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Childhood Maltreatment and Amygdala-Mediated Anxiety and Posttraumatic Stress Following Adult Trauma

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ABSTRACT

BACKGROUND: Childhood abuse (physical, emotional, and sexual) is associated with aberrant connectivity of the amygdala, a key threat-processing region. Heightened amygdala activity also predicts adult anxiety and posttraumatic stress disorder (PTSD) symptoms, as do experiences of childhood abuse. The current study explored whether amygdala resting-state functional connectivity may explain the relationship between childhood abuse and anxiety and PTSD symptoms following trauma exposure in adults.

METHODS: Two weeks posttrauma, adult trauma survivors (n = 152, mean age [SD] = 32.61 [10.35] years; women = 57.2%) completed the Childhood Trauma Questionnaire and underwent resting-state functional magnetic resonance imaging. PTSD and anxiety symptoms were assessed 6 months posttrauma. Seed-to-voxel analyses evaluated the association between childhood abuse and amygdala resting-state functional connectivity. A mediation model evaluated the potential mediating role of amygdala connectivity in the relationship between childhood abuse and posttrauma anxiety and PTSD.

RESULTS: Childhood abuse was associated with increased amygdala connectivity with the precuneus while covarying for age, gender, childhood neglect, and baseline PTSD symptoms. Amygdala-precuneus resting-state functional connectivity was a significant mediator of the effect of childhood abuse on anxiety symptoms 6 months posttrauma (B = 0.065; 95% CI, 0.013–0.130; SE = 0.030), but not PTSD. A secondary mediation analysis investigating depression as an outcome was not significant.

CONCLUSIONS: Amygdala-precuneus connectivity may be an underlying neural mechanism by which childhood abuse increases risk for anxiety following adult trauma. Specifically, this heightened connectivity may reflect attentional vigilance for threat or a tendency toward negative self-referential thoughts. Findings suggest that childhood abuse may contribute to longstanding upregulation of attentional vigilance circuits, which makes one vulnerable to anxiety-related symptoms in adulthood.

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Childhood maltreatment refers to experiences of abuse and/or neglect and is common. Approximately 40% of youth will experience some form of maltreatment (abuse or neglect) by the age of 18 years (1,2). The dimensional model of adversity and psychopathology argues that at least 2 distinct components of childhood maltreatment emerge: threat (referred to as childhood abuse in this article), which includes the presence of harm, and deprivation, which is often conceptualized as neglect and includes the absence of met needs (3,4). Experiences of childhood abuse, such as sexual or physical abuse (3,5), are related to adverse emotional, behavioral, neural, and psychopathological outcomes; these outcomes may occur immediately during childhood and often extend into adulthood (3,6)

Specifically, childhood abuse has been related to challenges in effective emotional processing, such as attenuated extinction in fear learning (3,5). Behaviorally, experiences of childhood abuse are associated with deficits in emotional regulation, such as poorer automatic regulation [i.e., slower adaptation to emotional conflict on a Stroop task (5)]. Other research has found that children who experience physical abuse were less accurate at differentiating between facial expressions of emotion but showed a bias toward recognizing angry faces (7). Psychophysiological data support such findings; children who experienced physical abuse exhibited selective attention (as measured by event-related potentials) to angry facial cues and had difficulties disengaging from such cues (8). This research suggests that children who experience abuse are conditioned to rapid orientation to angry and threatening cues and struggle to disengage from such stimuli. These emotional and attentional challenges persist into adulthood (9,10).

The longstanding impact of childhood abuse raises the question of how these early-life experiences affect future

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responses to stress and trauma. Just as experiencing abuse in childhood is common, so is adulthood trauma exposure. An estimated 70% of adults will experience at least one traumatic event during their lifetime, ranging from a natural disaster to combat exposure and physical violence (11,12). Trauma exposure increases an individual's likelihood of all psychiatric disorders, including generalized anxiety disorder, major depressive disorder, panic disorder, and posttraumatic stress disorder (PTSD) (13). More specifically, exposure to multiple traumatic events across the life span linearly increases risk for these adverse outcomes (14), such that a trauma history is often reported as a risk factor for PTSD after a subsequent trauma (15). However, a gap remains in integrating the interrelations between childhood abuse, neurobiological changes, and adult outcomes, particularly among those further exposed to adulthood trauma. Therefore, it is important to understand the neurobiological mechanisms by which childhood abuse may impact the development of psychopathology in the aftermath of adult trauma.

The Neurobiology of Childhood Maltreatment and Fear Processing

Researchers have also explored the neurobiological underpinnings of emotional processing deficits, but specific associations with abuse remain underexplored. Experiences of maltreatment have been associated with aberrant structure and function of the amygdala, a central node for threat detection and processing (3), such that studies across the life span have consistently found increased amygdala reactivity to negative stimuli following trauma in childhood (3,16). This indicates hyperactivity of the region at rest, an overactive fear response, and elevated activation during tasks that involve labeling and responding to emotions using faces as stimuli (3,17,18). Research has also documented significant associations between amygdala resting-state functional connectivity (rsFC) patterns and childhood maltreatment. Adults who experienced childhood emotional maltreatment (including both abuse and neglect, measured retrospectively) exhibit decreased amygdala rsFC with the precuneus and lateral occipital cortex (19). Van der Werff *et al.* (19) also found reduced positive rsFC of the amygdala with the left orbitofrontal cortex, insula, putamen, and hippocampus. During emotion identification, however, adults who had experienced child maltreatment (including both abuse and neglect) demonstrated greater amygdala-hippocampus and parahippocampal gyrus connectivity. The same study also found increased positive rsFC between the amygdala and the hippocampus as well as the prefrontal cortex (20). Similarly, greater rsFC of the amygdala with the hippocampus, parahippocampus, and right inferior temporal gyrus was evident in a small study of methamphetamine-dependent adults with a history of child maltreatment (21). Taken together, this work reveals a pattern of hyperactivity of the amygdala and greater connectivity of the amygdala with other threat-related regions (3,17,18).

Prior research highlights that experiences of childhood maltreatment are related to changes in emotional regulation and threat-processing circuitry, with the amygdala as a major region of interest. However, research has yielded mixed findings regarding the directionality of findings, i.e., whether childhood maltreatment is related to increased rsFC of the amygdala and other brain regions (20,21) or reduced connectivity (19,22). The difference in findings may lie in the types of maltreatment examined, with the few studies focusing on childhood abuse alone demonstrating reduced amygdala connectivity with the insula (23,24). However, there is limited research focusing on childhood abuse exclusively, and this must be further explored to better understand the negative associated sequelae.

Childhood Abuse and Anxiety-/Fear-Related Symptoms

In addition to alterations of neural threat–related regions, experiences of childhood maltreatment have been consistently linked to fear-/threat-related psychopathology in adolescence and adulthood (2,3,6,25,26). Childhood maltreatment predicts adult anxiety (27–32) and PTSD symptoms (13). The unique relationship between childhood abuse (as a subtype of maltreatment) and disorders related to anxiety remains unclear, but specificity is required for effective assessment and intervention. While some studies have examined specific types of childhood maltreatment, such as abuse or neglect (30,33), many studies have aggregated experiences of childhood maltreatment instead. While the aggregation approach is important in understanding the cumulative and summative risk of adverse experiences, it may obscure the differential effects of abuse or neglect (4). For example, some research has posited that physical abuse specifically is the type of child maltreatment most highly correlated with anxiety symptoms in adulthood (27), whereas experiencing sexual abuse in childhood is associated most strongly with depression and suicidal ideation (34). Thus, the current study focused on experiences of childhood abuse in part because of the risk for disorders of distress and dysregulation related to such experiences (3,35).

Childhood abuse may be related to psychopathology via maladaptive fear learning and generalization, increased emotional reactivity, and disruptions in emotional regulation (4,6). For example, children who experienced abuse struggle to discriminate between threat and safety cues compared with children with no history of abuse (36). This overgeneralization of fear has been associated with smaller volumes of important brain regions in the threat circuitry, including the amygdala and hippocampus (6). Atypical fear learning and overgeneralization has been observed in several forms of psychopathology, including PTSD and anxiety (6,36). In sum, the limited research that has specifically explored consequences of childhood abuse has shown the distinct effect of childhood abuse on anxiety and PTSD symptoms specifically, positing that disruptions in threat processing are one mechanism to explain the relationship (36).

The Current Study

While it is known that childhood abuse is related to emotional processing deficits, fear overgeneralization, increased anxiety, and PTSD risk (5,6,36) and that the amygdala is a key marker of such psychopathology (37–39), a few gaps still remain. Primarily, how rsFC of the amygdala is affected by childhood abuse remains unclear, obscuring its potential mechanistic role in this link. Moreover, the consequential impact of childhood

abuse specifically in the context of later stress in adulthood has not been fully explored, especially given the cumulative risk of childhood abuse with subsequent trauma exposure in adulthood leading to a dramatic increase in severity and chronicity of psychopathology (40). Thus, this current study aimed to further understand the impact of childhood abuse on adult threat circuitry and subsequent anxiety and posttraumatic stress symptoms. To address the gap in the literature, the first aim of the current study was to examine the relationship between childhood abuse and whole-brain amygdala rsFC. We examined this prospectively in a sample of injured adults recruited from a local emergency department, with imaging conducted 2 to 4 weeks posttrauma and symptom assessments gathered 6 months later. Given that some studies have shown increased relationship between childhood maltreatment and amygdala connectivity (20,21) and others have shown decreased connectivity (23,24), we did not have any a priori hypotheses regarding the rsFC directionality. However, based on previous research (20,23,24), we expected to observe significant amygdala rsFC with the hippocampus (19–21), prefrontal cortex, and insula (23,24).To understand the potential mechanistic role of amygdala rsFC in the effect of childhood abuse on anxiety-related symptoms, the second aim of this study was to examine its relevance to psychiatric disorders in which fear and threat detection and regulation are disrupted, particularly anxiety and PTSD. We integrated this into separate mediation models, examining childhood abuse as the predictor, amygdala rsFC from the first aim as the mediator, and anxiety and PTSD symptoms as outcomes. We also ran a sensitivity analysis with depression symptoms as an outcome. We anticipated that amygdala rsFC would mediate the relationship between childhood abuse and anxiety and PTSD symptoms. However, we did not expect amygdala rsFC to mediate the relationship between childhood abuse and depression symptoms given that the amygdala's primary role of fear and threat detection/regulation is not as strongly implicated in the development of depression (39). We also included childhood neglect and prior traumatic exposure as covariates in all mediation analyses. Because the participants had experienced a trauma very recently, we also covaried for posttraumatic stress symptoms from baseline.

METHODS AND MATERIALS

All protocols were approved by the Medical College of Wisconsin Institutional Review Board, and informed consent was obtained from participants prior to data collection.

Participants and Procedures

Participants (N = 215) were recruited from an emergency department at a level 1 trauma center as part of a longitudinal study (41–43) investigating neurobiological predictors of PTSD in adults. Participants were required to meet the following inclusion criteria: 1) speak English, 2) be between ages 18 and 65 years, 3) score 3 or higher on the Predicting PTSD Questionnaire (44), and 4) score 13 or above on the Glasgow Coma Scale (45). Exclusion criteria included moderate to severe traumatic brain injury, spinal cord injury, history of psychotic or manic symptoms, traumatic injuries resulting from a suicide attempt or self-harm, or a contraindication for magnetic resonance imaging (MRI) scanning (e.g., pregnancy). Within 2 to 4 weeks of recruitment from the emergency department, enrolled participants underwent functional and structural MRI scans and a battery of self-report measures. Six months posttrauma, participants self-reported symptoms of depression, anxiety, and PTSD. One hundred sixty-nine participants had usable resting-state functional MRI scans and self-reported childhood maltreatment, but 17 participants were missing self-reported depression, anxiety, and PTSD, leaving 152 participants. The most prevalent traumatic injuries were motor vehicle crash (69.5%), assault/altercation (11.8%), and being struck as a pedestrian (4.6%). Some participants met diagnostic criteria for the following disorders at the time of the trauma: generalized anxiety disorder (14.6%), specific phobia (11.8%), social anxiety (11.8%), and major depressive disorder (7.9%). Psychiatric medication usage (e.g., selective serotonin reuptake inhibitors, non–selective serotonin reuptake inhibitor antidepressants, stimulants, anxiolytics) was reported by 16.4% of participants.

Measures

Childhood Maltreatment. Childhood maltreatment was measured via the Childhood Trauma Questionnaire (CTQ)-Short Form (46,47), a retrospective, self-report measure that measures experiences of trauma in childhood. The CTQ-Short Form comprises 28 items, divided into 5 subscales: 1) physical abuse, 2) emotional abuse, 3) sexual abuse, 4) emotional neglect, and 5) physical neglect. Each item requires respondents to use a Likert scale from 1 to 5 (1 = "never true," and 5 = "very often true") to rate the frequency. The CTQ has been found to have strong general psychometric properties (e.g., Cronbach's alpha of 0.95) (47) and in the current sample (alpha = 0.73).

For the current analyses, we created 2 subscales within the CTQ: 1) abuse (sum of scores on emotional, physical, and sexual abuse items), and 2) neglect (made up of the emotional neglect and physical neglect items). This methodology has been used in prior research [e.g., (3,48)]. For the current study, the abuse subscale was used, and neglect was used as a covariate.

Anxiety and Depression. Anxiety and depression symptoms were measured via the 21-item Depression, Anxiety and Stress Scale (DASS-21) (49). The DASS-21 comprises 3 self-report subscales measuring depression, anxiety, and stress during the past week. Each subscale on the DASS-21 is made up of 7 questions and uses a 4-point Likert scale (0 = "did not apply to me at all," 4 = "applied to me very much"). The internal consistency of the DASS-21 has been shown to be excellent in the current sample (depression alpha = 0.90, anxiety alpha = 0.84, stress alpha = 0.89).

Posttraumatic Stress Symptoms

Baseline. Acute severity of traumatic distress at baseline (2 to 4 weeks posttrauma) was measured using the PTSD Checklist for DSM-5 (50), a validated self-report measure that captures acute symptoms. Participants rated how much they were bothered by the symptoms described in each of the 20 items using a 5-point Likert scale (1 = "not at all" to

5 = "extremely"). The PTSD Checklist for DSM-5 has been shown to have strong internal consistency (alpha = 0.94 to 0.95) (51), which was observed in the current sample (alpha = 0.95).

Six-Month Posttraumatic Symptoms. Posttraumatic stress symptoms at 6 months were assessed using the Clinician Administered PTSD Scale for DSM-5 (52). The Clinician Administered PTSD Scale for DSM-5 is considered to be the gold standard of PTSD assessment and has been shown to have good internal consistency (Cronbach's alpha 0.88) (52), which is observed in the current sample (alpha = 0.93).

Other Traumatic Exposure. The Life Events Checklist (LEC) (53) was used to capture prior trauma exposure. The LEC is a self-reported, validated measure that contains 17 items describing stressful, traumatic events. Four items (items 6–9) were excluded from the total calculation because they refer to experiences of physical or sexual assault and may be confounded with childhood maltreatment experiences. The LEC was used as a covariate in the analyses to isolate the role of childhood abuse in the model and avoid misattributing results to previous trauma exposure.

Neuroimaging Procedures

Acquisition. Images were collected using a GE Discovery MR750 3T scanner equipped with a 32-channel head coil. T1-weighted high-resolution anatomical scans were acquired (field of view = 240 mm; matrix = 256 × 224; slice thickness = 1 mm; 150 slices, repetition time/echo time = 8.2/3.2; flip angle = 12°, voxel size = 0.9375 × 1.071 × 1) for coregistration with functional images and structural analysis. Resting-state images were acquired during an 8-minute eyes-open scan (240 volumes; field of view = 22.4 mm; matrix = 64 × 64; slice thickness = 3.5 mm; 41 sagittal slices; repetition time/echo time =2000/25 ms; flip angle = 77°).

Functional MRI Data Preprocessing. Standard preprocessing procedures were completed using the MATLAB-based (version 2019b; The MathWorks, Inc.) SPM (version 12) CONN Toolbox. Preprocessing steps include discarding the first 3 repetition times, motion correction using a 6-parameter linear transformation, normalization to Montreal Neurological Institute (MNI 152) template, and spatial blurring with a 4-mm full width at half-maximum smoothing kernel. To address confounding effects of motion, volumes with framewise displacement over 0.3 mm were excluded from the analysis. Nuisance covariates (head motion parameters, white matter signal, and cerebrospinal fluid signal) were regressed out during the first level of analyses. Finally, participants were removed from analyses if more than 20% of the resting-state volumes were scrubbed.

Analytic Plan

Using the CONN Toolbox, we conducted a seed-to-voxel analysis (i.e., regression), which examined the effect of childhood abuse on resting-state connectivity between a bilateral amygdala seed and the rest of the brain. Age, gender, and childhood neglect were included as covariates. Significant clusters were identified using a height threshold of $p < .001$ (uncorrected) and a cluster-size threshold of $p < .05$ (false discovery rate–adjusted).

To examine the mediating effect of the amygdala rsFC on relationships between childhood abuse and adult posttrauma anxiety, PTSD, and depression symptoms, we used the PROCESS macro in SPSS 28, a computational macro that uses bootstrapping to analyze direct, indirect, and conditional effects (54,55). Model 4 was conducted to examine the indirect effect of childhood abuse on PTSD symptoms via amygdala rsFC (54). Connectivity values from significant clusters in the amygdala childhood abuse connectivity analysis described above were extracted from the CONN Toolbox to be used in the mediation analyses in PROCESS. Three mediation models examined the relationship between childhood abuse and anxiety, depression, and PTSD symptoms 6 months post-trauma, with rsFC of the amygdala as the mediator. Mediation analyses controlled for baseline PTSD symptoms and prior trauma exposure.

RESULTS

Table 1 summarizes participant demographic characteristics. Table 2 provides correlations between childhood threat, depression, anxiety, and PTSD (baseline and 6 months).

Neuroimaging Analyses

Amygdala rsFC. The seed-to-voxel analysis revealed that more severe childhood abuse was associated with increased bilateral amygdala connectivity with the bilateral precuneus (x = 8, y = −64, z = 50, k = 247, false discovery rate–corrected $p < .001$) (Figure 1) after adjusting for age, gender, and childhood neglect.

Mediation Analyses. Results of the mediation analyses indicated that amygdala-precuneus rsFC was a significant mediator of the effect of childhood abuse on anxiety symptoms (B = 0.062; 95% CI, 0.010–0.130; SE = 0.030), but not PTSD symptoms (B = 0.0004, 95% CI, −0.065 to 0.063; SE = 0.030) following adult trauma. Amygdala-precuneus rsFC did not mediate the effect of childhood abuse on depressive symptoms in our secondary model either (B = 0.023, 95% CI, −0.035 to 0.086; SE = 0.03). Results for the mediation analysis with anxiety symptoms as an outcome can be found in Table 3. Full mediation model and individual path results can are shown in Figure 2.

DISCUSSION

The current study investigated the relationship between childhood abuse and anxiety and PTSD following adult trauma and the potential mediating role of amygdala connectivity. Bilateral amygdala-precuneus rsFC mediated the relationship between childhood abuse and anxiety symptoms, covarying for age, gender, childhood neglect, and baseline PTSD symptoms; however, it did not mediate the relationship between childhood abuse and PTSD or depression as a secondary model. These findings contribute to a better understanding of how experiences of childhood abuse may be related to greater engagement of threat-processing circuitry,

Table 1. Demographic and Clinical Characteristics of Study Participants

Characteristic	Value
Gender, Women, *n* (%)	87 (57.2%)
Age, Years	
Mean (SD)	32.61 (10.35)
Range	18.1–58.6
Psychiatric Medication Use, %	
Yes	16.4%
No	83.6%
CTQ Abuse	
Mean (SD)	24.20 (11.67)
Range	15–70
CTQ Neglect	
Mean (SD)	18.87 (7.86)
Range	10–41
DASS Anxiety, 6 Months	
Mean (SD)	8.17 (9.51)
Range	0–42
DASS Depression, 6 Months	
Mean (SD)	7.58 (9.66)
Range	0–42
PCL-5 PTSD, 2 Weeks	
Mean (SD)	27.40 (18.44)
Range	0–73
CAPS-5 PTSD, 6 Months	
Mean (SD)	13.17 (11.41)
Range	0–57
LEC-5	
Mean (SD)	3.70 (2.27)
Range	0–10
Race, %	
Asian	1.3%
Black or African American	58.6%
More than one race	5.9%
White	27.6%
Did not disclose/unknown	6.6%
Hispanic Ethnicity, %	
Yes	8.6%
No	90.1%
Did not disclose/unknown	1.3%

Continuous and categorical variables are presented as mean (SD) and *n* (%), respectively.

CAPS-5, Clinician Administered PTSD Scale for DSM-5; CTQ, Childhood Trauma Questionnaire; DASS, Depression, Anxiety and Stress Scale; LEC, Life Events Checklist; PCL-5, PTSD Checklist for DSM-5.

and in turn to risk for developing anxiety in the aftermath of an adult trauma.

Broadly, our findings are consistent with previous research that has implicated the amygdala in childhood maltreatment (19,20) and with related brain regions, such as the precuneus. In addition to attention, the precuneus is further implicated in other processes relevant for emotion regulation, rumination, and anxiety [e.g., (56)]. The precuneus is a key node in the default mode network (57) implicated in episodic memory (58–60) and self-referential processing (60–62). More engagement in negative self-referential processing has been linked to anxiety (63,64), and individuals with anxiety have been found to have deficits in episodic memory (65,66). In light of these functions, stronger amygdala-precuneus connectivity could indicate that adults who experienced child abuse have an increased likelihood of engaging in negative self-referential thinking during periods of low external cognitive engagement or a tendency to recall negative thoughts or autobiographical memories. However, additional research is needed to fully understand how these neural processes uniquely contribute to anxiety.

Of note, prior literature has also found decreased connectivity between the amygdala and bilateral precuneus and the amygdala and the insula in adults with experiences of childhood emotional maltreatment versus those without experiences of childhood emotional maltreatment (19). These results, which are discrepant with those of the current study, may be explained by several factors, including the fact that Van der Werff *et al.* (19) had a smaller sample, which was grouped based on categorical experiences of maltreatment (i.e., a childhood emotional maltreatment group and a control group), and that the childhood emotional maltreatment group included experiences of both neglect and abuse (whereas the current study only investigated abuse).

The current findings are also consistent with similar but discrete task-based neuroimaging studies that implicate the amygdala and threat bias (67). More specifically, our finding of greater amygdala-precuneus connectivity in adults who experienced abuse as children adds to an existing body of task-based literature demonstrating that experiencing childhood maltreatment may affect how individuals orient to and process certain stimuli [e.g., angry faces (7,8)] and have selective attention to and delayed disengagement with certain facial emotions [e.g., anger (8)]. The precuneus has been implicated in visual attention (68), including allocating attention to salient and affective stimuli (69), and in memory-guided attention (70). In addition, while negative amygdala-precuneus connectivity has been observed in healthy adults (71,72), adults high on trait negative affectivity show greater amygdala-precuneus connectivity (73). Thus, stronger amygdala-precuneus rsFC may be an underlying neural mechanism that contributes to the tendency for anxious individuals to orient to negative stimuli when present (e.g., faces).

Individuals who have experienced early-life abuse may adaptively adopt a strategy of constant vigilance for potential threat, as reflected in findings that abuse-exposed children have difficulty discriminating between threat and safety cues (36). However, while potentially adaptive in a threat-laden environment, such preferential attention to potential threat in the environment has been shown to play a causal role in the onset and maintenance of anxiety (74–77). Thus, one possibility is that experiencing abuse as child has a longstanding impact on amygdala-precuneus connectivity such that this pathway is tonically upregulated even at rest, which may increase vulnerability to anxiety-related symptoms later in life.

While experiences of childhood abuse were related to changes in amygdala-precuneus connectivity and, in turn, later-in-life anxiety, childhood abuse was not related to adult

Table 2. Bivariate Correlations of Childhood Abuse, Anxiety, Depression, and PTSD

	Abuse, CTQ	2-Week PTSD Symptoms, PCL-5	6-Month Anxiety Symptoms, DASS	6-Month Depression Symptoms, DASS	6-Month PTSD, CAPS-5	Other Trauma Exposure, LEC
Abuse, CTQ	–	0.318[a]	0.370[a]	0.277[a]	0.354[b]	0.163[b]
2-Week PTSD Symptoms, PCL-5	–	–	0.487[a]	0.462[a]	0.503[a]	0.216[b]
6-Month Anxiety Symptoms, DASS	–	–	–	0.864[a]	0.059[a]	0.230[b]
6-Month Depression Symptoms, DASS	–	–	–	–	−0.498[a]	0.097
6-Month PTSD Symptoms, CAPS-5	–	–	–	–	–	0.180[b]
Other Trauma Exposure, LEC	–	–	–	–	–	–

CTQ, Childhood Trauma Questionnaire; DASS, Depression, Anxiety and Stress Scale; LEC, Life Events Checklist; PCL-5, PTSD Checklist for DSM-5; PTSD, posttraumatic stress disorder.

[a]$p < .001$.

[b]$p < .05$.

posttrauma PTSD and depression via amygdala-precuneus rsFC. There are a number of potential explanations for our only observing this relationship with symptoms of anxiety. First, changes in fear conditioning and attentional orientation (e.g., to more threatening stimuli) have mainly been observed in anxiety and PTSD, as opposed to depression (6,36). However, the current study did not find significant results using PTSD as an outcome. The current findings with anxiety are also consistent with previous work that has posited that abuse is most highly correlated with symptoms of anxiety later in life (27). More specifically, these observed patterns of connectivity (i.e., amygdala-precuneus connectivity) as they relate to childhood abuse may be a unique underlying mechanism that contributes to the development and maintenance of anxiety in adulthood. While the direct effects of childhood abuse on PTSD and depression were significant, amygdala connectivity was not an explanatory mechanism for these relationships. In other words, while experiences of childhood abuse predicted adult depression and PTSD, too, the way that childhood abuse is related to amygdala connectivity may distinctly underlie certain unique features of anxiety, but not PTSD or depression [e.g., bias toward negative emotional stimuli (8)]. Future studies can build on the current work by further investigating neurobiological underpinnings of related but discrete psychopathology (e.g., anxiety, PTSD, depression) and using task-based approaches.

Importantly, the current findings emerged while controlling for baseline acute PTSD symptoms and experiences of childhood neglect. By covarying for these variables, we were able to investigate the unique long-term effects of childhood abuse above and beyond the impact of more recent, acute PTSD symptoms. That is, experiences of childhood abuse have lasting effects on neural circuitry, thereby affecting mental health outcomes after adult trauma exposure (even when controlling for acute posttraumatic stress symptoms). The current study supports the theory that experiences of

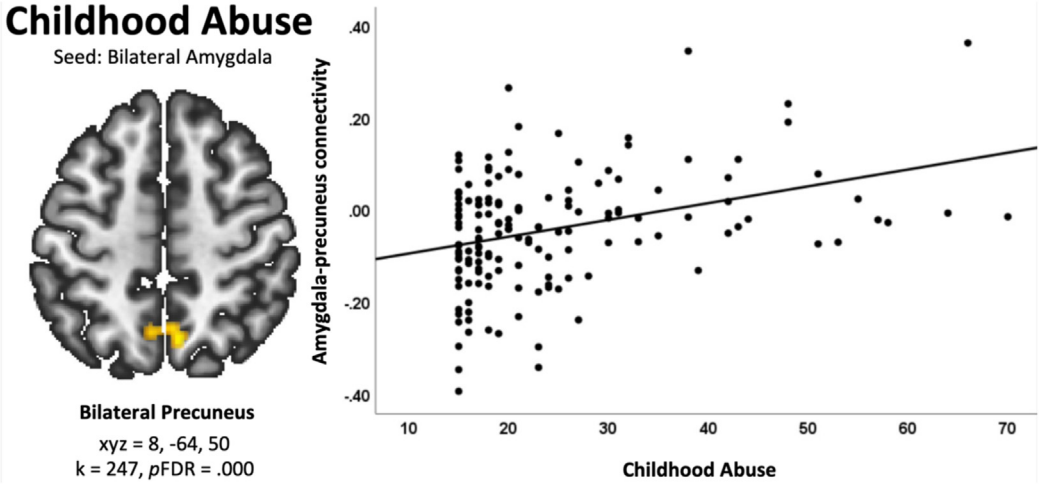

Figure 1. Whole-brain connectivity analysis results. Childhood abuse was associated with greater connectivity between the bilateral amygdala and bilateral precuneus. Significant clusters were identified using a voxelwise threshold of $p < .001$ and a cluster threshold of false discovery rate (FDR)–adjusted $p < .05$. Graph is displayed for illustrative purposes to depict the direction of the association.

Table 3. Model Summary of the Indirect Effect of Childhood Abuse on Anxiety Symptoms

	Outcome					
	M – rsFC			Y – Anxiety Symptoms		
Predictor	*B*	SE	*p* Value	*B*	SE	*p* Value
Childhood Abuse	0.004	0.0009	<.0001[a]	0.123	0.061	.043[b]
rsFC	–	–	–	16.13	5.41	.003[a]
Constant	−0.137	0.026	<.0001[a]	−1.592	1.87	.40
	R^2 = 0.130, $F_{2,149}$ = 10.47		.0001[b]	R^2 = 0.358, $F_{3,148}$ = 26.71		.0001[a]
Total Indirect Effect	*B* = 0.062, SE = 0.030, 95% CI 0.010–0.130					

B values are unstandardized.
M, mediator; rsFC, resting-state functional connectivity; Y, outcome variable.
[a]$p < .001$.
[b]$p < .05$.

childhood abuse contribute to developing negative downstream mental health outcomes, including anxiety (4). However, the current findings increase the specificity of this relationship by pointing to one possible underlying mechanism: changes in rsFC of the amygdala. Results of the current study may aid in the development of more targeted, mechanistic screenings and treatments in adulthood.

Limitations

The current study has several limitations. First, we used a retrospective measure of childhood maltreatment, which may be affected by participants' memory. Second, the current study used different forms of reporting at different time points such that 2-week PTSD symptoms were self-reported, whereas 6-month symptoms were assessed clinically. Third, the current sample is composed entirely of individuals who had recently experienced a traumatic event; therefore, we did not have a nontrauma control group, and our findings may have limited generalizability across other noninjury types of trauma. Fourth, we controlled for previous trauma exposure to isolate the role of childhood maltreatment in our sample. To do this, we used the LEC but excluded 4 items (items 6–9) that ask about experiences of sexual or physical assault because we are unable to determine whether such experiences did, in fact, occur during childhood. Finally, while evidence suggests that the timing of childhood maltreatment can be predictive of outcomes (78), the current study was not designed to make temporal inferences regarding moderating effects of timing of maltreatment.

Conclusions

The current study provides evidence that increased amygdala-precuneus connectivity may be an underlying neural mechanism that links childhood abuse with anxiety following trauma later in life. These findings suggest that experiences of childhood abuse may contribute to enhanced attentional vigilance for potential threat or changes in episodic memory or self-referential processing via amygdala-precuneus connectivity, which in turn contributes to symptoms of anxiety in the aftermath of adult trauma exposure; however, future task-based studies should explore this further. Better understanding of how these constructs are related may help to inform the development of more targeted, mechanistic treatments.

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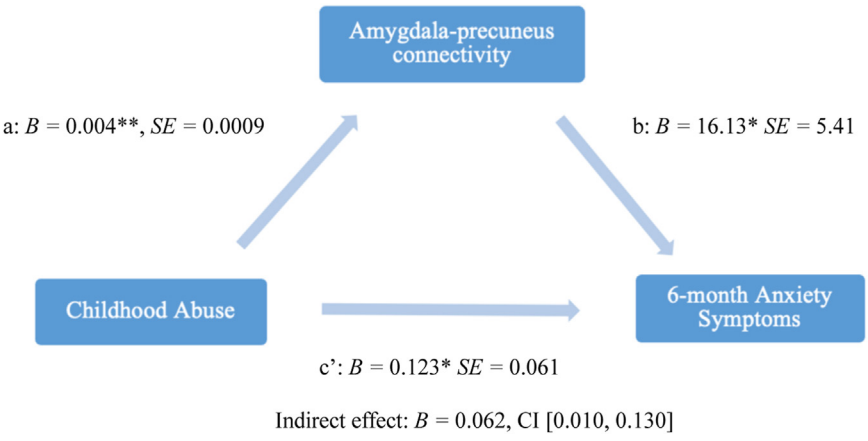

Figure 2. Mediational model, PROCESS model 4. *$p < .05$, **$p < .001$.

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