in this sample.

Although the purpose of this investigation was not to examine effects of race or other, additional, environmental factors as part of deprivation, it is well-documented that certain populations in the United States, namely black Americans, commonly experience worse mental health outcomes and increased levels of stress in lower SES environments than white Americans living in the United States. Race and perceived socioeconomic standing may be related, and different racial groups may perceive their social standing differently, which may have physical and mental health associations (Singh-Manoux et al, 2003; Singh-Manoux et al, 2005; Ostrove et al, 2000; Reitzel et al, 2013; Wilkinson, 2006; Chen & Paterson, 2006). Further research needs to be done to determine how additional demographic and environmental factors that can affect ROIS relevant to stress in adulthood resting state functional connectivity at rest.

Future Directions

At present, more information is needed regarding the functioning of this central, visceral neural circuit and dimensions of adversity as there is much that still needs to be determined. Future analysis must also be done on varying measures of adulthood SES to determine what type of effect it may have resting-state functional connectivity, and if it may potentially act as a moderating agent on childhood adversity. Additionally, further research needs to be done to capitalize on advanced in drawing manual and creating automatic segmentations of regions of interest (Banihashemi et al, 2015; Wu et al, 2019; Banihashemi et al, 2022).

Conclusion

As highlighted by this investigation, threatening experiences in childhood might influence this central, visceral network. However, no signficant relationship was detected with perceived social standing within the participants community or compared to others within the United States, as measured by the MacArthur ladder on this central visceral network. Additionally, it seems as if there higher connectivity within this central visceral network as a result of adulthood income. This finding could be important in understanding adulthood moderating effects on adversity. These findings have functional imaging implications that suggest potential alterations in emotion regulation and processing (particularly of stress), responses to threatening stimuli and stressors. Specifically, among the relationships seen in our analysis, the Amyg-sgACC and BNST-PVN play an important role in the relationship between threatening experiences in childhood and connectivity in adulthood. Adulthood income was seen to have a positive relationship on resting state connectivity in the Amyg-sgACC and BNST-PVN. These findings highlight that adversity and SES may result in altered patterns of resting-state connectivity between these ROIS. These alterations could lead to changes in neural responses to stress and emotional processing. Alterations could also contribute to risk for later affective disorders. Further research in this area may be signficant to broaden understanding of neural links between how childhood adverse experiences mechanistically affect the neural pathways, as well as contribute to disorders.

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