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Cocaine-Related Attentional Bias following Trauma Cue Exposure among Cocaine Dependent Inpatients with and without Posttraumatic Stress Disorder

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Abstract

AIMS—Although the co-occurrence of posttraumatic stress disorder (PTSD) and cocaine dependence is associated with a wide range of negative clinical outcomes, little is known about the mechanisms that underlie this association. This study investigated one potential mechanism – attentional bias to cocaine imagery following trauma cue exposure.

DESIGN—Male and female cocaine dependent inpatients with and without PTSD were exposed to both a neutral and personalized trauma script on separate days, followed by a visual dot-probe task. A 2 (PTSD vs. non-PTSD) × 2 (neutral vs. trauma script) × 2 (male vs. female) design was used to examine hypotheses.

SETTING—Participants were recruited from a residential substance use disorder (SUD) treatment center.

PARTICIPANTS—Participants were 60 trauma-exposed cocaine dependent inpatients, 30 with current PTSD and 30 without a history of PTSD.

MEASUREMENTS—Attentional bias was assessed using a visual dot-probe task depicting cocaine-related imagery following both a neutral script and personalized trauma script.

FINDINGS—Following neutral script exposure, PTSD (vs. non-PTSD) participants exhibited an attentional bias away from cocaine imagery. This effect was reversed following trauma script exposure, with PTSD participants exhibiting a greater attentional bias toward the location of cocaine imagery than non-PTSD participants. Severity of subjective distress following trauma script exposure predicted level of attentional bias among PTSD participants.

CONCLUSIONS—Cocaine appears to serve an emotion-regulating function among posttraumatic stress disorder patients and may be a potential target for brief posttraumatic stress disorder-substance use disorder interventions that can facilitate residential substance use disorder treatment retention.

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INTRODUCTION

High rates of posttraumatic stress disorder (PTSD) are found among individuals with substance use disorders (SUD). Among SUD patients, rates of current PTSD range from 25% to 42% [1–3] – substantially higher than rates found in the general population [4,5]. A PTSD-SUD diagnosis is associated with a range of negative clinical outcomes, including worse SUD treatment outcomes [6–10]. However, little is known about the mechanisms underlying the association between PTSD and poor treatment outcomes among SUD patients. Individual differences in cognitive processing may be particularly relevant in this regard.

Specifically, theoretical literature has acknowledged the role of cognitive biases in substance use relapse [11–15], and studies have found evidence of heightened attentional biases toward drug-related cues among substance users in general [16–19]. However, no studies have examined drug-related attentional bias among SUD patients with PTSD. Research on the function of substance use within PTSD may elucidate how such a bias could develop among SUD patients with (vs. without) PTSD.

Specifically, research suggests that individuals with PTSD may use substances to regulate emotional distress [20–24]. For example, there is evidence that SUD patients with (vs. without) PTSD are more likely to use substances in response to unpleasant emotions [23]. Further, alcohol use coping motives have been found to mediate the association between PTSD symptoms and alcohol problems [21,22,24], and difficulties in emotion regulation have been found to explain the association between PTSD symptom severity and marijuana use coping motives [20].

Such findings are consistent with the negative reinforcement model of substance use, which states that the primary motive for substance use is the avoidance of or escape from emotional distress [25,26]. Given the high levels of emotion dysregulation and avoidance found in PTSD [27,28], individuals with PTSD may be particularly motivated to use substances as a way of reducing distress. Further, as substances are used to avoid emotional distress, they may gain motivational significance due to their ability to predict escape from distress, leading to the allocation of attention toward cues that signify such reward. Therefore, when individuals with a PTSD-SUD diagnosis experience emotional distress (e.g., following trauma-cue exposure), they may be more likely to notice and become preoccupied with substance-relevant stimuli in their environment (consistent with findings that induced negative affect increases attentional bias to substance-related cues) [29–31]. This attentional bias for substance-related cues, in-line with both negative reinforcement [25,26] and incentive-sensitization [14,32] models of addiction, would then be followed by enhanced responding (i.e., cravings) to these cues, increasing the risk for relapse.

Based on this model, this study sought to test the hypothesis that cocaine dependent inpatients with PTSD would exhibit a greater attentional bias to cocaine-related imagery following exposure to a personalized trauma script (relative to neutral script exposure), compared to cocaine dependent inpatients with a history of traumatic exposure but no PTSD. Additionally, given evidence of gender differences in the clinical presentation of PTSD-SUD [33], cocaine use [34], and anxiety-relevant information processing biases [35,36], we explored the moderating role of gender in this relationship. Finally, we hypothesized that the level of attentional bias would be explained by the severity of distress reported by PTSD-SUD inpatients following trauma script exposure.

METHOD

Participants

Participants were 60 cocaine dependent inpatients with ($n = 30$) and without ($n = 30$) current PTSD in residential SUD treatment (see Table 1 for demographic information).

Materials

Interview-based measures—The Life Events Checklist (LEC) [37] is a 17-item measure assessing exposure to potentially traumatic events. After completing the LEC, participants were asked to identify the event resulting in the most distress currently. This event was used as the index event for the assessment of PTSD and for the personalized trauma script (see below).

The Clinician-Administered PTSD Scale (CAPS) [37,38] is a structured PTSD diagnostic interview and the most widely-used PTSD measure [39]. Frequency items are rated from 0 (never or none/not at all) to 4 (daily or almost every day/more than 80%). Intensity items are rated from 0 (none) to 4 (extreme). The Item Severity ≥ 4 rule, which requires that symptoms must have a severity rating (frequency + intensity) of ≥ 4 to be considered, was used to establish PTSD diagnoses. The CAPS is reliable and demonstrates convergent validity with other established PTSD measures [40,41]. The CAPS was administered by trained interviewers. All interviews were reviewed by a PhD-level clinician (MTT), with diagnoses determined in consensus meetings.

Personalized trauma and neutral scripts—During the initial assessment session, participants were asked specific questions about the event they identified on the LEC. Prior to the first experimental session, a one-minute script generated from this interview was recorded onto an audiotape. The method for generating this personalized trauma script followed the procedures developed by Lang et al. [42,43]. The script is designed to maximize emotional responses by depicting events in a salient, emotion-focused form in second person present tense. This procedure has been used with PTSD [44–46] and PTSD-SUD [47] patients, reliably inducing emotional responses. A one-minute neutral script describing activities involved in getting up in the morning was also developed. Consistent with Keane et al. [45], the neutral script was standardized and consistent across participants.

Visual dot-probe task—The dot-probe has extensive support as a measure of attentional bias within anxious [48–51], substance-using [52–54], and PTSD [55–57] samples. The dot-probe is preferable to other attentional bias tasks (e.g., the Stroop task) for the examination of attentional biases in substance use, as it better corresponds to real-world conditions where substance-related cues may compete for attention [17]. The dot-probe task was developed and presented using E-Prime 2.0 (Psychology Software Tools, Inc., Pittsburgh, PA) on a laptop computer. Pictorial stimuli for this study consisted of 20 cocaine-related images (e.g., crack rocks, powder cocaine, crack pipes) chosen based on clinical experiences with this particular patient population, and 40 images of furniture.

At the beginning of each trial, a fixation cross was displayed in the center of the screen for 500 ms, followed by a blank screen inter-stimulus interval of 250 ms before the picture onset. Picture pairs were then presented side by side for 500 ms. Immediately following the images, a dot-probe appeared in the left or right position, remaining until the participant responded. Participants were asked to indicate where the dot appeared by pressing one of two response keys. Following a response, a feedback screen was presented for 1500 ms and displayed reaction time (RT) and response accuracy (correct/incorrect).

This dot-probe consisted of 5 practice trials and 240 experimental trials. Experimental trials consisted of furniture (neutral) and cocaine (stimulus) pairings. A total of 6 conditions existed: neutral-neutral with left or right dot-probe placement, stimulus-neutral with left or right dot-probe placement, and neutral-stimulus with left or right dot-probe placement. Each condition was represented equally (40 trials each) and images were presented randomly for each trial. The dot-probe task was presented on two separate days following the trauma or neutral script.

For the post-neutral and post-trauma script dot-probe tasks, an attentional bias index score was obtained by calculating the difference in RTs for trials where the dot-probe appeared in the same location as the cocaine image (congruent trials) from trials where the dot-probe appeared opposite from the cocaine image (i.e., in the place of the neutral image; incongruent trials). Higher scores suggest a greater attentional bias, with positive scores indicating an attentional bias towards cocaine images and negative scores reflecting the avoidance of such images. Internal consistency estimates were calculated using procedures outlined by Schmukle [58]. Specifically, the 160 critical trials were divided into 40 quadruplets consisting of one of each kind of critical trial. A bias index was then calculated for each quadruplet, and Cronbach's alpha was calculated using these values. Consistent with past dot-probe studies [58], internal consistency estimates for the post-neutral script ($\alpha = .30$) and post-trauma script ($\alpha = .26$) dot-probe tasks were low (overall $\alpha = .27$).

Self-report measures—All participants completed the 21-item version of the Depression Anxiety Stress Scales [59], a reliable and valid assessment of the severity of depression, anxiety, and stress symptoms [60]. Internal consistency of each of these scales was excellent ($\alpha = .87-.90$). Participants also completed a self-report measure that assessed past-year substance use frequency (across 10 substances). This measure has been used in multiple studies of inpatient substance users [61–64]. Internal consistency for this measure within this sample was adequate ($\alpha = .72$). Both measures were included to identify covariates for analyses and to establish the unique relationship between PTSD and post-trauma script cocaine-related attentional bias.

Procedure

All procedures were approved by the institution's Institutional Review Board. Inclusion criteria included: 1) current cocaine dependence on the SCID-IV (administered to all patients upon entry into the treatment center separate from this study) and reporting cocaine as their drug of choice; 2) Criterion A traumatic exposure; 3) a Mini-Mental Status Exam [65] score of ≥ 24 ; and 4) no current psychotic disorder. Eligible participants were recruited no sooner than 72 hours from treatment entry to limit interference of withdrawal symptoms on study engagement. Those meeting inclusion criteria were given information about the study, following which written informed consent was obtained. This study involved three sessions (completed within the first two weeks of treatment) conducted on three separate days.

Initial assessment session—Participants completed the LEC and were asked to identify and describe the event they currently experience as most distressing. This portion of the session was audiotaped. The CAPS was then administered. Afterwards, participants scheduled their two experimental sessions and were reimbursed \$10.

Experimental sessions—The procedures for the two experimental sessions were the same, with the exception of the particular script presented prior to the dot-probe. Script presentation was counterbalanced, and the order of script presentation was equally balanced across groups. At the start of the session, participants rated their level of distress on a scale

from 1 (no distress) to 5 (extreme distress). Participants then listened to the tape (consistent with procedures described by Keane et al. [45]), following which they rated their level of distress. They then completed the dot-probe task, followed by a final distress rating. Participants were reimbursed \$10 for each experimental session.

Analysis Plan

Dot-probe data were prepared by identifying and removing outlier RT data and RT data from trials with errors. Next, a series of paired t-tests was conducted within each group to examine mean differences in left and right dot-probe placement RTs for the trials used to calculate the attentional bias score. In the absence of significant differences, these RTs are averaged to create single RT scores for the congruent and incongruent trials of both dot-probe tasks. Although it has been argued that RTs on neutral-neutral trials can be used to determine whether an attentional bias is due to vigilance for or difficulty disengaging attention from cues [66], Mogg et al. [67] have advised against this approach, demonstrating that evidence of disengagement (i.e., a difference in incongruent RTs relative to neutral-neutral trial RTs) may also be due to a slowing effect of threat cues on motor responses. Consequently, we did not utilize neutral-neutral trial RT data.

To identify potential covariates for analyses, a series of chi-square, independent t-tests, and correlational analyses was conducted to explore associations between the independent and dependent variables of interest (PTSD and both post-neutral script and post-trauma script attentional bias scores) and demographic factors, depression, anxiety, and stress symptom severity, past year cocaine and overall substance use severity, number of traumatic events experienced, pre-neutral and pre-trauma script distress, and psychotropic medication use [68].

To examine between-group differences in attentional bias, a 2 (PTSD vs. non-PTSD) $\times$ 2 (neutral vs. trauma script) $\times$ 2 (male vs. female) repeated measures analysis of covariance (ANCOVA) was conducted, with post-hoc one-tailed independent t-tests examining between-group differences in attentional bias indices (using adjusted means). To examine if distress following the trauma script significantly predicted post-trauma script attentional bias within the PTSD group, a hierarchical regression analysis was conducted with pre-trauma script distress entered in the first step of the equation and post-trauma script distress entered in the second step.

RESULTS

Preparation of Dot-Probe Data

RT data are presented in Table 2. RT data from trials with errors (< 1% of the data) were discarded. RT data were also excluded if < 200 ms, > 2000 ms, and > 3 standard deviations above the mean (< 1% of the data) [52,69–71].

Results of analyses examining mean differences in RT as a function of left or right dot-probe placement for the congruent and incongruent trials of both the post-trauma and post-neutral script dot-probe tasks revealed no significant differences for either group (t_s [29] < 1.90, p_s > .05). Thus, scores were averaged to create single RT scores for congruent and incongruent trials of each dot-probe task. Post-neutral and post-trauma script attentional bias scores were not significantly correlated with one another, $r = -.05$, $p = .72$.

Counterbalancing

We examined if post-neutral and post-trauma script attentional bias scores differed as a function of the order in which the trauma script was presented. No significant differences

were found on post-neutral, $t(58) = 1.67, p = .10$, or post-trauma script, $t(58) = 0.49, p = .63$, attentional bias scores, demonstrating counterbalancing was effective.

Manipulation Check

A 2 (pre- vs. post-script distress) $\times$ 2 (PTSD vs. non-PTSD) repeated measures analysis of variance (ANOVA) demonstrated that the trauma script resulted in a significant increase in distress (mean pre-script distress = 1.73 ± 1.12 ; mean post-script distress = 2.28 ± 1.34), $F(1,59) = 10.62, p = .002$ across all participants. Further, there was no significant between-group difference in the increase in distress following trauma script presentation, $F(1,58) = 2.91, p = .09$, suggesting that the trauma script was equally effective in increasing distress among PTSD and non-PTSD participants. The neutral script resulted in a reduction in distress across both groups (mean pre-script distress = 1.90 ± 1.13 ; mean post-script distress = 1.48 ± 0.77 ; $F(1,59) = 16.80, p = .001$).

Identification of Covariates

Individuals reporting an annual income of over (vs. under) \$10,000 exhibited a greater post-neutral script attentional bias, $t(58) = 2.16, p = .04$, and age was significantly associated with post-neutral script attentional bias, $r = .26, p = .048$. Further, participants with (vs. without) PTSD exhibited significantly more severe depression, anxiety, and stress symptoms and were significantly more likely to be female (Table 1). Thus, these variables were included as covariates in primary analyses, with the exception of gender which was included as a fixed factor in the primary analyses to examine its role as a moderator, in addition to controlling for its effect.

Primary Analyses

Between-group differences in attentional bias—As predicted, results of the repeated measures ANCOVA revealed a significant PTSD status by script interaction, $F(1,51) = 11.20, p = .002, \eta_p^2 = .12$. Whereas non-PTSD participants exhibited a greater attentional bias following the neutral script than PTSD participants (*means* = $21.68 [SE = 7.78]$ vs. $-9.28 [SE = 6.52]$, respectively; $t[58] = 3.05, p = .002$), PTSD participants exhibited a greater attentional bias following trauma script presentation than non-PTSD participants (*means* = $15.84 [SE = 7.04]$ vs. $-2.76 [SE = 8.39]$, respectively; $t[58] = 1.70, p = .047$). No evidence was found for the moderating role of gender, $F(1,51) = 0.15, p = .70, \eta_p^2 = .00$.

Given findings of gender differences in PTSD, we reran the repeated measures ANCOVA among women and men separately. The pattern of findings did not change. Both women and men with PTSD exhibited a greater attentional bias following trauma script presentation. Finally, given concerns about the validity of results due to the inclusion of multiple covariates [72], we reran analyses without covariates. The significant PTSD status by script interaction remained, $F(1,56) = 7.09, p = .01, \eta_p^2 = .11$.

Association between post-trauma script distress and attentional bias among PTSD participants—Findings indicate that the inclusion of post-trauma script distress significantly improved the model, accounting for an additional 14% of the variance in post-trauma script attentional bias above and beyond pre-trauma script distress, $\beta = 0.40$, Adjusted $R^2 = .08, \Delta F(1,27) = 4.46, ps = .04$.

Discussion

Results suggest that in the absence of PTSD-related cues, cocaine dependent patients with PTSD may be motivated to avoid cocaine-related cues, potentially due to an awareness that the stimulant effect of cocaine may worsen certain PTSD symptoms (e.g., hyperarousal)

[73]. However, in the context of trauma-related cues, PTSD-SUD patients may become preoccupied with cocaine cues, potentially due to a motivation to regulate emotional distress with cocaine. The emotion-regulatory function of cocaine within PTSD is further supported by our finding that post-trauma script distress among PTSD participants significantly predicted attentional bias for cocaine images.

Surprisingly, the non-PTSD group exhibited an opposite effect from the PTSD group following neutral and trauma script exposure. Specifically, non-PTSD participants exhibited an attentional bias toward cocaine images following neutral script exposure and an attentional bias away from cocaine images following trauma script exposure. This finding may speak to the different function of cocaine among cocaine-dependent patients without PTSD. At baseline, cocaine-dependent patients without PTSD may have been motivated to obtain cocaine due to its known ability to elevate mood or as a result of some other positive reinforcement-based motivation. Unlike PTSD patients, however, those without PTSD may not rely on cocaine as a method of regulating distress (i.e., negative reinforcement); consequently, they would not be motivated to use the drug following trauma-cue exposure. This possibility is consistent with Field and Powell's [31] findings that heavy social drinkers who did not use alcohol to cope failed to exhibit an attentional bias toward alcohol cues following exposure to a stressor. Nonetheless, it is also possible that this finding was spurious, resulting from how we assessed attentional bias. The internal consistency and test-retest reliability of the dot-probe task have been questioned [58] (consistent with the low internal consistency found in this study), and its inability to determine whether an attentional bias stems from a vigilance for or difficulty disengaging from a stimulus has been criticized [66]. Thus, results should be considered preliminary and in need of replication using other attentional bias measures, such as eye-fixation monitoring [74].

Other limitations should also be considered. We only examined cocaine-dependent patients; therefore, it is unclear if similar processes operate among individuals with PTSD dependent on other substances. Research in this area is needed, given evidence that alcohol-dependent patients with PTSD respond differently to trauma-related cues than cocaine-dependent patients with PTSD [75]. Also, this was a non-random, treatment-seeking sample. Thus, findings may not generalize to all active cocaine users and require replication with non-treatment seeking cocaine users from the general population. In addition, in the absence of data on key cocaine use characteristics (e.g., route of administration, duration of use, weekly amount used), we cannot be sure that our sample is representative of cocaine users in general. Likewise, given that this was an inner-city, predominantly African-American sample, findings require replication in diverse samples. It also warrants mention that our sample size was small, resulting in low power to find significant effects. Future studies with larger samples would allow us to explore the mediating role of emotional distress in the relationship between PTSD and cocaine-related attentional bias, as well as the specific PTSD symptom clusters driving this effect.

We also did not have access to data on other co-occurring disorders and, thus, could not control for additional diagnoses. Given evidence that PTSD frequently co-occurs with other disorders [76,77], greater psychiatric comorbidity among our PTSD participants may have influenced findings. However, it is important to note that past studies have demonstrated that the worse outcomes observed among PTSD-SUD patients cannot be attributed to the higher rates of comorbidity within this population [9,10,78], and we were able to demonstrate that the effect of PTSD on post-trauma script attentional bias was independent of depression, anxiety, and stress symptom severity. Nonetheless, future studies should examine the effect of co-occurring psychopathology on drug-related attentional bias among SUD patients with PTSD. It will also be important for future studies to utilize comparison groups of SUD patients with co-occurring disorders other than PTSD to establish that our findings cannot be

attributed simply to the presence of severe psychopathology. We also did not examine whether attentional biases correspond to actual negative clinical outcomes (e.g., treatment drop-out) – an important next step in this line of research.

Despite limitations, findings speak to the potential utility of attention modification interventions within residential SUD treatment. Attention modification interventions have been found to be efficacious for numerous anxiety disorders in relatively few sessions [79,80], making them particularly suitable for residential SUD treatment centers where patient stays may be brief. Acceptance- and mindfulness-based interventions may also assist patients in responding more flexibly to their internal and external environment, limiting reliance on emotionally-avoidant behaviors [81,82]. Finally, given evidence that PTSD-SUD patients may be most at-risk for relapse in the context of emotional distress, PTSD-SUD treatments may benefit from incorporating the practice of emotion regulation skills following activation of emotional distress in session.

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Table 1

Descriptive Data for PTSD (n = 30) and Non-PTSD (n = 30) Participants

	PTSD	Non-PTSD	Test of Significance
Age	44.57 (6.14) ^a	44.27 (6.96) ^a	$t(58) = 0.18$
Gender	26.7% Male	83.3% Male	$\chi^2(1) = 19.46^{***}$
Racial/Ethnic Background			$\chi^2(2) = 2.00$
Black/African-American	96.7%	96.7%	
White	0%	3.3%	
Other	3.3%	0%	
Past-Year Income Level			$\chi^2(7) = 4.33$
0–\$9,999	86.7%	73.3%	
\$10,000–\$49,999	10%	13.3%	
\$50,000–\$99,999	3.3%	13.4%	
Psychotropic Medication Use	36.7%	16.7%	$\chi^2(1) = 3.07$
Depression Symptom Severity	15.73 (10.58) ^a	10.33 (9.44) ^a	$t(58) = -2.09^*$
Anxiety Symptom Severity	15.33 (11.64) ^a	7.6 (8.25) ^a	$t(58) = -2.97^{**}$
Stress Symptom Severity	22.67 (12.19) ^a	11.4 (7.72) ^a	$t(58) = -4.28^{***}$
Past Year Cocaine Use Frequency	4.77 (0.57) ^a	4.47 (0.73) ^a	$t(58) = -1.78$
Past Year Substance Use Frequency	14.31 (6.24) ^a	15.56 (8.12) ^a	$t(58) = 0.67$
Number of Traumatic Events	5.93 (2.78) ^a	4.67 (2.73) ^a	$t(58) = -1.78$
PTSD Criterion A Traumatic Events			$\chi^2(5) = 4.43$
Serious Accident	3.3%	3.3%	
Life-Threatening Illness	6.7%	3.3%	
Death of or Injury to Another	20%	40%	
Physical Assault	16.7%	13.3%	
Assault Involving a Weapon	23.3%	26.7%	
Sexual Assault	30%	13.3%	

^a Means are presented followed by standard deviations in parentheses.* $p < .05$.** $p < .01$.*** $p < .001$.

Table 2

Post-Trauma and Neutral Script Selective Attentional Bias Indices and Raw Reaction Time Data for PTSD and Non-PTSD Participants for Post-Trauma and Post-Neutral Script Congruent and Incongruent Trials with Left and Right Dot-Probe Placement

Trials (240 trials/condition)	PTSD (n=30)		Non-PTSD (n=30)	
	Mean	SD	Mean	SD
Post-Neutral Script				
Attentional Bias Index	0.66 (−9.28) ^a	30.70 (6.52) ^b	6.81 (21.68) ^a	34.01 (7.78) ^b
Left Congruent	450.21	92.85	382.21	70.42
Right Congruent	446.48	96.88	381.33	17.69
Left Incongruent	453.73	100.05	392.58	106.93
Right Incongruent	444.27	89.01	384.58	76.02
Post-Trauma Script				
Attentional Bias Index	5.17 (15.84) ^a	42.31 (7.04) ^b	5.92 (−2.76) ^a	20.81 (8.39) ^b
Left Congruent	460.51	133.78	386.10	76.37
Right Congruent	462.73	138.19	394.68	85.64
Left Incongruent	476.07	207.40	400.76	78.39
Right Incongruent	457.51	129.82	391.85	75.45

^aData in parentheses reflect adjusted means;

^bData in parentheses reflect standard errors of the adjusted means.