Published in final edited form as:
Behav Res Ther. 2014 October ; 61: 35–42. doi:10.1016/j.brat.2014.07.003.

Treatment of co-occurring PTSD-AUD: Effects of exposure-based and non-trauma focused psychotherapy on alcohol and trauma cue-reactivity

Elizabeth Nosen[a], **Andrew K. Littlefield**[1,b], **Julie A. Schumacher**[a], **Paul R. Stasiewicz**[c], and **Scott F. Coffey**[a]

Department of Psychiatry and Human Behavior, The University of Mississippi Medical Center

Department of Psychiatry and Human Behavior, The University of Mississippi Medical Center and G.V. (Sonny) Montgomery VA Medical Center

Research Institute on Addictions, University at Buffalo

Abstract

Laboratory studies have shown that exposure to trauma memories increases both craving and salivation responses to alcohol cues among individual with co-occurring posttraumatic stress disorder (PTSD) and alcohol dependence (AD). The purpose of the present study was to examine 1) whether this cue reactivity is dampened following exposure-based treatment for PTSD and 2) how changes in reactivity to trauma cues correspond to changes in alcohol cue-reactivity.

Adults with current PTSD and AD (N=120) were randomly assigned to 9–12 sessions of either Trauma-focused Exposure Therapy (EXP) for PTSD or Health & Lifestyles (HLS, a non-trauma focused comparison treatment), concurrent with 6-week residential AD treatment-asusual. Participants completed trauma and alcohol cue-reactivity laboratory sessions before and after treatment.

Compared to HLS, individuals receiving EXP showed significantly greater reductions in negative affect elicited by trauma cues following treatment. Both treatments demonstrated similar, moderate to large reductions in craving and salivary reactivity over time. Interestingly, latent change in trauma cue-elicited distress over the course of treatment predicted latent change in both trauma cue-elicited alcohol craving and salivation.

Overall, findings highlight the utility of integrating trauma-focused therapies like EXP into substance use treatment in the interests of reducing PTSD symptoms and distress associated with trauma cues.

Published by Elsevier Ltd.

Correspondence concerning this article should be addressed to Scott F. Coffey, Department of Psychiatry and Human Behavior, The University of Mississippi Medical Center, 2500 North State St. Jackson, MS 39216. scoffey@umc.edu.
Dr. Littlefield is now in the Department of Psychology, Texas Tech University

Approximately 40% of individuals seeking treatment for a substance use disorder (SUD) meet diagnostic criteria for comorbid posttraumatic stress disorder (PTSD), a mental health issue characterized by flashbacks of traumatic events, intense anxiety, hyperarousal and avoidance behavior (Dansky, Roitzsch, Brady, & Saladin, 1997; Reynolds et al., 2005). Substance users with PTSD demonstrate poorer treatment outcomes, improving less and relapsing faster following standard addictions treatment (e.g., Brown, Stout, Mueller, 1996; 1999; Ouimette, Finney, & Moos, 1999; Read, Brown & Kahler, 2004). Accordingly, developing effective PTSD treatments for substance users has been a priority among researchers and clinicians in recent years.

Exposure-based psychotherapy (EXP) is considered a 'gold standard' treatment for PTSD among non-substance users (Powers et al., 2010). EXP specifically focuses on desensitizing emotional reactivity to painful memories and real-life trauma reminders via sustained imaginal and in-vivo exposure (e.g., Foa, Hembree & Rothbaum, 2007). Interestingly, while several psychotherapeutic interventions specifically designed to address concurrent PTSD and SUD have emerged, EXP is one of the only treatments demonstrating added benefit over and above traditional, intensity-matched SUD treatments in randomized controlled trials (RCTs; see Torchalla et al., 2011 and van Dam et al., 2012 for reviews of the predominantly non-EXP treatment literature). Five clinical trials of EXP for PTSD-SUD have been published to date (Brady, Dansky, Back, Foa & Carroll, 2001; Foa et al., 2014; Najavits, Schmitz, Gotthardt & Weiss, 2005; Triffleman; 2000; Mills et al., 2012), with at least two more forthcoming (Coffey et al., submitted; Sannibale et al., in press)). Thus far, all demonstrate that exposure-based treatment for individuals with PTSD-SUD are associated with significant reductions in symptoms of PTSD, depression and substance use during treatment. More importantly, 3 of the 4 RCTs (Mills et al., 2012; Coffey et al., submitted; Sannibale et al., 2013) demonstrate that the reduction in PTSD symptoms associated with EXP is significantly greater than reductions observed in matched non-trauma comparison treatments.

Is EXP succeeding where other therapies for PTSD-SUD have failed *because* of its desensitizing effects on trauma-cue reactivity? The self-medication model (Khantzian, 1985; 1997) argues that individuals with PTSD may be vulnerable to abusing substances in effort to relieve, escape or avoid trauma-related negative affect and other PTSD symptoms. Several drug conditioning models suggest that repeated pairings of trauma-related memories with alcohol or drug use may produce conditioned drug responses such as alcohol craving. These models propose that negative emotional cues and negative emotional states may act as conditioned stimuli that are capable of eliciting conditioned drug responses (Siegel, 1983; Stewart, de Wit, & Eikelboom, 1984). This view acknowledges the role of conditioned drug responses as mediating variables in alcohol and drug consumption. In turn, the conditioning models posit that repeated exposure to negative emotional cues in the absence of alcohol and drugs should decrease conditioned drug responses. The two-factor model of substance use (Stasiewicz & Maisto, 1993) extends these drug conditioning models by emphasizing aversive emotional learning and includes conditioned emotional responses as mediating variables in alcohol and drug consumption. In the case of PTSD-SUD, repeated exposure to negative emotional cues that are linked to past specific aversive conditioning events is

predicted to decrease the magnitude of the conditioned emotional responses (e.g., fear, anxiety), which are assumed to play a central role in motivating drug use. Despite their differences, all of models are consistent with a large body of laboratory-based cue-reactivity research that indicates that presentation of trauma cues to individuals with PTSD-SUD increases distress, negative emotional responses, and conditioned drug responses (e.g.,craving, salivation), even when no alcohol cues are present (e.g., Coffey et al., 2002; 2006; 2010; Nosen et al., 2012).

Specifically, alcohol and drug cues (e.g., seeing or smelling an alcoholic beverage or drug of choice) have been shown to reliably increase craving and salivation among substance users in multiple studies (e.g. Monti et al., 1987; Thomas, Drobes & Deas, 2005). Consistent with the self-medication, two-factor, and drug conditioning models, negative mood induction has also been shown to increase substance craving in alcohol and drug users (e.g., Sinha, Catapano,& O'Malley, 1999; Sinha et al., 2008), often to a level equivalent to those elicited by drug and alcohol cues alone (e.g., Childress et al., 1987, 1994; Litt, Cooney, Kadden & Guapp, 1990; Rubonis et al., 1994; Cooney, Litt, Morse, Bauer & Guapp, 1997).

In an early investigation of applications to co-occurring PTSD and SUD, Coffey et al. (2002) presented combinations of trauma imagery, in-vivo alcohol and neutral cues (neutral imagery, water) to an alcohol dependent (AD)-PTSD sample. Compared to neutral cues, participants reported elevated alcohol craving in response to *both* trauma imagery and alcohol cues. Coffey et al. (2010) examined whether this reactivity extends to salivation, a physiological indicator of alcohol craving. Consistent with classical conditioning, AD-PTSD individuals showed increased salivary responding in response to trauma cues, even when no alcohol cue was present. Interestingly, this and other studies (e.g., Coffey, Stasiewicz, Hughes & Brimo, 2006; Nosen et al., 2012) have found that, relative to either cue type presented alone, the presentation of alcohol and trauma cues in combination produces the largest increases in craving and distress, suggesting that individuals exposed to both trauma and alcohol cues concurrently may show especially elevated symptom levels.

This work has important treatment implications, such that desensitization to trauma cues via EXP imaginal and in-vivo exposure techniques could be associated with a concomitant decrease in cue-elicited negative affect and alcohol craving (see Stasiewicz & Maisto, 1993). To date, only one small pilot study has examined whether trauma and alcohol cue-elicited distress and craving is dampened following exposure EXP in individuals with comorbid SUD and PTSD (Coffey et al., 2006). Coffey et al. examined changes in trauma and alcohol cue reactivity following 6 sessions of imaginal exposure vs. relaxation training in a subsample of 12 AD-PTSD individuals receiving outpatient substance use treatment. Consistent with expectations, individuals completing imaginal exposure reported decreased alcohol and trauma cue-elicited craving and distress at post-treatment while cue-reactivity did not change among those receiving relaxation training. This study is limited by several factors, however, including a small sample size and failure to assess physiological indices of craving (which reduce demand effects and provide a stronger test of conditioning models).

In the present study, we replicate and extend this work by examining treatment-related changes in cue-reactivity within the context of an RCT (Coffey et al., submitted) comparing

EXP and non-trauma-focused therapy for PTSD-SUD. Consistent with previous work, Coffey et al., (submitted) observed that EXP was associated with significantly greater reductions in self-reported symptoms of PTSD, depression and alcohol craving over 6-month follow-up, with no differences observed in substance use. In the present study, we examine changes in trauma and alcohol cue-reactivity from pre- to post-treatment. As both treatment conditions received concurrent residential addictions treatment, we hypothesized that both treatments would be associated with reductions in alcohol-cue elicited craving and salivation over time. We also hypothesized that relative to those in a non-trauma focused comparison treatment condition, individuals completing EXP would show reduced distress and negative affect in response to trauma imagery cues. Finally, we took advantage of the longitudinal design to investigate correlated change between trauma cue-elicited distress and cravings by employing latent difference score (LDS) models (McArdle, 2009). In line with current models of PTSD-SUD comorbidity, we anticipated that across treatment groups, decreases in distress and negative affect elicited by trauma cues would be associated with decreases in trauma cue-elicited craving and salivation.

Method

Participants

Adults meeting DSM-IV criteria for alcohol dependence and PTSD were recruited from a community residential chemical dependency treatment facility (see Coffey et al., submitted, for details). All participants reported that their preferred substance was alcohol; 81% also met abuse or dependence criteria for other substances. Participants were required to be abstinent from drugs and alcohol for at least four days immediately preceding each cue-reactivity assessment. Individuals experiencing a psychotic disorder or current manic episode were excluded, as were individuals deemed to be at high risk for suicide. Other exclusion criteria included previous exposure-based PTSD treatment and current use of medications that could interfere with craving, treatment, or salivation responses. See Table 1 for demographics.

Measures

Screening—Individuals whose scores were ≥ 44 on the *PTSD Checklist* (PCL; Blanchard, Jones-Alexander, Buckley & Forneris, 1996) and ≥ 8 on the *Alcohol Use Disorders Identification Test* (AUDIT; Babor, de la Fuente, Saunders, & Grant, 1992) were invited to participate in a comprehensive eligibility assessment.

Diagnosis—The *National Women's Study (NWS) PTSD Module* (Resnick, 1996), as adapted by Dansky, Bryne and Brady (1999), was used to identify PTSD Criterion A events. Past month PTSD was evaluated using the *Clinician Administered PTSD Scale* (CAPS; Blake et al., 1995), a structured clinical interview considered the "gold standard" for PTSD assessment (Weathers, Keane, & Davidson, 2001). Substance use disorders were diagnosed using the *Computerized Diagnostic Interview Schedule* (C-DIS; Robins et al., 2000), a structured assessment for DSM-IV Axis I disorders with sound psychometric properties (e.g., Vandiver & Sher, 1991). Diagnostic criteria for other co-occurring mood, eating, and

anxiety disorders were assessed with the *Mini-International Neuropsychiatric Interview* (MINI; Sheehan et al., 1998).

Self-report—The *Impact of Event Scale-Revised* (IES-R; Weiss & Marmar, 1997) and the *Alcohol Dependence Scale* (ADS; Skinner & Horn, 1984) were administered pre- and post-treatment. The IES-R and ADS are widely used measures of PTSD and AUD symptoms, respectively; both display solid psychometric properties (e.g., Drake, McHugo, & Biesanz, 1995; Rash, Coffey, Baschnagel, Drobes, & Saladin, 2008).

Cue reactivity—Distress, alcohol craving and salivation were assessed after each cue reactivity trial during the laboratory sessions. Negative affect was rated following each cue trial using a 0–100 *subjective units of distress scale* (SUDS) and using the *Positive and Negative Affect Scale* (PANAS; Watson, Clark, & Tellegen, 1988). The PANAS asks participants to rate how much they are experiencing 20 emotion descriptors on a scale from 1 “very slightly or not at all” to 5 “extremely” and produces a negative affect subscale ranging from 10–50.

Self-reported cue-elicited *alcohol craving* was assessed with three Likert scale items (Kozlowski, Pillitteri, Sweeney, Whitfield, & Graham, 1996). Participants rated three statements: “I crave a drink right now,” “I have a desire for a drink right now,” and “I want a drink right now”; on a 0 to 10 scale. Items demonstrated high internal consistency ($\propto$ = .97 following NN condition) and were averaged to produce a single craving score.

Salivary flow was utilized as a physiological measure of cue-elicited craving. This method is described fully by Monti and colleagues (1987). In brief, three pre-weighed dental cotton rolls were inserted under the tongue and between the inner check and lower gum on each side of the mouth, and weighed again following the presentation of each cue combination. Magnitude of salivation is calculated by subtracting the pre- from post-trial weight. One-minute test-retest reliability for salivary flow collected via cotton swabs is $r = 0.68$ (Navazesh & Christensen).

Procedure

Assessment—Prospective participants scoring above the cut-offs on the AUDIT and PCL were invited to complete the C-DIS, NWS PTSD module, CAPS, MINI, IES-R, and ADS during an assessment session. Individuals meeting inclusion/exclusion criteria were asked to describe their worst traumatic event using multiple sensory dimensions (i.e., physical sensations, thoughts, emotions, olfactory sensations, visual details, and avoided activities and events), which provided information for a 60-second audiotaped narrative to be used in their laboratory session. Participants were then scheduled for their first laboratory session within the next week.

Laboratory sessions—Participants completed two lab sessions, one occurring approximately the first week of beginning residential SUD treatment (before completing the study treatment protocol) and one approximately six weeks later (after completing both the residential SUD program and the study treatment protocol). In order to control for diurnal variations that may affect cue reactivity, laboratory sessions were scheduled between 1:00

p.m. and 3:00 p.m. Upon arrival to the laboratory, participants were asked to remove any gum and were given a urine drug screen (UDS; Instant Technologies, Inc., Norfolk, VA) to assess for recent drug use. Expired air samples were analyzed (Alco-sensor IV, Intoximeters, Inc., St. Louis, MO) to assess for current alcohol intoxication. Participants who reported or tested positive for the metabolites of cocaine, opiates, benzodiazapines, amphetamines, methamphetamine, oxycodone, propoxyphene, barbiturates and MDMA were rescheduled. However, participants who tested positive for THC and reported marijuana use in the past 30 days, but not the past 4 days, were allowed to participate in the laboratory session due to the long half-life of THC. Participants were then seated in a sound attenuated experimental room and provided detailed instructions of the cue-reactivity procedure, which has been used frequently and is described in detail elsewhere (Coffey et al., 2010).

Briefly, participants were presented four counterbalanced imagery-in vivo cue combinations (i.e., trauma imagery cue followed by an alcohol cue, TA; trauma imagery cue followed by a neutral cue, TN; neutral imagery cue followed by an alcohol cue, NA; and neutral imagery cue followed by a neutral cue, NN). The trauma imagery cue was a 60-second narrative description of the participant's subjectively rated worst traumatic event, the alcohol cue was their preferred alcoholic beverage, and the neutral cues were a 60-second narrative about changing a light bulb and a bottle of water. Prior to the presentation of these cue combinations, participants were led through a practice trial using an NN combination. Dental cotton rolls were inserted into participants' mouths and they were instructed to close their eyes and listen to the narrative. Following the imagery presentation, the experimenter placed the beverage cue in front of the participant, and they were instructed to open their eyes and continue imagining the scene described in the narrative as vividly as possible for 2 minutes. Immediately following the 3-minute imaginal/in vivo cue exposure, the dental cotton rolls were removed and participants were instructed to complete self-report measures (i.e., craving, PANAS and SUDS). Following the practice trial, this procedure was repeated for the four cue combinations (i.e., TA, TN, NA, NN). Participants provided a final craving rating at the end of the session in order to assure their safety upon dismissal.

Treatments—A full description of study treatments is provided in Coffey et al. (submitted). Therapy was administered by one of four clinicians with doctoral degrees in clinical psychology or one of five advanced clinical psychology Ph.D. candidates. *Trauma-focused exposure therapy* (EXP; Foa et al., 2007) utilizes psycho-education, breathing re-training, imaginal and in vivo exposure techniques to reduce PTSD symptoms. Consistent with Foa et al. (2007), 9–12 sessions of EXP were provided. Participants whose IES-R scores were reduced by 70% or more by the end of the 8th session were assigned to complete 9 sessions, the remainder were assigned to completed 12 sessions. *Healthy Lifestyles Sessions (HLS)* was the active non-trauma comparison condition. HLS provides education about a variety of health-related topics, including sleep hygiene, progressive muscle relaxation, starting/maintaining an exercise program, personal role identification, healthy eating and nutrition, diabetes, monitoring goals and values, cancer and HIV. Participants receiving HLS treatment were yoked to those in the EXP condition and assigned to complete 9 or 12 sessions depending on their corresponding EXP participant. Approximately one half of the participants receiving EXP were also provided a single 90 min Motivational

Enhancement Therapy for PTSD (MET) session prior to beginning EXP. The other half of the EXP participants and all of the HLS participants were provided a 60 min relaxation session prior to the first scheduled treatment session. As MET did not (and was not expected to) produce differences in symptoms over treatment (see Coffey et al., submitted, for details), EXP individuals receiving MET and relaxation were collapsed into a single EXP condition. To note, patterns of statistical significance were identical when analyses were run with the two EXP groups separate and collapsed.

Sessions in both EXP and HLS conditions were 60 minutes and provided twice weekly, concurrently with participants' residential addictions treatment program. Substance use treatment-as-usual (TAU) consisted of group therapy (∼ 3 hours/day), recreation therapy, AA and NA meetings, individual drug and alcohol counseling sessions and related homework. TAU was provided by drug and alcohol counselors unaffiliated with the current study.

Analyses

As the aim of the present study was to examine the effects of treatment on cue-reactivity (not treatment efficacy per se), analyses focus on the 87 individuals receiving an adequate "dose" of treatment (i.e., at least 8 sessions; Foa, et al., 2007). To examine the effects of treatment on cue-reactivity over time, four 2 × 2 × 2 × 2 ANOVA examined differences on the dependent measures (i.e., craving, salivation, PANAS negative affect subscale, SUDS) as a function of treatment assignment (EXP vs PE), lab session (pre- vs. post-treatment), trauma cue type (trauma vs. neutral) and alcohol cue type (alcohol vs. neutral). Significant interactions were follow-up by *t*-tests, where appropriate. We estimated latent difference score models (see McArdle, 2009, Selig & Preacher, 2009) in Mplus version 6.11 (Muthén & Muthén, 1998–2011) to examine correlations between latent change in trauma cue-elicited negative affect (PANAS), distress (SUDs), craving and salivation based on reactivity to the trauma-neutral (TN) trial. The TN trial was selected for analyses because it provides the clearest examination of reactivity to trauma reminders in the absence of alcohol cues. LDS models capture inter-individual differences in intra-individual change across two time points. More specifically, the model is specified such that change in variable X across two time points is expressed as a latent variable ΔX. At time t, variable X is the sum of X at the previous time and change in X, i.e., $X[t] = X[t-1] + \Delta X[t]$ (see equation 5 in Selig & Preacher). This model permits the exploration of the correlated change between trauma cue-elicited distress and cravings (e.g., the extent to which change in SUDs predicts change in salivation). As noted by King et al. (2006), the LDS model allows for an optimally reliable index of change unlike traditional change score analysis that use simple difference scores (see King et al. for more details). Given the relatively small sample size for latent variable models, a relatively straightforward version of a LDS was used (see McArdle and Nesselroade, 1994 for the original description and Selig & Preacher for an applied example) and treatment groups were combined.

Results

Preliminary analyses

Of the 120 participants randomized to condition, a significantly greater proportion of participants received an adequate therapy "dose" (at least 8 sessions) of HLS (92%), compared to EXP (63%), χ^2 (120) = 10.72, p =.001. Of the 87 individuals completing at least 8 treatment sessions, individuals assigned to EXP (n = 52) completed an average of 10.07 (1.58) sessions, whereas those assigned to HLS (n = 35) completed an average 9.74 (1.36). There were no differences in rates of lab session participation in the full sample, χ^2 (120) = 1.17, p =.56. Among treatment completers, 84 (EXP *n = 50; HLS n = 34*) completed the pre-treatment lab session, 74 (EXP *n = 45; HLS n = 29*) completed the post-treatment lab session and 72 completed both sessions (EXP *n = 43; HLS n = 29*).

To examine whether individuals particularly distressed by trauma and alcohol cues were especially likely to drop out of treatment, 4 (trial) × 2 (completion status) ANOVAs examined treatment completion status (at least 8 sessions) as a predictor of cue reactivity (post-trial craving, salivation, PANAS-negative affect and suds) at the first lab session. There was not a significant main effect of completion status for any dependent variable, F's (1, 112) ≤ 2.11, p's ≥ .15, nor were there any significant interactions with cue trial, F's (3, 336) ≤ 2.18, p's ≥ .11. Thus, initial cue reactivity was not predictive of treatment dropout.

Three missing values on the post-treatment PANAS (n = 2) were replaced with predicted values using the Expectation-Maximization (EM) algorithm (Gold & Bentler, 2000). Two HLS participants were missing salivation data for one or more trials and were excluded only from relevant analyses. Thus, sample sizes for subsequent analyses range from 31 – 33 and 41–50 for participants receiving HLS and EXP, respectively. Table 1 displays baseline demographics and symptoms by treatment group. T-tests indicated that there were no significant differences between individuals receiving EXP and HLS at baseline on alcohol use patterns (ADS total score, days since last drank alcohol, average drinks per week) and PTSD symptoms (CAPS total score, IES-R), *t's* (114) ≤ 1.40, p's ≥ .16. Chi-square tests on categorical baseline variables revealed that individuals assigned to EXP were more likely to have a comorbid (non-PTSD) anxiety disorder diagnosis, $\chi^2(87) = 6.23$, p = .01, whereas those assigned to HLS were more likely to have a comorbid eating disorder diagnosis, $\chi^2(87) = 6.23$, p = .03; no other significant differences were observed. As neither anxiety nor eating disorder diagnostic status was significantly related to cue-reactivity outcome variables, these variables were not used in analyses as covariates. Groups did not differ on pre-treatment demographics, including age, gender, education, employment status or income.

Cue Reactivity

Change in cue reactivity across the two laboratory sessions was examined using a series of 2 (treatment) × 2 (time) × 2 (alcohol cue type) × 2 (trauma cue type) repeated measures ANOVAs with craving, salivation, PANAS negative affect and distress as dependent variables. Tables 2 and 3 display descriptors and statistics, respectively.

Cue-elicited alcohol craving—There was a statistically significant 3-way time/trauma cue/alcohol cue interaction effect on cue-elicited alcohol craving. There were also significant 2-way interactions between time/alcohol cue, time/trauma cue, trauma cue/alcohol cue and treatment/alcohol cue, plus significant main effects of time, trauma cue and alcohol cue. Interpreting the 3-way interaction, this indicates that change in cue-elicited craving over time depends in part on both the alcohol cue and the trauma cue. Craving elicited by alcohol and trauma cues generally decreased from pre- to post-treatment (see time/trauma; time/alcohol cue interactions), to a similar degree in both treatment conditions. Alcohol cues elicited stronger craving than trauma cues overall (see trauma/alcohol cue interaction), but particularly at post-treatment. That is, before treatment the combination of alcohol and trauma cues elicited the strongest craving (stronger than alcohol alone), while post-treatment trauma cues did not elevate craving over and above alcohol alone. Interpreting the significant treatment/alcohol cue interaction, this indicates that collapsed across time and trauma cue, individuals assigned to complete PE expressed less alcohol-cue craving reactivity. That is, PE and HLS individuals reported similar craving levels in response to neutral (water) cues, but PE individuals reported significantly lower craving levels in response to alcohol cues. Main effects of time, trauma and alcohol cue reflect that across conditions, cravings were lower at post-treatment and for neutral cue conditions.

Cue-elicited salivation—Examining salivation responses, there were significant 2-way interactions between time/alcohol cue, time/trauma cue, and treatment/trauma cue, plus significant main effects of time, trauma cue and alcohol cue. This indicates that for both treatments, salivation elicited by alcohol and trauma cues generally decreased from pre- to post-treatment (time/trauma; time/alcohol cue interactions). Interpreting the significant treatment/alcohol cue interaction, this indicates that collapsed across time and alcohol cue, individuals assigned to complete PE expressed less trauma-cue salivation reactivity. That is, PE and HLS individuals reported similar salivation levels in response to neutral (water) cues, but PE individuals reported significantly lower salivation levels in response to trauma cues. Main effects of time, trauma and alcohol cue reflect that across conditions, salivation was lower at post-treatment and for neutral cue conditions.

Cue-elicited negative affect and distress (PANAS negative affect and SUDS ratings)—Similar patterns of results were observed when using either the PANAS negative affect subscale or the single item SUDS (0–100) scale as indices of distress. For both measures, there were significant 2-way trauma/alcohol cue, time/alcohol cue, time/trauma cue, treatment/trauma cue and time/treatment interactions. There were also significant main effects of alcohol cue, trauma cue, time and treatment. Interactions can be interpreted such that overall, both trauma and alcohol cues were more distressing than neutral cues (see main effects), with trauma cues eliciting more distress than alcohol cues (trauma/alcohol interaction). Over the course of treatment, distress elicited by both trauma and alcohol cues decreased significantly in both treatments (time/alcohol, time/trauma interactions), with EXP resulting in significantly greater reductions in both alcohol and trauma cue-elicited distress than HLS (time/treatment; treatment/trauma interactions).

Correlations Between Latent Change in Cue-elicited Craving and Distress

Consistent with hypotheses, parameters from the LDS models showed that changes in SUDs ratings from pre- to post-treatment positively predicted change in craving, $B = .28$, $p = .001$ and change in salivation, $B = .20$, $p = .02$. Interestingly, changes in PANAS negative affect predicted change in salivation, $B = .26$, $p = .002$, but not subjective craving, $B = .11$, $p = .22$.

Discussion

The purpose of the present study was to examine effects of exposure-based (EXP) and non-trauma focused psychotherapy on alcohol and trauma-cue reactivity. Specifically, we examined whether providing concurrent trauma-specific therapy (trauma-focused exposure therapy; EXP) in supplement to standard residential substance use treatment would decrease alcohol and trauma cue-elicited negative affect, craving and salivation among individuals with co-occurring PTSD and alcohol dependence. At pre-treatment, results revealed a pattern of cue-reactivity consistent with previous work using this paradigm (Coffey et al., 2002; 2006; Saladin et al., 2003). That is, both trauma and alcohol cues elicited urges to drink and salivation, with the presence of both types of cue evoking greater craving and salivation than either cue paired with a neutral counterpart. Pre-treatment distress and negative affect reactivity followed a similar pattern, such that both trauma and alcohol cues evoked higher SUDS and negative affect ratings than neutral comparison cues; the combination of trauma and alcohol cues again elicited the highest distress.

Compared to non-trauma-focused treatment, EXP produced significantly greater decreases in distress and negative affect elicited by trauma and alcohol cues, measured by either the single-item SUDs scale or the PANAS negative affect subscale. This is consistent with hypotheses and with scores of evidence indicating that EXP is an effective therapy for PTSD (Powers et al., 2010). It also echoes the larger RCT symptom outcomes, which found that EXP produced significantly greater decreases in PTSD and depression symptoms (Coffey et al., submitted).

Also consistent with hypotheses, both trauma- and non-trauma focused therapies were associated with significant and equivalent reductions in symptoms of cue-elicited craving and salivation following treatment. Specifically, craving and salivary responses to both trauma and alcohol cues was significantly reduced at post-treatment, to a similar extent across treatment type. These results mirror the effects of treatment found in the larger RCT (Coffey et al., submitted), which indicated that both trauma and non-trauma focused treatment produced significant and equivalent decreases in substance use behavior. Interestingly, we found that latent change in trauma cue-elicited distress (SUDS, negative affect) predicted latent change in trauma-cue elicited craving and salivation from pre- to post-treatment. Thus, individuals who showed the greatest reductions in distress and negative affect reactivity to trauma cues also tended to show the greatest reductions in trauma cue-elicited craving and salivary responses. These data support Stasiewicz and Maisto's (1993) suggestion that cue exposure treatment for substance users should go further than exposure to substance use cues and should include exposure to the conditioned stimuli associated with past aversive conditioning experiences.

Overall, results are congruent with previous controlled trials demonstrating that relative to comparison conditions, exposure-based trauma-focused therapy significantly reduce PTSD symptoms and evidence similar decreases in SUD symptoms (Mills et al., 2012; Triffleman, 2000). This is the first study to demonstrate that cue-reactivity paradigms are sensitive to these specific treatment effects. Results show that both self-reported craving and salivary responses to alcohol and trauma cues are significantly decreased following residential substance use treatment (either trauma-focused or not) and that EXP produces superior decreases in distress elicited by trauma and alcohol cues. Importantly, results demonstrate that contrary to some common concerns, exposure treatment does not increase alcohol or trauma cue-elicited alcohol craving or salivation.

That *both* types of treatment reduced craving and salivation responses to trauma cues is a departure from the one small pilot study previously examining this topic. Coffey et al. (2006) found that among PTSD-AD individuals receiving outpatient treatment for substance use, imaginal exposure decreased self-report craving responses to trauma cues, but the non-trauma focused comparison condition (relaxation training) did not. There are several plausible explanations for this. For one, the HLS condition used in the present study was considerably more involved and arguably included more valuable nonspecific therapeutic factors (e.g., opportunities for warmth, empathy, personal reflection) than the relaxation training used by Coffey et al., 2006; improvements in mental health and substance use in the comparison condition could be attributable to these factors. Substance use treatment also differed. In contrast to Coffey et al.'s (2006) outpatient treatment sample, participants in the current study were enrolled in a more intensive, residential substance use treatment facility with compulsory abstinence, random drug testing policies and daily attention to helping the client effectively navigate high relapse-risk situations. To the extent that substance use treatment was more effective in the current study, global, non-specific declines in urges to drink may have been more common. Indeed, both self-reported alcohol dependence and craving declined following treatment, as did craving responses to even neutral cues. Demand effects may also have been greater in the current study, such that substance users successfully completing an intensive residential program may plausibly be more reluctant to admit to cue-elicited cravings. Finally, differences in sample sizes may have contributed to differences in study outcomes—with a sample of 12, Coffey et al. (2006) may have been more strongly influenced by individual differences in treatment responses.

Either way, continued exploration of mechanisms driving the maintenance of PTSD and substance use symptoms is warranted. Current results suggest that alcohol and trauma cue-elicited craving and salivation decrease post-treatment, regardless of whether trauma symptoms are explicitly targeted. Although decreases in trauma cue-elicited distress over the course of treatment were associated with decreases in trauma cue-elicited craving and salivation (and were modeled as predictors of change in craving and salivation), true causal directionality of symptom change remains unclear. Temporal analyses tend to find that improvements in PTSD symptoms predict subsequent improvements in SUD (Back, Brady, Jaanimägi, & Jackson, 2006; Hein et al., 2010), but there are also studies that show that PTSD symptoms naturally decline among PTSD-SUD individuals receiving SUD (not PTSD) treatment (e.g., Coffey, Schumacher, Brady, Dansky Cotton, 2007). Examination of

mediations and moderators of cue reactivity may also yield insight. Treatment response may differ, for example, among individuals who drink to avoid or cope with PTSD symptoms vs. individuals who drink for other reasons (Lehavot Stappenbeck, Luterek, Kaysen & Simpson, 2013).

It would be valuable for future work to examine the generalizability of these findings to other treatment modalities. In particular, we examined the specific effects of just one type of trauma-focused therapy, the explicit goals of which are to reduce distress associated with imaginal and in-vivo trauma cues through exposure. Thus, though it is logical that EXP would produce significantly greater reductions in negative affect reactions to trauma cues in comparison to non-trauma focused treatment, it is quite plausible that other trauma-focused therapies would produce similar outcomes. Indeed, meta-analyses suggest that EXP is more effective than waitlists or treatment-as-usual but it is not superior to other well-studied trauma-focused therapies such as Cognitive Processing Therapy (Benish, Imel & Wampold, 2008). Comparison of cue-reactivity following other well-supported trauma-focused treatments may provide insight into unique or shared mechanisms of change, given that EXP explicitly attempts to reduce trauma-cue reactivity while these other therapies do not.

Several limitations are also important to note. First, we are not able to compare patterns in cue reactivity to individuals who did not receive any type of treatment supplemental to the standard residential alcohol use program or to individuals receiving less intensive alcohol dependence treatment. As such, we are not able to pinpoint the causal factor driving the decrease in craving and salivation cue responses (where there were no treatment group differences). We also did not employ any diagnostic control groups. As such, it cannot be determined whether patterns in cue-reactivity are unique to individuals with PTSD-AD. Individuals with comorbid depression, for example, may display negative affective response to trauma narratives similar to those receiving non-trauma focused treatment. Similarly, results cannot be generalized to those with active mania, suicidal ideation, psychosis or individuals taking anti-anxiety or -craving medications, given that these individuals were excluded from participation. Additional follow-up laboratory sessions were also not completed. As such, it is unknown how patterns of cue reactivity relate to long-term symptom improvement or relapse rates.

Finally, reliability of the cue-combinations is uncertain. Navazesh & Christensen (1982) found test-retest reliability of $r = .68$ for the general method of measuring salivary flow used in the current study, but reliability has not been established for this method used specifically in the context of alcohol or trauma cues. Similarly, we do not know the reliability of the cue reactivity procedures. Unlike in picture paradigms, where participants are shown multiple images belonging to a similar category (e.g., mutilation images), the imagery/in-vivo stimuli were unique for each individual. If the cue combinations were presented multiple times, one would actually predict reliability to be poor due to habituation effects. This concern is why we counterbalanced presentation of the cue combinations, but nevertheless, uncertainty regarding the cue-related psychometrics remains a limitation.

Overall, this study demonstrates that alcohol and trauma-cue-reactivity paradigms are sensitive to treatment effects following integrated psychotherapy for PTSD-AD. Consistent

with previous controlled trials, results reveal that craving and salivation responses to trauma and alcohol cues decrease following both trauma and non-trauma focused treatment. Results also show that trauma-focused exposure therapy produces significantly greater decreases in distress triggered by trauma cues, which is consistent with theorized mechanisms of change in EXP. Findings highlight the utility of integrating trauma-focused therapies like EXP into substance use treatment in the interests of reducing PTSD symptoms and distress associated with trauma cues.

Acknowledgments

This research was supported, in part, by National Institute on Alcohol Abuse and Alcoholism grant R01AA016816 (PI: Coffey). The authors wish to thank M. Trost Friedler, Jackie Lampley, and the staff and patients of Harbor House Recovery Center for their cooperation on this study.

References

Babor, TF.; de la Fuente, JR.; Saunders, J.; Grant, M. The Alcohol Use Disorders Identification Test: Guidelines for use in primary care. Geneva: World Health Organization; 1992. WHO Publication No. 92.4.

Back SE, Brady KT, Jaanimägi U, Jackson JL. Cocaine dependence and PTSD: A pilot study of symptom interplay and treatment preferences. Addictive Behaviors. 2006; 31(2):351–354. [PubMed: 15951125]

Benish SG, Imel ZE, Wampold BE. The relative efficacy of bona fide psychotherapies for treating post-traumatic stress disorder: a meta-analysis of direct comparisons. Clinical psychology review. 2008; 28(5):746–758. [PubMed: 18055080]

Blake DD, Weathers FW, Nagy LM, Kaloupek DG, Gusman FD, Charney DS, et al. The development of a clinician-administered PTSD scale. Journal of Traumatic Stress. 1995; 8:75–90. [PubMed: 7712061]

Blanchard EB, Jones-Alexander J, Buckley TC, Forneris CA. Psychometric properties of the PTSD Checklist (PCL). Behaviour Research and Therapy. 1996; 34:669–673. [PubMed: 8870294]

Brady KT, Dansky BS, Back SE, Foa EB, Carroll KM. Exposure therapy in the treatment of PTSD among cocaine-dependent individuals: Preliminary findings. Journal of Substance Abuse Treatment. 2001; 21(1):47–54. [PubMed: 11516926]

Brown PJ, Stout RL, Gannon-Rowley J. 15Substance Use Disorder-PTSD Comorbidity: Patients' Perceptions of Symptom Interplay and Treatment Issues. Journal of Substance Abuse Treatment. 1998; 15(5):445–448. [PubMed: 9751003]

Brown PJ, Stout RL, Mueller T. Posttraumatic stress disorder and substance abuse relapse among women: A pilot study. Psychology of Addictive Behavior. 1996; 10:124–128.

Brown PJ, Stout RL, Mueller T. Substance use disorder and posttraumatic stress disorder comorbidity: Addiction and psychiatric treatment rates. Psychology of Addictive Behavior. 1999; 13:115–122.

Childress AR, Ehrman R, McLellan AT, MacRae J, Natale M, O'Brien CP. Can induced moods trigger drug-related responses in opiate abuse patients? Journal of substance abuse treatment. 1994; 11(1): 17–23. [PubMed: 8201629]

Childress AR, McLellan AT, Natale M, O'Brien CP. Mood states can elicit conditioned withdrawal and craving in opiate abuse patients. NIDA Res Monogr. 1987; 76:137–144. [PubMed: 3125443]

Coffey SF, Saladin ME, Drobes DJ, Brady KT, Dansky BS, Kilpatrick DG. Trauma and substance cue reactivity in individuals with comorbid posttraumatic stress disorder and cocaine or alcohol dependence. Drug and Alcohol Dependence. 2002; 65(2):115–127. [PubMed: 11772473]

Coffey SF, Schumacher JA, Brady KT, Cotton BD. Changes in PTSD symptomatology during acute and protracted alcohol and cocaine abstinence. Drug and alcohol dependence. 2007; 87(2):241–248. [PubMed: 17008029]

Coffey SF, Schumacher JA, Stasiewicz PR, Henslee AM, Baillie LE, Landy N. Craving and physiological reactivity to trauma and alcohol cues in posttraumatic stress disorder and alcohol

dependence. Experimental and Clinical Psychopharmacology. 2010; 18(4):340–349. [PubMed: 20695690]

Coffey SF, Stasiewicz PR, Hughes PM, Brimo ML. Trauma-Focused Imaginal Exposure for Individuals With Comorbid Posttraumatic Stress Disorder and Alcohol Dependence: Revealing Mechanisms of Alcohol Craving in a Cue Reactivity Paradigm. Psychology of Addictive Behaviors. 2006; 20(4):425–435. [PubMed: 17176177]

Coffey SF, Schumacher JA, Nosen Elizabeth, Henslee AM, Lappen A, Stasiewicz P. Trauma-focused Exposure Therapy for Chronic Posttraumatic Stress Disorder in Alcohol and Drug Dependent Patients: A Randomized Clinical Trial. (submitted manuscript).

Cooney NL, Litt MD, Morse PA, Bauer LO, Gaupp L. Alcohol cue reactivity, negative-mood reactivity, and relapse in treated alcoholic men. Journal of abnormal psychology. 1997; 106:243–250. [PubMed: 9131844]

Crawford JR, Henry JD. The Positive and Negative Affect Schedule (PANAS): Construct validity, measurement properties and normative data in a large non-clinical sample. British Journal of Clinical Psychology. 2004; 43(3):245–265. [PubMed: 15333231]

Creamer M, Bell R, Failla S. Psychometric properties of the Impact of Event Scale - Revised. Behaviour Research and Therapy. 2003; 41:1489–1496. [PubMed: 14705607]

Dansky BS, Saladin ME, Brady KT, Kilpatrick DG, Resnick HS. Prevalence of victimization and posttraumatic stress disorder among women with substance use disorders: comparison of telephone and in-person assessment samples. Substance Use & Misuse. 1995; 30(9):1079–1099.

Dansky BS, Roitzsch JC, Brady KT, Saladin ME. Posttraumatic stress disorder and substance abuse: use of research in a clinical setting. Journal of Traumatic Stress. 1997; 10(1):141–148. [PubMed: 9018685]

Drake RE, McHugo GJ, Biesanz JC. The test-retest reliability of standardized instruments among homeless persons with substance use disorders. Journal of Studies on Alcohol. 1995; 56:161–167. [PubMed: 7760561]

Foa, E.; Hembree, E.; Rothbaum, BO. Prolonged exposure therapy for PTSD: Emotional processing of traumatic experiences therapist guide. USA: Oxford University Press; 2007.

Foa EB, Yusko DA, McLean CP, Suvak MK, Bux DA, Oslin D, Volpicelli J. Concurrent naltrexone and prolonged exposure therapy for patients with comorbid alcohol dependence and PTSD: a randomized clinical trial. JAMA. 2013; 310(5):488–495. [PubMed: 23925619]

Gold MS, Bentler PM. Treatments of Missing Data: A Monte Carlo Comparison of RBSHI, Iterative Stochastic Regression Imputation, and Expectation-Maximiazation. Stuctural Equation Modeling: A Multidisciplinary Journal. 2000; 7:319–355. http://dx.doi.org/10.1207/S15328007SEM0703_1.

Hien DA, Jiang H, Campbell AN, Hu MC, Miele GM, Cohen LR, Nunes EV. Do treatment improvements in PTSD severity affect substance use outcomes? A secondary analysis from a randomized clinical trial in NIDA's Clinical Trials Network. The American journal of psychiatry. 2010; 167(1):95. [PubMed: 19917596]

Institute of Medicine. Treatment of posttraumatic stress disorder: An assessment of the evidence. Washington, DC: The National Academies Press; 2007.

Kazdin AE. Treatment outcomes, common factors, and continued neglect of mechanisms of change. Clinical Psychology: Science and Practice. 2005; 12:184–188.

Kazdin AE. Mediators and mechanisms of change in psychotherapy research. Annu. Rev. Clin. Psychol. 2007; 3:1–27. [PubMed: 17716046]

Khantzian EJ. The self-medication hypothesis of addictive disorders: focus on heroin and cocaine dependence. Am J Psychiatry. 1985; 142(11):1259–1264. [PubMed: 3904487]

Khantzian EJ. The self-medication hypothesis of substance use disorders: A reconsideration and recent applications. Harvard Review of Psychiatry. 1997; 4(5):231–244. [PubMed: 9385000]

Kilpatrick DG, Acierno R, Resnick HS, Saunders BE, Best CL. A 2-year longitudinal analysis of the relationships between violent assault and substance use in women. Journal of consulting and clinical psychology. 1997; 65(5):834. [PubMed: 9337502]

King LA, King DW, McArdle JJ, Saxe GN, Doron-LaMarca S, Orazem RJ. Latent difference score approach to longitudinal trauma research. Journal of Traumatic Stress. 2006; 6:771–785. [PubMed: 17195976]

Kozlowski LT, Pillitteri JL, Sweeney CT, Whitfield KE, Graham JW. Asking questions about urges or cravings for cigarettes. Psychology of Addictive Behaviors. 1996; 10:248–260.

Lehavot K, Stappenbeck CA, Luterek JA, Kaysen D, Simpson TL. Gender Differences in Relationships Among PTSD Severity, Drinking Motives, and Alcohol Use in a Comorbid Alcohol Dependence and PTSD Sample. Psychology of Addictive Behavior. 2013

Litt MD, Cooney NL, Kadden RM, Gaupp L. Reactivity to alcohol cues and induced moods in alcoholics. Addictive Behaviors. 1990; 15(2):137–146. [PubMed: 2343787]

McArdle JJ. Latent variable modeling of differences and changes with longitudinal data. Annual Review of Psychology. 2009; 60:577–605.

McArdle, JJ.; Nesselroade, JR. Using multivariate data to structure developmental change. In: Cohen, SH.; Reese, HW., editors. Life-span developmental psychology: Methodological contributions. Hillsdale, NJ: Erlbaum; 1994. p. 223-267.

Mills KL, Teesson M, Back SE, Brady KT, Baker AL, Hopwood S, Ewer PL. Integrated Exposure-Based Therapy for Co-occurring Posttraumatic Stress Disorder and Substance Dependence: A Randomized Controlled Trial Exposure Therapy for PTSD and Substance Dependence. JAMA: The Journal of the American Medical Association. 2012; 308(7):690–699.

Monti PM, Binkoff JA, Abrams DB, Zwick WR, Nirenberg TD, Liepman MR. Reactivity to alcoholics and non-alcoholics to drinking cues. Journal of Abnormal Psychology. 1987; 96:122–126. [PubMed: 3584660]

Muthén, LK.; Muthén, BO. Mplus user's guide. 6th ed.. Los Angeles, CA: Muthén & Muthén; 1998–2011.

Najavits LM, Schmitz M, Gotthardt S, Weiss RD. Seeking safety plus exposure therapy: An outcome study on dual diagnosis men. Journal of Psychoactive Drugs. 2005; 37(4):425–435. [PubMed: 16480170]

Navazesh, Christensen. A comparison of whole mouth resting and stimulated salivary measurement procedures. Journal of Dental Research. 1982; 61:1159–1162.

Norman SB, Tate SR, Anderson KG, Brown SA. Do trauma history and PTSD symptoms influence addiction relapse context? Drug and Alcohol Dependence. 2007; 90:89–96. [PubMed: 17459611]

Nosen E, Nillni YI, Berenz EC, Schumacher JA, Stasiewicz PR, Coffey SF. Cue-elicited affect and craving: advancement of the conceptualization of craving in co-occurring posttraumatic stress disorder and alcohol dependence. Behav Modif. 2012; 36(6):808–833. [PubMed: 22619397]

Ouimette PC, Finney JW, Moos RH. Two-year posttreatment functioning and coping of substance abuse patients with posttraumatic stress disorder. Psychology of Addictive Behaviors. 1999; 13:105–114.

Powers MB, Halpern JM, Ferenschak MP, Gillihan SJ, Foa EB. A meta-analytic review of prolonged exposure for posttraumatic stress disorder. Clinical Psychology Review. 2010; 30(6):635–641. [PubMed: 20546985]

Rash CJ, Coffey SF, Baschnagel JS, Drobes DJ, Saladin ME. Psychometric properties of the IES-R in a sample of traumatized substance users. Addictive Disorders. 2008; 33:1039–1047.

Read JP, Brown PJ, Kahler CW. Substance use and posttraumatic stress disorder: Symptom interplay and effects on outcome. Addictive Behaviors. 2004; 29:1665–1672. [PubMed: 15451135]

Reynolds M, Mezey G, Chapman M, Wheeler M, Drummond C, Baldacchino A. Co-morbid post-traumatic stress disorder in a substance misusing clinical population. Drug and Alcohol Dependence. 2005; 77:251–258. [PubMed: 15734225]

Resnick, H. Psychometric review of National Women's Study (NWS) Event History-PTSD Module. In: Stamm, BH., editor. Measurement of stress, trauma, and adaptation. Lutherville, MD: Sidran Press; 1996. p. 214-217.

Resnick HS, Kilpatrick DG, Dansky BS, Saunders BE, Best CL. Prevalence of civilian trauma and posttraumatic stress disorder in a representative national sample of women. Journal of Consulting and Clinical Psychology. 1993; 61:984–991. [PubMed: 8113499]

Robins, LN.; Cottler, LB.; Bucholz, KK.; Compton, WM.; North, CS.; Rourke, KM. Diagnostic Interview Schedule for the DSM-IV (DIS-IV). St. Louis, MO: Washington University; 2000.

Rubonis AV, Colby SM, Monti PM, Rohsenow DJ, Gulliver SB, Sirota AD. Alcohol cue reactivity and mood induction in male and female alcoholics. Journal of Studies on Alcohol and Drugs. 1994; 55(4):487.

Saladin ME, Drobes DJ, Coffey SF, Dansky BS, Brady KT, Kilpatrick DG. PTSD symptom severity as a predictor of cue-elicited drug craving in victims of violent crime. Addictive Behaviors. 2003; 28(9):1611–1629. [PubMed: 14656549]

Sannibale C, Teesson M, Creamer M, Sitharthan T, Bryant RA, Sutherland K, et al. Randomized controlled trial of cognitive behavior therapy for comorbid posttraumatic stress disorder and alcohol use disorders. Addiction. in press.

Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M. Development of the Alcohol Use Disorders Screening Test (AUDIT). WHO collaborative project on early detection of persons with harmful alcohol consumption. II. Addiction. 1993; 88:791–804. [PubMed: 8329970]

Selig JP, Preacher KJ. Mediation models for longitudinal data in developmental research. Research in Human Development. 2009; 6:144–164.

Sheehan DV, Lecrubier V, Sheehan KH, Amorim P, Janavs J, Weiller E, et al. The Mini-International Neuropsychiatric Interview (MINI): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. Journal of Clinical Psychiatry. 1998; 59:22–23. [PubMed: 9881538]

Siegel, S. Classical conditioning, drug tolerance, and drug dependence. In: Israel, Y.; Glaser, FB.; Kalant, H.; Popham, RE.; Schmidt, W.; Smart, RG., editors. Research advances in alcohol and drug problems. Vol. 7. New York: Plenum; 1983. p. 207-246.

Sinha R, Catapano D, O'Malley S. Stress-induced craving and stress response in cocaine dependent individuals. Psychopharmacology. 1999; 142(4):343–351. [PubMed: 10229058]

Sinha R, Fox HC, Hong KA, Bergquist K, Bhagwagar Z, Siedlarz KM. Enhanced negative emotion and alcohol craving, and altered physiological responses following stress and cue exposure in alcohol dependent individuals. Neuropsychopharmacology. 2008; 34(5):1198–1208. [PubMed: 18563062]

Skinner, HA.; Horn, JL. Alcohol Dependence Scale: Users guide. Toronto: Addiction Research Foundation; 1984.

Stasiewicz PR, Maisto SA. Two-factor avoidance theory: The role of negative affect in the maintenance of substance use and substance use disorder. Behavior Therapy. 1993; 24:337–356.

Stewart J, De Wit H, Eikelboom R. Role of unconditioned and conditioned drug effects in the self-administration of opiates and stimulants. Psychological review. 1984; 91(2):251. [PubMed: 6571424]

Stewart S, Pihl RO, Conrod PJ, Dongier M. Functional assocations between trauma, ptsd and substance-related disorders. Addictive Behavior. 1998; 23:797–812.

Tate SR, Norman SB, McQuaid JR, Brown SA. Health problems of substance-dependent veterans with and those without trauma history. Journal of substance abuse treatment. 2007; 33(1):25–32. [PubMed: 17588486]

Thomas SE, Drobes DJ, Deas D. Alcohol cue reactivity in alcohol-dependent adolescents. Journal of Studies on Alcohol and Drugs. 2005; 66(3):354.

Triffleman E. Gender differences in a controlled pilot study of psychosocial treatments in substance dependent patients with post-traumatic stress disorder: Design considerations and outcomes. Alcoholism Treatment Quarterly. 2000; 18(3):113–126.

Vandiver T, Sher KJ. Temporal stability of the Diagnostic Interview Schedule. Psychological Assessment: A Journal of Consulting and Clinical Psychology. 1991; 3:277–281.

Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: The PANAS scales. Journal of Personality and Social Psychology. 1988; 54(6): 1063–1070. [PubMed: 3397865]

Weathers, FW.; Keane, TM. Psychological assessment of traumatized adults. In: Saigh, PA.; Bremner, JG., editors. Posttraumatic stress disorder: A comprehensive text. Boston: Allyn & Bacon; 1999. p. 219-247.

Weathers FW, Keane TM, Davidson JR. Clinician-administered PTSD scale: A review of the first ten years of research. Depression and Anxiety. 2001; 13:132–156. [PubMed: 11387733]

Weathers, F.; Litz, B.; Herman, D.; Huska, J.; Keane, T. The PTSD Checklist (PCL): Reliability, validity, and diagnostic utility; San Antonio, TX. Paper presented at the Annual Convention of the International Society for Traumatic Stress Studies; 1993 Oct.

Weiss, DS.; Marmar, CR. The Impact of Event Scale-Revised. In: Wilson, JP.; Keane, TM., editors. Assessing psychological trauma and PTSD. New York: Guilford Press; 1997. p. 399-411.

Highlights

- We examined changes in trauma/alcohol cue-reactivity after psychotherapy for PTSD-SUD
- Exposure therapy reduced distress elicited by trauma cues more than non-trauma therapy
- Both therapies were associated with reduced craving and salivation reactivity
- Change in trauma cue-elicited distress predicted change in craving, salivation
- Findings support integration of exposure-based PTSD therapies into SUD treatment

Table 1

Mean (SD) participant characteristics at baseline among treatment completers (≥ 8 sessions)

	EXP (*N* = 52)	**HLS (*N* = 35)**
Age	**35.37 (9.98)**	**32.63 (9.75)**
Gender (% Female)	**42%**	**49%**
Race		
White/Caucasian	77%	83%
Black/African American	19%	17%
Other	2%	0%
Education		
Did not complete high school	6%	11%
High school graduate or GED	19%	29%
Some college	44%	37%
≥ 2 or 4-year college degree	29%	23%
Employment prior to treatment		
Full-Time	19%	37%
Part-Time	13%	9%
Unemployed	52%	49%
Homemaker	6%	0%
Student	10%	3%
Retired	0%	3%
Average household income	$35,062 ($35,742)	$26,600 ($25,702)
Alcohol Dependence Scale	26.15 (9.17)	25.80 (9.40)
Days since last drink of alcohol	16.40 (9.86)	19.86 (13.11)
Average # drinks per week	52.32 (53.36)	39.72 (35.19)
Current co-occurring drug use		
Cocaine use disorder	51%	68%
Amphetamine use disorder	17%	26%
Marijuana use disorder	41%	37%
Sedative use disorder	46%	23%
Opiate use disorder	38%	40%
Hallucinogen use disorder	0%	3%
Any co-occurring drug use disorder	81%	80%
Major Depression/Dysthymia	35%	32%
Other anxiety disorder [a]	75%	54%
Anorexia or Bulimia Nervosa [a]	0%	11%
CAPS Total Score	79.48 (16.49)	77.06 (18.19)

	EXP (*N* = 52)	**HLS (*N* = 35)**
Age	**35.37 (9.98)**	**32.63 (9.75)**
Gender (% Female)	**42%**	**49%**
Impact of Event Scale-Revised	48.86 (15.30)	46.14 (13.91)
Beck Depression Inventory	30.10 (10.34)	30.54 (10.20)
Beck Anxiety Inventory	25.72 (13.71)	26.94 (12.28)

[a]Treatment groups differed significantly at baseline, $p<.05$

Table 2

Alcohol Craving, Salivation and Negative Affect and Distress Ratings for the Four Trial Types among Treatment Completers

	Trauma-focused exposure therapy (*N*= 43)				Healthy Lifestyles Session (*N*=29)			
	Pre-treatment		Post treatment		Pre treatment		Post treatment	
Trial type and measure	***M***	***SD***	***M***	***SD***	***M***	***SD***	***M***	***SD***
Trauma-Alcohol								
Craving (0–10)	5.95	3.23	1.98	2.52	7.23	3.03	3.54	3.01
Salivation	1.22	1.26	.63	.48	1.83	1.55	1.18	.96
SUDS (0–100)	80.02	20.50	28.44	19.28	80.64	18.17	58.71	22.63
PANAS NA	34.55	9.78	17.27	6.79	36.21	6.54	27.57	8.91
Trauma-Neutral								
Craving	4.71	3.02	1.15	1.84	5.28	3.58	1.94	2.38
Salivation	.93	1.09	.57	.53	1.22	1.23	1.03	.82
SUDS (0–100)	69.70	22.76	19.63	14.55	68.14	25.09	51.00	27.78
PANAS NA	33.95	9.09	15.65	5.97	33.34	7.82	26.93	10.32
Neutral-Alcohol								
Craving	4.73	3.38	1.87	2.53	5.36	2.90	3.12	2.83
Salivation	1.15	1.26	.73	.69	1.17	1.02	1.05	.83
SUDS (0–100)	40.77	27.65	15.26	13.06	37.71	24.45	34.36	21.40
PANAS NA	23.09	10.00	13.62	4.41	22.96	8.69	17.54	5.55
Neutral-Neutral								
Craving	2.75	2.77	.84	1.73	2.52	2.41	1.61	2.17
Salivation	0.77	0.73	0.63	0.59	0.95	0.89	0.98	0.96
SUDS (0–100)	21.30	18.30	8.86	9.96	13.83	16.69	18.07	21.58
PANAS NA	18.32	8.45	11.29	2.35	15.76	6.25	14.38	6.03

SUDS = subjective units of distress scale (0–100); PANAS NA = Positive and Negative Affect Scale, negative subscale .

† $p \leq .10$

* $p \leq .05$

** $p \leq .01$

Table 3

2 × 2 × 2 × 2 ANOVA Results

	Craving			Salivation			Negative Affect (PANAS)			SUDs		
	***F* (1, 68)**	***p***	η_p^2	***F* (1, 68)**	***p***	η_p^2	***F* (1, 68)**	***p***	η_p^2	***F* (1, 68)**	***p***	η_p^2
Treatment	3.00	.09	.04	3.28	.08	.05	8.43	.005	.11	9.18	.003	.12
PrePost	80.47	<.001	.54	8.41	.005	.11	138.91	<.001	.67	142.94	<.001	.68
PrePost * Treatment	.76	.39	.01	1.00	.32	.01	21.84	<.001	.24	44.27	<.001	.39
TraumaCue	67.98	.001	.50	10.16	.002	.13	207.30	<.001	.75	273.05	<.001	.80
TraumaCue * Treatment	3.68	.06	.05	7.45	.01	.10	8.36	.01	.11	5.94	.02	.08
AlcCue	108.62	.001	.61	22.59	<.001	.25	38.06	<.001	.36	115.20	<.001	.63
AlcCue * Treatment	4.34	.04	.06	.04	.83	.00	1.86	.18	.03	2.37	.13	.03
PrePost * TraumaCue	44.03	.001	.39	9.37	.003	.12	50.32	<.001	.43	83.03	.00	.55
PrePost * TraumaCue * Treatment	2.14	.15	.03	.46	.50	.01	5.58	.02	.08	2.06	.16	.03
PrePost * AlcCue	14.38	.00	.17	9.56	.003	.12	3.74	.06	.05	8.19	.01	.11
PrePost * AlcCue * Treatment	.01	.91	.00	.00	.97	.00	1.73	.19	.02	1.05	.31	.02
TraumaCue * AlcCue	4.50	.04	.06	.19	.67	.00	11.72	.001	.15	6.57	.01	.09
TraumaCue * AlcCue * Treatment	.002	.97	.00	2.74	.10	.04	.56	.46	.01	1.16	.29	.02
PrePost * TraumaCue * AlcCue	6.71	.01	.09	.27	.60	.00	4.49	.04	.06	2.79	.10	.04
PrePost * TraumaCue * AlcCue * Treatment	.47	.49	.01	.64	.43	.01	.02	.88	.00	.88	.35	.01

Note: SUDS = subjective units of distress scale (0–100); PANAS = Positive and Negative Affect Scale, negative subscale; Treatment = between-subject treatment condition (PE vs. HLS); PrePost= within-subject time condition (Lab 1 vs. Lab 2); TraumaCue = within-subject trauma cue condition (trauma vs. neutral imagery); AlcCue = within-subject alcohol cue condition (alcohol vs. neutral imagery)