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Prior Sexual Trauma Exposure Impacts Posttraumatic Dysfunction and Neural Circuitry Following a Recent Traumatic Event in the AURORA Study

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ABSTRACT

BACKGROUND: Prior sexual trauma (ST) is associated with greater risk for posttraumatic stress disorder after a subsequent traumatic event; however, the underlying neurobiological mechanisms remain opaque. We investigated longitudinal posttraumatic dysfunction and amygdala functional dynamics following admission to an emergency department for new primarily nonsexual trauma in participants with and without previous ST.

METHODS: Participants ($N = 2178$) were recruited following acute trauma exposure (primarily motor vehicle collision). A subset ($n = 242$) completed magnetic resonance imaging that included a fearful faces task and a resting-state scan 2 weeks after the trauma. We investigated associations between prior ST and several dimensions of posttraumatic symptoms over 6 months. We further assessed amygdala activation and connectivity differences between groups with or without prior ST.

RESULTS: Prior ST was associated with greater posttraumatic depression ($F_{1,1120} = 28.35$, $p = 1.22 \times 10^{-7}$, $\eta_p^2 = 0.06$), anxiety ($F_{1,1113} = 17.43$, $p = 3.21 \times 10^{-5}$, $\eta_p^2 = 0.05$), and posttraumatic stress disorder ($F_{1,1027} = 11.34$, $p = 7.85 \times 10^{-4}$, $\eta_p^2 = 0.04$) severity and more maladaptive beliefs about pain ($F_{1,1113} = 8.51$, $p = .004$, $\eta_p^2 = 0.02$) but was not related to amygdala reactivity to fearful versus neutral faces (all $ps > .05$). A secondary analysis revealed an interaction between ST and lifetime trauma load on the left amygdala to visual cortex connectivity (peak Z value: -4.41, corrected $p < .02$).

CONCLUSIONS: Findings suggest that prior ST is associated with heightened posttraumatic dysfunction following a new trauma exposure but not increased amygdala activity. In addition, ST may interact with lifetime trauma load to alter neural circuitry in visual processing regions following acute trauma exposure. Further research should probe the relationship between trauma type and visual circuitry in the acute aftermath of trauma.

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Approximately 1 in 3 women and 1 in 8 men in the United States have experienced rape, sexual assault, or childhood sexual abuse (CSA) during their lifetime (1–6). Sexually traumatic events carry the greatest conditional risk for posttraumatic stress disorder (PTSD) development compared with all other types of trauma (7–9) and are associated with greater general posttraumatic dysfunction (i.e., depression, anxiety) than other types of trauma (2,10–12). Furthermore, sexual trauma (ST) may compound risk for psychopathology after a new, subsequent trauma [e.g., motor vehicle collision; (13,14)]. Given that 50% to 90% of the population will experience a traumatic event in their lifetime (7,15,16), the likelihood of experiencing a subsequent traumatic event after prior ST is high. Although recent neuroimaging studies conducted in the early aftermath of trauma have revealed several neural predictors of posttraumatic dysfunction, whether and how prior

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ST may modulate these effects in individuals is still unknown. Understanding the interplay between prior ST and subsequent trauma may contribute to more accurate predictive models of individual susceptibility to PTSD.

The fact that ST is likely to result in PTSD is well established by existing literature. Prior work has found that approximately 94% of female rape survivors met symptomatic criteria for PTSD 2 weeks posttrauma, with approximately 50% continuing to meet criteria 3 months later (17,18). ST is also associated with increased depression and anxiety (2,19,20) as well as symptoms of dissociation (21). Significant associations between CSA and psychological distress in adults have been described, including anxiety, depression, PTSD, and dissociation (22–24). The apparent preexisting elevated risk for psychopathology in survivors of ST may affect the course of posttraumatic dysfunction after a new trauma and may be better elucidated through the identification of neural signatures. In particular, identifying neural signatures of risk for PTSD through functional neuroimaging may contribute to the ability to implement targeted early interventions for those most at risk.

Prior research suggests that the amygdala, a region critical to threat learning and expression, may be a major neural substrate of PTSD vulnerability (25,26). Earlier functional neuroimaging studies of PTSD conducted in small samples have shown that the amygdala is hyperactive in response to emotional stimuli, leading to symptoms of hyperarousal, heightened fear, and impairments in emotional regulation in individuals with the disorder (27,28). More recent work conducted with larger samples further suggests that reactivity to fearful faces may help to distinguish between biotypes of PTSD risk (29). Studies with large samples have also found neighborhood disadvantage in children to be related to blunted amygdala reactivity (30) and greater PTSD symptoms in a highly trauma-exposed population to be related to faster amygdala habituation to repeated fearful faces (31), suggesting that childhood adversity (e.g., CSA) may be predictive of a more blunted than a hyperactive response. In prospective studies, amygdala reactivity to emotional stimuli has emerged as predictive of PTSD when magnetic resonance imaging (MRI) scans were done both prior to exposure to a traumatic event (32) and in the early aftermath of trauma (33). Alterations in amygdala connectivity to regions including the prefrontal cortex (PFC) and dorsal anterior cingulate cortex have also been demonstrated in individuals with PTSD (34,35). In women, decreased functional connectivity (FC) between the right amygdala and left ventromedial PFC during threat processing was associated with PTSD (36). In the early aftermath of trauma, greater resting-state FC (rsFC) between the dorsal lateral PFC and an arousal network, which encompassed the amygdala, hippocampus, mamillary bodies, midbrain, and pons, was associated with reduced PTSD symptoms 3 months later (37). Furthermore, the interconnections between the amygdala and visual circuitry are particularly relevant for processing of threat-relevant visual stimuli in PTSD, and recent work, including in the AURORA study, has identified the role of the structure of the ventral visual stream in PTSD symptoms over time (38,39). For example, a study comparing visual processing in individuals with and without PTSD found that activity in response to visual scenes was lower in participants with PTSD in the ventral stream of the visual system (40). Thus, prior research suggests that amygdala reactivity and connectivity to other brain regions, which are important for the appraisal and regulation of threat, may play an important role in the development of posttraumatic psychopathology.

Despite the importance of previous imaging work, lack of consideration for potential effects of prior ST is a critical limitation of the current literature. Understanding the modulatory effects of prior ST on future PTSD symptom development and amygdala function in the acute aftermath of a new trauma may help inform more targeted clinical and neuromodulatory interventions. ST has previously been linked to alterations in amygdala function that may be important for understanding PTSD vulnerability. More specifically, prior work found that adolescent girls who had experienced physical or sexual assault and had greater amygdala reactivity to faces showed less symptom improvement after therapy (41). Furthermore, physical and sexual assault victims with greater amygdala reactivity to negative stimuli had more PTSD symptoms (42). However, these studies examined the effects of a single trauma episode and did not consider previous life events or subsequent traumatic events. The lack of neuroimaging studies of ST survivors after later trauma, particularly longitudinal neuroimaging studies, represents a gap in knowledge that must be filled to elucidate potential mechanisms of vulnerability to adverse neural sequelae in ST survivors following other traumatic event.

In the current study, we investigated the impact of prior ST on posttraumatic pathology including PTSD, depression, anxiety, and dissociation following an acute traumatic event requiring an emergency department (ED) evaluation in a multisite, longitudinal study. We also assessed differences in amygdala reactivity to fearful compared with neutral faces and amygdala rsFC between those with and without a history of ST. We hypothesized that individuals with a history of ST would show greater symptoms of posttraumatic dysfunction persisting for 6 months following the acute trauma. We also hypothesized that those with ST would have greater activation in the amygdala to fearful compared with neutral faces than the group without ST. We anticipated that ST would modulate the rsFC of the amygdala to other regions involved in threat processing (i.e., PFC, hippocampus, visual cortex). The study findings demonstrate that prior ST exacerbates the psychological impact of subsequent trauma and contributes to variability in the neural circuitry of PTSD in the early aftermath of trauma, making it an important consideration in the evaluation of recent trauma victims.

METHODS AND MATERIALS

Participants

Participants were recruited from EDs across the United States as part of a longitudinal, multisite parent study of adverse neuropsychiatric sequelae (the AURORA study) (43). Participants who were 18 to 65 years of age were recruited from an ED after experiencing a qualifying traumatic event including a motor vehicle collision, sexual assault, physical assault, a fall of 10 feet or more, or a mass casualty incident. Other traumatic events were also qualifying if the event involved actual or threatened death, serious injury, or sexual violence exposure, either by direct exposure, witnessing, or learning about it, as reported by the participant and agreed upon by the research assistant who was doing the assessment. Full details of the recruitment protocol have been described previously (43).

A total of 2626 participants who were recruited for the AURORA study between September 2017 and July 31, 2020, were included in this investigation (see the Supplement for details on the overall sample). A subset of participants (*n* = 436) were invited to complete an MRI data collection session. Additional MRI exclusion criteria included a history of seizures, epilepsy, Alzheimer's disease, dementia, or Parkinson's disease, and any MRI contraindication (e.g., metal or ferromagnetic implants, pregnancy, claustrophobia). MRI participants were scanned within 2 weeks of their ED visit for acute trauma at 1 of 5 imaging sites. Of the invited participants, 54 participants did not provide task or resting-state functional MRI (fMRI) data and were therefore excluded. We excluded an additional 92 participants for incomplete scan data, motion criteria, or for other behavioral, anatomical, or technical reasons (complete criteria are detailed in the Supplement). Complete data on ST, our primary variable of interest, were missing for an additional 48 participants; therefore, we excluded these participants from analyses (see details below for classification of ST). The final imaging sample consisted of 242 participants (Table 1). Most participants were recruited after a motor vehicle collision (70.3%), and slightly more than half (55.4%) reported having experienced at least 1 instance of prior ST as indexed by the Life Events Checklist for DSM-5 and the Childhood Trauma Questionnaire (see details below). In the final sample, only 2 participants (0.83%) were recruited from the ED following a sexual assault, and index trauma type did not differ between the prior ST group and the group without prior ST (*p* = .61) (see Table 1). Thus, we were unable to consider the polyvictimization aspect of prior ST in relation to posttraumatic dysfunction. Participants provided written informed consent, and all study procedures were approved by each site's institutional review board.

Measures

Detailed information on the psychometric measures included is provided in the Supplement and in prior AURORA study data (44–46). In the current study, ST was defined as reporting having personally experienced at least 1 instance of one of the following: 1) CSA, 2) rape or sexual assault, or 3) another unwanted sexual experience. CSA was assessed using an abbreviated form of the Childhood Trauma Questionnaire—Short Form (47). Prior rape, sexual assault, or other unwanted sexual experience was assessed by the Life Events Checklist for DSM-5 (48,49). If a participant answered affirmatively to any 1 of these 3 questions, they were coded as "yes" for ST, regardless of whether they were missing data for either or both of the other questions. However, given the potential for individuals not to report prior ST (50,51), participants had to have denied all 3 experiences to be coded as "no" for ST. Otherwise, they were coded as "missing." This method achieved good internal reliability (Cronbach's α = 0.74). In additional analyses, we also calculated total Childhood Trauma Questionnaire—Short Form and Life Events Checklist for DSM-5 scores without the ST items.

Table 1. Participant Demographics and Sample Characteristics in the Imaging Sample (*n* = 242)

Characteristic	Prior Sexual Trauma, *n* = 134	No Prior Sexual Trauma, *n* = 108	*p* Value (ANOVA, χ^2)
Gender			.001
Man	32 (23.88%)	48 (44.44%)	
Woman	102 (76.12%)	60 (55.56%)	
Age, Years	35.79 (12.50)	33.86 (12.63)	.24
Race/Ethnicity			.35
Non-Hispanic Black	52 (38.81%)	54 (50.47%)	
Non-Hispanic White	52 (38.81%)	33 (30.84%)	
Hispanic	24 (17.91%)	16 (14.95%)	
Other	6 (4.48%)	4 (3.74%)	
Educational Attainment			.17
Some high school or less	10 (7.46%)	4 (3.70%)	
High school graduate or GED	29 (21.64%)	36 (33.33%)	
Some college or associate degree	53 (39.55%)	44 (40.74%)	
College graduate	29 (21.64%)	17 (15.74%)	
Graduate school	13 (9.70%)	7 (6.48%)	
Income			.37
<$19,001	36 (28.57%)	21 (19.44%)	
$19,001–$35,000	40 (31.75%)	38 (35.19%)	
$35,001–$50,000	19 (15.08%)	16 (14.81%)	
$50,001–$75,000	11 (8.73%)	15 (13.89%)	
$75,001–$100,000	11 (8.73%)	6 (5.56%)	
>$100,000	9 (7.14%)	12 (11.11%)	
CTQ Total	14.94 (11.01)	4.10 (5.07)	<.001
LEC-5 Total	12.90 (9.58)	6.54 (7.15)	<.001
Index Trauma Event Type			.61
Motor vehicle collision	89 (66.42%)	81 (75.00%)	
Physical assault	17 (12.69%)	10 (9.26%)	
Fall < 10 ft	8 (5.97%)	5 (4.63%)	
Nonmotorized collision	7 (5.22%)	2 (1.85%)	
Animal-related	5 (3.73%)	2 (1.85%)	
Other	4 (2.99%)	4 (3.70%)	
Fall ≥ 10 ft	1 (0.75%)	3 (2.78%)	
Sexual assault	1 (0.75%)	1 (0.93%)	
Mass/public trauma	1 (0.75%)	0 (0.00%)	
Burns	1 (0.75%)	0 (0.00%)	
Poisoning	0 (0.00%)	0 (0.00%)	

Values are presented as mean (SD) or *n* (%).

ANOVA, analysis of variance; CTQ, Childhood Trauma Questionnaire; LEC-5, Life Events Checklist for DSM-5.

Participants reported posttraumatic symptoms across several domains retrospectively (past 30 days) in the ED and at 2 weeks (past 14 days), 8 weeks, 3 months, and 6 months (past 30 days) after trauma. PTSD symptoms were assessed using the PTSD Symptom Checklist for DSM-5 (PCL-5) (52). Baseline (i.e., pretrauma) PTSD symptoms or a probable diagnosis of PTSD were not exclusionary criteria. Anxiety symptoms were assessed with the Participant-Reported Outcomes Measurement Information System Anxiety Scale Short Form 7a, and depression symptoms were assessed with the Participant-Reported Outcomes Measurement Information System Depression Short Form 8b scale (53,54). Dissociative symptoms were measured with a modified version of the Brief Dissociative Experiences Scale–Modified (55,56). Symptoms that may be considered consistent within a cognitive domain (i.e., maladaptive beliefs about one's pain) (57) were assessed with the Rumination subscale of the Pain Catastrophizing Scale (58).

MRI Procedures

MRI data were obtained from participants within approximately 2 weeks after trauma exposure as described in our prior reports (29,37,38,59). Detailed information on acquisition parameters by site and imaging processing are available in the Supplement. Briefly, fMRIPrep was used to preprocess task and resting-state fMRI data. During the fMRI task, participants passively viewed fearful and neutral faces in block presentations with a fixation cross presented between each block. Group-level statistical modeling was completed on the fearful > neutral faces contrast extracted for the amygdala using the CIT168 atlas (60). Additional supplemental analyses were completed on data extracted for the insula (61) and hippocampus (62). The resting-state fMRI data were further processed within the AFNI program 3dTproject to perform linear detrending, censoring of non–steady-state volumes identified by fMRIPrep, bandpass filtering (0.01–0.1 Hz), and regression of the white matter, corticospinal fluid, and global signal to account for potential physiological noise. The mean fMRI signal time course was extracted separately from the left and right medial amygdala as defined by the Brainnetome atlas (63), and z-transformed Pearson correlation coefficients were calculated between each region of interest (ROI) and the rest of the brain (i.e., 2 voxelwise connectivity maps for the left/right amygdala per participant). Group-level statistical modeling was completed in AFNI using the separate voxelwise connectivity maps.

Statistical Analyses

Statistical analyses were completed in R 4.1.1 (https://www.R-project.org/) through R Studio 2021.09.0+351 and AFNI (https://afni.nimh.nih.gov/). Hypotheses related to effects of prior ST on posttraumatic stress, depression, anxiety, dissociation, and maladaptive beliefs about pain symptoms were assessed with repeated-measures analyses of covariance (ANCOVAs) with time point (i.e., pretrauma or week 2, week 8, month 3, or month 6 follow-up sessions) as our within-subjects factor and prior ST (i.e., yes/no) as our between-subjects factor. ANCOVAs were first conducted with demographic covariates (age at time of ED admission, yearly income, education level) and were Bonferroni corrected at a corrected alpha level of 0.05 for significance (5 models per comparison, thus critical p value = .05/5). Secondary ANCOVAs included covariates for trauma variables (Childhood Trauma Questionnaire total score without the sexual abuse variable and Life Events Checklist for DSM-5 standard total score without sexual assault variables) to account for effects of other trauma exposures, and results were also Bonferroni corrected at a corrected alpha level of 0.05 for significance.

Hypotheses related to ROI activation to fearful > neutral faces were assessed with one-way ANCOVAs using the same covariates as in previous models (primary models only included demographic covariates; secondary models included both demographic and trauma-related covariates, Bonferroni corrected at a corrected alpha level of 0.05 for significance, 2 models per comparison, thus critical p value = .05/2). To assess hypotheses related to seed-based rsFC, we used AFNI's 3dttest++, assessing voxelwise FC for our a priori ROIs (left and right amygdala) as a function of history of ST. For primary models, analyses included covariates for scanner site, age, income level, and education level. We again covaried for overall prior trauma as well as PCL-5 scores at week 2 in secondary models with a corrected alpha level of 0.05 maintained by setting a cluster-forming threshold of $p < .005$. Gender was not included as a covariate given the high known multicollinearity of sex/gender with prevalence of ST (in the current sample, history of ST for 32 men [23.9%] and 102 women [76.1%]). Exploratory analyses investigated the interaction between other lifetime trauma and prior ST on amygdala reactivity and rsFC.

RESULTS

Participant Demographic and Psychological Characteristics

Sample characteristics including participant demographics and trauma history are presented in Table 1. Childhood trauma (excluding CSA) and lifetime trauma (excluding rape or sexual assault and other unwanted sexual experience) levels were significantly higher among participants who also reported a history of ST. There were significantly more women compared with men among the individuals who experienced ST than among those who did not experience ST (p = .001). The samples did not differ significantly on age, race/ethnicity, income, educational attainment, or index trauma event type.

Participants with a history of ST in the imaging subsample had significantly greater posttraumatic dysfunction across time points (Figure 1 and Table 2). Main effects of ST were largest for depression ($F_{1,1068} = 64.11$, $p = 3.06 \times 10^{-15}$, $\eta_p^2 = 0.06$) followed by anxiety ($F_{1,1062} = 50.49$, $p = 2.20 \times 10^{-12}$, $\eta_p^2 = 0.05$), PTSD ($F_{1,981} = 36.17$, $p = 2.55 \times 10^{-9}$, $\eta_p^2 = 0.04$), dissociation ($F_{1,1063} = 17.55$, $p = 3.03 \times 10^{-5}$, $\eta_p^2 = 0.02$), and maladaptive beliefs about pain ($F_{1,1055} = 16.01$, $p = 6.73 \times 10^{-5}$, $\eta_p^2 = 0.02$) after adjusting for demographic covariates (age, income, and education level). After including additional trauma-related covariates to control for all previous lifetime trauma excluding ST, we observed smaller main effects of ST, but these remained significant except for dissociation (p = .14) (Table 2). There was a significant effect of time point (i.e., pretrauma, week 2, week 8, month 3, and month 6) on all symptoms when adjusting for demographic and trauma covariates, such that symptoms generally increased from pretrauma to week 2 before decreasing over time. The interaction between time point and ST was not significant in any of the models. When we assessed effects of ST in the overall sample (N = 2178), effects varied slightly, but overall, the same

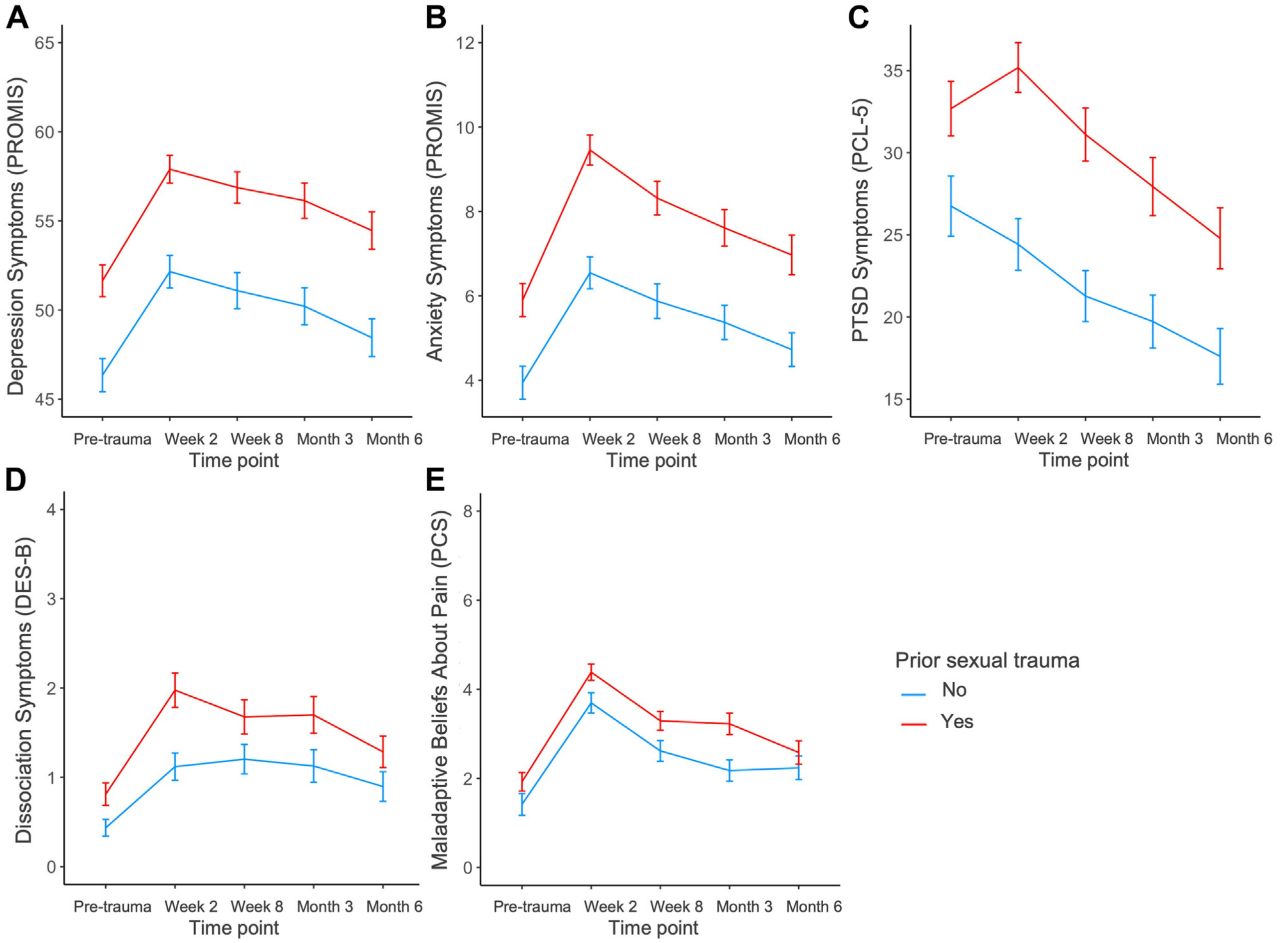

Figure 1. Posttraumatic dysfunction and prior sexual trauma in the 6 months following acute trauma in the imaging sample (n = 242). **(A)** Total depression symptoms (Participant-Reported Outcomes Measurement Information System [PROMIS] Short Form). **(B)** Total anxiety symptoms (PROMIS Short Form). **(C)** Total posttraumatic stress disorder (PTSD) symptoms (PTSD Symptom Checklist for DSM-5 [PCL-5]). **(D)** Total dissociation symptoms (Brief Dissociative Experiences Scale–Modified [DES-B]). **(E)** Total symptoms of maladaptive beliefs about pain (Pain Catastrophizing Scale [PCS] Rumination subscale). For all symptom types, the group with history of sexual trauma presented with higher symptoms when adjusting for demographic covariates. When trauma-related covariates were included in models, only the effect of sexual trauma on dissociation symptoms became nonsignificant (p = .14). Plots are presented without adjustment for covariates. Lines indicate mean scores, and error bars indicate ±1 standard error.

findings were observed (see Supplemental Results; Tables S1, S3, S4). These data suggest that prior ST exacerbates the severity of posttraumatic symptoms across domains over a period of at least 6 months from the time when a new trauma exposure occurred.

Given the observed main effect of prior ST on total PCL-5 scores, we further explored effects of ST on PCL-5 symptom clusters, with previously used covariates (primary models included only demographic covariates, whereas secondary models included both demographic and trauma-related covariates). In primary models, the effect of ST was significant on each symptom cluster (Table 3), with the largest effect observed for criterion D (negative alterations in cognition and mood). In secondary models controlling for overall lifetime trauma, the effect of ST remained significant only for criterion D. These follow-up results suggest that the effect of prior ST on posttraumatic stress may be driven by symptoms of negative thoughts and feelings.

Reactivity to Fearful and Neutral Faces and ST

We did not observe statistically significant effects of prior ST on neural reactivity to fearful faces within the left ($F_{1,218}$ = 1.61, p = .21) or right ($F_{1,218}$ = 1.91, p = .17) amygdala in primary or secondary models ($F_{1,205}$ = 0.55, p = .46 and $F_{1,205}$ = 1.28, p = .26, respectively). Additional ROIs were explored and are detailed in Table S5. These findings suggest that prior ST does not affect neural reactivity to fearful faces within these brain regions after a recent trauma.

Seed-based rsFC and ST

We did not observe a significant effect of prior ST on amygdala connectivity to other brain regions (all $ps > .05$). However, in exploratory post hoc tests, we found that there was an interaction between ST and lifetime trauma on amygdala-to-visual cortex connectivity (peak Z value: -4.41, corrected $p < .01$, X = −6.5, Y = −104.5, Z = 13.5) (Figure 2). More specifically,

Table 2. Prior Sexual Trauma and Posttraumatic Dysfunction in First 6 Months Following Trauma in the Imaging Sample (n = 242)

	Demographic Covariates		Trauma and Demographic Covariates	
Symptom Type	F Value	p Value	F Value	p Value
Depression, PROMIS				
Time point	14.77	9.48×10^{-12}	14.75	1.00×10^{-11}
Sexual trauma	64.11	3.06×10^{-15}	23.41	1.51×10^{-6}
Time point × sexual trauma	0.09	.99	0.10	.98
Anxiety, PROMIS				
Time point	19.68	1.22×10^{-15}	19.98	7.43×10^{-16}
Sexual trauma	50.49	2.20×10^{-12}	11.07	9.09×10^{-4}
Time point × sexual trauma	0.67	.61	0.65	.62
PTSD, PCL-5				
Time point	10.13	4.92×10^{-8}	9.22	2.59×10^{-7}
Sexual trauma	36.17	2.55×10^{-9}	6.05	.01
Time point × sexual trauma	0.97	.42	1.16	.33
Dissociation, DES-B				
Time point	11.53	3.65×10^{-9}	11.13	7.76×10^{-9}
Sexual trauma	17.55	3.03×10^{-5}	2.15	.14
Time point × sexual trauma	0.85	.49	0.54	.71
Maladaptive Beliefs About Pain, PCS				
Time point	34.84	2.35×10^{-27}	33.96	1.23×10^{-26}
Sexual trauma	16.01	6.73×10^{-5}	6.24	.01
Time point × sexual trauma	0.92	.45	0.81	.52

DES-B, Brief Dissociative Experiences Scale–Modified; PCL-5, PTSD Checklist for DSM-5; PCS, Pain Catastrophizing Scale (Rumination subscale); PROMIS, Participant-Reported Outcomes Measurement Information System (Anxiety Scale Short Form 7a and Depression Short Form 8b); PTSD, posttraumatic stress disorder.

the non-ST group showed a positive relationship between lifetime trauma and amygdala-to-visual cortex connectivity ($r_{100} = 0.20$, $p = .04$), while the ST group showed a negative relationship ($r_{110} = -0.25$, $p = .01$). Of note, the prior models of reactivity to fearful faces did not show a significant interaction between lifetime trauma and ST on left or right amygdala reactivity ($p = .73$ and $p = .41$, respectively). These data suggest that the past occurrence of ST alters the influence of prior traumatic experiences on neural connectivity patterns after a recent trauma.

DISCUSSION

ST is a known risk factor for the development of adverse neuropsychiatric sequelae, but how it may modulate the impact of a subsequent trauma is unclear. In this investigation, symptoms of PTSD, depression, anxiety, dissociation, and maladaptive beliefs about pain in the early aftermath of acute trauma were significantly higher in individuals with a history of ST than in individuals without a history of ST. Contrary to our hypotheses, history of ST was not associated with differences in amygdala reactivity to fearful faces. However, there was an interaction between history of ST and exposure to other traumas on amygdala-to-visual cortex rsFC. The current findings suggest a need to consider history of ST in the development of predictive models of adverse neuropsychiatric sequelae and treatment in the early aftermath of trauma.

Table 3. Prior Sexual Trauma and Types of PCL-5 Symptom Clusters in the Imaging Sample (n = 242)

	Demographic Covariates		Trauma and Demographic Covariates	
Symptom Cluster	F Value	p Value	F Value	p Value
Intrusion	9.00	.003	1.59	.21
Avoidance	6.19	.01	0.68	.41
Negative Alterations in Cognition and Mood	21.30	6.65×10^{-6}	4.47	.04
Hyperarousal	10.38	.001	1.79	.18

PCL-5, PTSD Checklist for DSM-5.

Of particular note in this study is the interaction effect between ST and lifetime trauma exposure in predicting amygdala-to-visual cortex rsFC. Emerging work has begun to highlight the importance of visual circuitry and extrinsic connectivity of visual systems in relation to trauma and stress-related disorders (37–39,64). Given that visual cortex activity is modulated by the amygdala, the visual symptoms of PTSD may be related to dysregulated visual cortex activity (65,66). Altered connectivity between the amygdala and visual cortex has also been observed in individuals with PTSD (67,68). Specifically, hyperactivity of the amygdala and associated enhancement of visual perceptual processing of trauma-related stimuli may be related to visual re-experiencing and intrusive symptoms such as flashbacks and may partially support hypervigilance and attention to threat-related cues (66,67,69). A study of patients with mood and anxiety disorders found that blood oxygen level–dependent activity in the amygdala and ventral visual cortex covaried significantly with trauma such that individuals with high trauma showed the

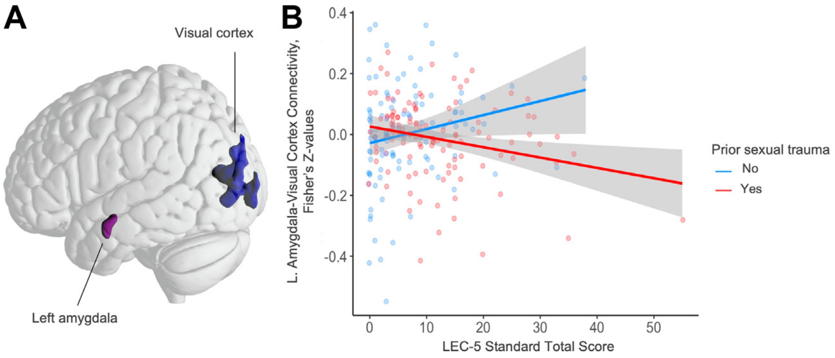

Figure 2. Left amygdala to visual cortex connectivity and prior sexual trauma (ST) in imaging sample (n = 242). **(A)** After accounting for both demographic and trauma-related covariates, we found that the effect of prior ST on left amygdala-to-visual cortex connectivity in a resting state had an interaction with overall lifetime trauma load. **(B)** In the group with ST, stronger connectivity was negatively associated with overall lifetime trauma load, and in the group without ST, the opposite pattern was found. LEC-5, Life Events Checklist for DSM-5.

smallest blood oxygen level–dependent changes in response to emotional versus neutral scenes in these regions (70). Given that highly traumatized participants with prior ST in this study showed reduced amygdala–visual cortex rsFC, this pattern may reflect a posttraumatic outcome that is tied more to negative cognition/depression. Prior research has found decreased rsFC of the amygdala to the visual cortex in major depressive disorder (71). Furthermore, the largest effects of prior ST were on criterion D components of PTSD (i.e., negative cognitions/mood) and depression symptoms. These results may also be interpreted in light of other findings of lower activity in the ventral visual stream during a picture-viewing task in individuals with PTSD versus trauma-exposed control subjects without PTSD (40) given that the group with ST in our sample was significantly more likely to meet criteria for a probable diagnosis of PTSD. One speculative hypothesis in light of these findings is that high polytrauma that includes ST promotes avoidance behaviors to minimize exposure to trauma-related cues, which in turn inhibits extinction memory processes and promotes more frequent negative thoughts about the trauma. Future research that involves specifically testing visual threat memory processes in trauma survivors with ST is needed to fully elucidate this potential mechanism.

These findings are consistent with a large body of previous literature that demonstrated that ST is a risk factor for later mental health disorders. As in prior work (72–75), the current study found that individuals with a history of ST have increased posttraumatic symptom severity across a number of domains (e.g., PTSD, depression, and anxiety). The group with prior ST had higher symptoms prior to the new trauma as well as elevated symptoms after the acute traumatic event, suggesting that the acute phase after a new trauma may be an especially vulnerable period for this population and that ST may thus have especially deleterious effects on mental health. In general, interpersonal traumas result in higher rates of PTSD than noninterpersonal traumas such as motor vehicle collisions or natural disasters (9,76–78). Furthermore, prior literature suggests that sexual assault is by its nature unique even when compared with other types of interpersonal trauma because it is a crime that violates and “disrupts the sense of autonomy, control, and mastery over one’s body” (79). This unique nature of ST may explain why it is a singularly important risk factor for later psychopathology, and taken together with prior literature, the current results suggest that history of ST exacerbates posttraumatic dysfunction following a new trauma. Thus, care providers should be especially sensitive to the possibility of heightened distress both in the short- and long-term following events such as motor vehicle collisions in individuals with prior ST.

We did not observe differences in amygdala reactivity to fearful faces between individuals with and without a history of ST. We initially hypothesized that ST would be associated with greater amygdala reactivity given that a large body of prior work has found amygdala hyperactivity in people with PTSD (e.g., 28,80). Furthermore, in previous analyses of AURORA study data, amygdala reactivity to fearful faces was related to PTSD symptom presentations (29). However, there is also evidence that repeated trauma and childhood adversity may be related to blunted rather than elevated amygdala reactivity (30,81). In the current study, although some participants were exposed to prior ST and others were not, all participants in the current study had been recently exposed to a traumatic event. It is possible that trauma-exposed individuals, regardless of prior ST, exhibit comparably high levels of reactivity to threat-related/emotional stimuli due to the recency of their traumatic event. It may also be true that prior ST modulates amygdala reactivity at a later time scale than was assessed in the current study. Additional longitudinal studies are required to assess whether prior ST may modulate amygdala reactivity to threat in the months after trauma exposure.

Several limitations of the current study should be noted. First, we are unable to determine whether observed neurobiological alterations are preexisting risk factors or the result of the acute trauma because MRIs could not be obtained prior to the ED visit. Although our study design allows for greater understanding of the possible neurobiological mechanisms present in the early aftermath of acute trauma, it remains impractical and expensive to implement a fully prospective longitudinal study design of acute trauma. Without pre-existing knowledge of who will go on to experience a traumatic event that brings them to the ED, scanning individuals as early as 2 weeks after such a trauma is likely to be one of the most practical ways of studying the progression of posttraumatic symptoms and possible biological alterations during the acute phase of trauma exposure. Second, we applied stringent exclusion criteria for categorizing ST that might have excluded certain individuals who experienced prior ST but chose to decline to answer these questions due to distress or other concerns. Third, the available measure assessing dissociation was likely insufficient to comprehensively assess the range of symptoms of dissociation that have been linked to traumatic sexual experiences (82,83). As noted in the Methods and Materials, only 2 of the 8 items of the Brief Dissociative Experiences Scale–Modified were included, and both items assessed derealization. It is possible that a more extensive measure that also assesses depersonalization could have revealed the hypothesized effects of ST on dissociation more strongly. Fourth, although we observed effects of prior ST on neural connectivity and posttraumatic symptoms, many of the effect sizes were small to moderate in size. Thus, although the differences are significant, it may be important to consider how these factors interact with one another as opposed to focusing on individual effects. Fifth, our connectivity analyses used resting-state data, and our inferences are thus limited by a lack of concurrent behavioral/task-specific data. Future research should leverage task-related connectivity approaches to probe the relationship between the amygdala and visual circuitry in participants with different trauma backgrounds. Finally, it is possible that the developmental timing (e.g., in childhood, adolescence, or adulthood) of prior ST might have affected the current findings. Information on the timing of prior trauma exposure was not available, and thus, we are unable to fully delineate the impact of ST timing on posttraumatic reactions.

In conclusion, the current study investigated the impact of prior ST on posttraumatic dysfunction and alterations in neural circuitry following an acute trauma. We found that prior ST was related to greater symptoms of depression, PTSD, anxiety, dissociation, and maladaptive beliefs about pain that persisted during the 6 months following acute trauma. In addition, we found that there was an interaction between ST and other lifetime trauma on amygdala-to-visual cortex FC during a resting-state MRI scan. These findings suggest that prior ST is an important determinant in the progression of symptoms following a later trauma and that it may also be related to alterations in visual circuitry modulated by amygdala activity. Particular care should be taken in the treatment of individuals with prior ST following traumatic events. Furthermore, increased understanding of interactions between threat and visual processing brain regions after trauma may open new avenues for neuroscience-based interventions in the early aftermath of trauma.

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