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Treatment of Co-occurring Posttraumatic Stress Disorder and Substance Use Disorders

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Abstract

There is a significant need for advanced understanding of treatment of co-occurring posttraumatic stress disorder (PTSD) and substance use disorders (SUD). Approximately half of individuals seeking SUD treatment meet criteria for current PTSD, and individuals with co-occurring PTSD-SUD tend to have poorer treatment outcomes compared with those without such comorbidity. However, there is not sufficient empirical evidence to determine a best course of treatment for these individuals. This paper provides a review of the literature relevant to the treatment of co-occurring PTSD-SUD. To date, treatment studies have focused primarily on non-exposure-based psychosocial treatments, exposure-based psychosocial treatments, and medication trials. The most promising outcome data thus far are for psychosocial treatments that incorporate an exposure therapy component; however, further research is needed, particularly as related to how best to implement these approaches in real-world treatment settings.

Keywords

Posttraumatic stress disorder; PTSD; Substance use; Substance abuse; Substance dependence; Addiction; Alcohol; Alcoholism; Cocaine; Prolonged exposure; Comorbidity; Anxiety; Treatment; Selective serotonin reuptake inhibitors; SSRI; Cognitive behavioral therapy; CBT

Introduction

There is a significant clinical need for a better understanding of the etiology and treatment of co-occurring posttraumatic stress disorder (PTSD) and substance use disorders (SUD). Approximately half of individuals seeking treatment for SUD meet current criteria for PTSD [1], an estimate more than 5 times greater than the U.S. lifetime prevalence rate [2]. In addition, the prognosis for individuals in SUD treatment who have co-occurring PTSD is poorer compared with those without PTSD. For example, individuals with co-occurring PTSD report more intense cravings for drugs/alcohol [3–6] and tend to relapse more quickly than individuals without PTSD upon completion of SUD treatment [1]. Unfortunately, there

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is not currently a “gold standard” of care for individuals presenting with both diagnoses. The objective of the current paper is to review the available literature on potential etiological pathways of, and treatment approaches for, comorbid PTSD-SUD, as well as provide a summary of limitations and associated future directions in this area of study.

Possible Etiological Pathways of Co-Occurring PTSD and SUD

There have been a number of conceptualizations of potential pathways for the development of co-occurring psychiatric disorders [7, 8]. The primary etiological models investigated in relation to PTSD-SUD co-occurrence are the shared liability and causal models. We will provide a brief review of the evidence for each model.

Shared Liability Model

The shared liability model presumes that individuals with greater common liability would be more likely to develop both disorders [8]. There is empirical support that PTSD and SUD share common risk. For example, Wolf and colleagues examined the factor structure of several internalizing and externalizing disorders (including PTSD, alcohol dependence, and substance dependence) in over 3000 male twin pairs from the Vietnam Era Twin Registry (VETR). They found that PTSD, but no other anxiety/mood disorders, significantly loaded on both the internalizing and externalizing factors and that common genetic liability exists between PTSD and SUDs [9]. It is possible that the shared genetic liability between PTSD and SUDs is due to common genetic risk for exposure to traumatic events (which have been found to be approximately 36 % heritable [10]) and/or common genetic risk for PTSD (which has been found to be approximately 30 % heritable after accounting for trauma exposure [11]) following a traumatic event. Emerging research has found that only one-fifth of familial liability (ie, shared environmental and genetic factors) for PTSD overlaps with that for trauma exposure [12]; however, few genetic studies investigate trauma exposure and PTSD separately in relation to SUDs.

Available research from the VETR has found that there is shared genetic and/or environmental liability between combat exposure and alcohol consumption [13], as well as between combat exposure and alcohol and cannabis dependence [14]. Similarly, studies have indicated genetic/environmental factors common to PTSD and alcohol consumption [13], and to PTSD and both alcohol and drug dependence [15]. It is not entirely clear what specific factors account for this shared liability. One possible mediator is trait-level neuroticism [16, 17], which is significantly related to PTSD [18–20] and SUD [21, 22]; however, further research is needed to better understand common liability factors.

Causal Model

Some literature suggests that preexisting SUD is related to increased odds of subsequent PTSD and/or traumatic event exposure, but findings are inconsistent. For example, individuals with a pre-existing alcohol use disorder (37.5 %) or SUD (41.5 %) met criteria for PTSD at higher rates following the Oklahoma City bombing than those without prior SUD [23]. Kaysen and colleagues found a lifetime history of alcohol problems was related to greater PTSD symptom severity following an assault [24]. Other work has found modest or no support for a relationship between SUD and subsequent odds of developing PTSD among trauma-exposed individuals [25, 26]. Some work has found that SUD does not predict subsequent trauma exposure [25], while other studies have found support for substance use behavior being related to increased odds of trauma, particularly sexual assault [27–29]. There is some support for a potential relationship between substance use behavior/SUD and subsequent trauma exposure and PTSD; however, a causal test of the relationship has yet to be conducted.

More often, studies indicate PTSD predicts subsequent SUD, as it is consistent with the self-medication hypothesis, or the theory that individuals use substances to cope with psychiatric distress [30]. PTSD precedes SUD in retrospective [2, 31] and prospective studies [26]. Cross-sectional studies have demonstrated links between PTSD and using substances to cope with negative affect [32], and that self-medication motives for use is a potential mediator of the relationship between PTSD and problem drinking/drug use [33]. Human laboratory studies provide further support for the self-medication hypothesis. For example, individuals with PTSD and co-occurring alcohol/cocaine dependence evidence increased self-reported craving in response to personalized trauma cues, even when an alcohol/drug cue is not present [3, 5]. Furthermore, alcohol dependent individuals with PTSD experience increased physiological indices of craving (ie, salivation) in response to a personalized trauma cue compared with neutral cues, with an additive effect being observed for trauma and alcohol cues that are presented together [34•]. Results of a recent daily monitoring study indicate that on days of greater PTSD symptoms, individuals experience higher subjective craving for alcohol [6]. Taken together, there is a larger body of literature supporting PTSD as a potential causal mechanism for the development of SUD than vice versa; however, causality cannot be determined.

Finally, it is important to recognize that once an individual meets criteria for both disorders, they influence each other. For example, past studies have shown that within-individual increases in PTSD symptoms are associated with increases in subjective craving [6], while improvements in PTSD symptoms are related to decreased substance use [35]. Brown and colleagues reported that patients perceive a strong interrelationship between symptoms of PTSD and SUD in that when symptoms of one condition worsen, symptoms of the other condition also worsen. Likewise, when symptoms of one condition improve, symptoms of the other condition improve [36, 37]. In a prospective study during the first 28 days of monitored abstinence, PTSD symptom severity significantly decreased in individuals with PTSD and a SUD despite the fact that these individuals were not receiving treatment for their PTSD symptoms [38]. In summary, the nature of PTSD-SUD co-occurrence is still largely unknown, but it is clear that there are negative implications for comorbid PTSD-SUD and that these individuals likely represent a group with unique treatment needs.

Treatment of Co-Occurring PTSD and SUD

Non-Exposure-Based Psychosocial Treatment Approaches

One of the most widely recognized and studied non-exposure based treatments for co-occurring substance abuse and PTSD is Seeking Safety (SS), which consists of an average of 25 60–90 minute sessions covering a wide variety of topics such as decreasing risky behaviors, setting boundaries, and coping with substance triggers, to name a few [39]. SS, in the context of the Herman's model of trauma recovery [40], is a Stage I treatment in which the primary goal is to establish safety, broadly defined. Exploration of past traumas (eg, exposure therapy) is explicitly excluded from this treatment approach [41].

A handful of recently published studies found limited support for SS among individuals with co-occurring PTSD-SUD. For example, a pilot study of 9 Operation Iraqi Freedom/ Operation Enduring Freedom (OIF/OEF) veterans who received an abbreviated (10-session) SS protocol revealed that 8 of the 9 participants experienced improvements in PTSD symptoms, all improved on depressive symptoms, and 5 reported a reduction in drinking days following the intervention [42]. However, the sample size was limited, and there was no control condition. Lynch and colleagues conducted an investigation of SS among 114 incarcerated women and found that those who received SS (n=59) compared with a waitlist control evidenced greater improvement in PTSD and depressive symptoms [43]. However,

there was no assessment of substance use outcomes, the treatment groups were not randomly assigned, and the comparison condition was a waitlist.

Among studies with larger samples and more rigorous control conditions, SS does not appear to be better than SUD treatment alone for PTSD-SUD. Although SS has evidenced significant improvements in PTSD symptoms and substance abuse in a number of studies, it does not demonstrate better outcomes than relapse prevention, a SUD-only treatment, or health education interventions alone in randomized controlled trials [44•, 45]. In Hien et al [45], SS produced an 18 % reduction in PTSD symptom severity on a psychometrically sound questionnaire (compared with a 26 % reduction in PTSD symptom severity for those in the relapse prevention condition), while Hien et al [44•], a large study consisting of 353 subjects, reported a 35 % reduction in PTSD symptom severity following SS during follow-up compared with a 33 % reduction in PTSD symptom severity for those in a women's health education condition. Similarly, Zlotnick and colleagues, in a study comparing SS/treatment-as-usual (TAU) to TAU alone, found both conditions exhibited equal improvements in PTSD and SUD outcomes, with SS/TAU not being superior to TAU alone [46].

In a more recent investigation of SS, 98 male veterans presenting to an outpatient substance use clinic at a Veterans Affairs (VA) medical center who met criteria for a current SUD and subclinical or clinical levels of PTSD symptoms were randomized to a SS or TAU condition within the VA system [47]. TAU consisted of twice weekly abstinence-based recovery groups and a variety of other groups and individual appointments as deemed necessary by the patients and treatment providers. The SS condition consisted of the same treatment approach with the exception of the recovery groups being replaced by SS groups. Following treatment, there were no group differences in PTSD symptoms or alcohol use; however, participants in SS reported fewer days of illicit drug use compared with TAU, as well as better treatment attendance and satisfaction. It should be noted that TAU recovery groups were conducted by individuals with a bachelor's or master's degree, while SS groups were conducted by a Ph.D.-level therapist. Taken together, SS has evidenced limited benefit above and beyond TAU conditions among studies with more rigorous methodologies and should likely not be considered a stand-alone treatment for individuals suffering from co-occurring PTSD-SUD.

Transcend is another treatment approach that has been described in the literature as an option for treating co-occurring PTSD-SUD. Transcend is a 12-week eclectic, partial hospitalization program for veterans that includes concepts from psychodynamic, cognitive behavioral therapy (CBT), and 12-step treatment programs. Patients first complete a VA SUD treatment program, then begin the Transcend protocol, which is a group treatment divided into 6 weeks of skills development and 6 weeks of group “trauma processing.” In the one published study of Transcend, the treatment was associated with improvements in PTSD and SUD outcomes among 46 male veterans, producing a 14 % PTSD symptom reduction at 6-month follow-up on a well-validated structured clinical interview for PTSD. Results from the study must be interpreted with caution since there was no control group employed in the design and no follow-up studies have been conducted to our knowledge [48].

Two studies have examined a non-exposure-based CBT approach for treating co-occurring PTSD-SUD. McGovern and colleagues adapted a CBT-based treatment (ie, Integrated CBT) initially developed for individuals with co-occurring PTSD and serious mental illness for use among individuals with PTSD-SUD [49]. Integrated CBT is an 8–12 session protocol that includes modules such as breathing retraining, PTSD psycho-education, and CBT coping skills (eg, relapse prevention, cognitive restructuring) [49]. Results of a recent

randomized controlled trial comparing Integrated CBT to individual addiction counseling among 53 individuals with PTSD and SUD receiving intensive outpatient treatment in the community indicated that Integrated CBT was related to greater improvements in PTSD and SUD outcomes (validated by urinalysis) compared with individual addiction counseling, particularly among those with more severe PTSD symptoms. However, as assessed with a well-validated semi-structured clinical interview, the treatment groups did not appear to differ at 6-months follow-up, with the Integrated CBT group evidencing a 39 % reduction in PTSD symptom severity post-treatment and the individual addiction counseling group evidencing a 41 % symptom reduction. It is worth noting that treatment completion was significantly better in the individual addiction counseling condition. Both treatments were delivered by trained community counselors with master's level degrees or lower, which may speak to the dissemination potential for Integrated CBT [50].

In summary, there is modest, preliminary support for Integrated CBT as a potential treatment for PTSD-SUD, particularly in the initial post-treatment phase; however, further research needs to be conducted to establish whether Integrated CBT outperforms SUD treatment alone. With regard to SS, results of randomized controlled trials have indicated that it is not more effective than relapse prevention or healthy living interventions alone; therefore, pursuing dissemination or further in depth study of SS is likely not warranted, given more promising results of other treatment approaches.

Exposure-Based Psychosocial Treatment Approaches

There have been a number of treatment protocols introduced for treating co-occurring PTSD-SUD that involve varying degrees of exposure-based interventions. Prolonged Exposure (PE) [51•], a CBT approach, is one of the most effective treatments for PTSD [52•] and is the basis for PTSD-SUD interventions that incorporate exposure-based principles. PE includes psycho-education, breathing retraining, in vivo exposure, and imaginal exposure [51•]. In the psycho-education phase of PE, the therapist explains the criteria for PTSD, presents a CBT model for understanding PTSD onset and maintenance, and gives an overview of the treatment mechanisms presumed to underlie PE. The therapist then instructs the client on breathing retraining, a relaxation skill enabling clients to regulate their physiological arousal and distress following exposure sessions. Exposure consists of both *in vivo* and imaginal exposure. *In vivo* exposure involves clients and therapists working together to create a list of feared/avoided, yet safe, trauma-related situations that the client can systematically, and repeatedly engage in until the anxiety in those situations diminishes. Finally, imaginal exposure consists of clients repeatedly recounting their most bothersome trauma to the therapist in the present tense for 45–60 minutes without stopping. The imaginal exposure sessions are audiotape-recorded, and clients listen to the recordings daily. Typically, PE occurs for 9–12, 60- or 90-minute sessions and has been shown to be an effective and lasting treatment for PTSD [53•].

Preliminary work indicates that PE may be successful and feasible within PTSD-SUD populations. For example, Triffleman [54] investigated Substance Dependence PTSD Therapy (SDPT), which involves a 5-month twice-weekly treatment, consisting of an initial phase of cognitive-behavioral coping skills training for SUD, followed by a second phase of cognitive-behavioral PTSD treatment, which included exposure-based exercises. SDPT was compared with a manual-based 12-step facilitation treatment but, similar to studies reviewed above, no differences were found on either PTSD or SUD outcome measures. Overall, PTSD symptoms decreased over the course of treatment (32 %–43 % symptom reduction across both treatments), and substance use behavior decreased over the follow-up period, but not during the course of treatment [54]. Results from the study must be interpreted with caution due to the very small number of subjects in the study (n=12).

Concurrent Treatment of PTSD and Cocaine Dependence [55, 56] is an example of a PTSD-SUD treatment that more explicitly relies on PE procedures. Specifically, CTPCD is a 16-session treatment that combines PE with Coping Skills Training [57], a well-established CBT treatment for alcohol dependence. In CTPCD, patients first complete 5 sessions of Coping Skills Training in conjunction with PTSD-focused psycho-education and PE treatment rationale. Therapists incorporate in vivo exposure homework exercises starting at session 6 of treatment, and imaginal exposure exercises are conducted in-session, and for homework beginning at session 7. Coping Skills Training is continued throughout the treatment protocol. Results of a study conducted by Brady and colleagues found that CTPCD led to treatment gains for PTSD symptoms and cocaine use during and after the 16-session treatment protocol, with gains being maintained at 6-months post-treatment [56]. A 59 % reduction in PTSD symptom severity at 6-month follow up was documented through a psychometrically sound questionnaire. However, in spite of promising results, this study is limited by a small sample size (n=39) and its lack of a control condition.

In a small sample of men with PTSD-SUD (n=5), Najavits and colleagues [58] investigated SS combined with exposure-based PTSD therapy, where patients were allowed to select how much of each treatment component they received. There was no control condition, and the sample size was negligible; however, participants evidenced positive PTSD and SUD treatment outcomes. Importantly, patients rated the exposure-based sessions as being the most useful treatment component, suggesting that exposure-based approaches may be well-tolerated by PTSD-SUD patients.

Given the initial promise of combined PTSD-SUD treatments that incorporate exposure-based therapies, it is important to pursue research to better understand how such treatments may be useful and best implemented. One potential long-term complication is a possible hesitation by treatment providers to learn and/or deliver exposure-based therapy to individuals with a SUD [49]. However, there is growing evidence that exposure therapy is not harmful for individuals with SUD and rather is useful for treating SUD that co-occurs with PTSD. For example, Coffey and colleagues found that a brief imaginal exposure intervention (6 sessions) among individuals with PTSD and alcohol dependence was related to decreased trauma cue-elicited craving in the laboratory, even when no SUD intervention was provided. In addition, PTSD symptoms decreased 49 % in the exposure condition compared with a 4 % decrease in the guided relaxation condition [59]. Similarly, treatments incorporating exposure-based components have not led to worsened SUD outcomes [56, 60]. Therefore, further study on exposure-based PTSD treatment in the context of SUD is needed. Table 1 provides a compilation of the reviewed psychosocial treatment studies.

Medication-Based Treatment Approaches

The literature examining pharmacological approaches to treating PTSD-SUD is limited (Table 2). Brady and colleagues examined sertraline compared with placebo in 94 individuals with PTSD and alcohol dependence over a 12-week trial [61]. They found no significant group differences in alcohol consumption or PTSD symptom severity between the 2 groups, although sertra-line evidenced a non-significant trend towards greater improvements in re-experiencing and hyperarousal PTSD symptoms at the end of treatment.

Petrakis and colleagues examined the effects of naltrexone and disulfiram, 2 medications for alcohol dependence, among 93 veterans with PTSD and alcohol dependence [62]. The study took place over 12 weeks and consisted of 4 randomly assigned groups: placebo, naltrexone, disulfiram with placebo, and disulfiram with naltrexone. Results indicated that both active medications were related to decreased drinking days and longer periods of abstinence, with no significant differences being detected across the active conditions. Disulfiram was related to greater decreases in PTSD symptoms, although all conditions evidenced significant

decreases in symptom severity. A combination of disulfiram and naltrexone proved to be less effective for PTSD compared with either medication alone.

Alderman and colleagues [63] investigated the use of top-iramate, an anti-convulsant medication not approved for treatment of PTSD, among 43 male combat veterans with PTSD (with or without alcohol use problems) over the course of 8 weeks, with 29 participants completing the study. The authors reported a significant reduction in PTSD symptom severity over the course of the trial, although no patients reached full PTSD remission. Similarly, there was no significant reduction in drinking behavior. The results from this study must be interpreted with caution given the absence of a control condition.

Petrakis and colleagues [64] examined paroxetine in comparison to desipramine among 88 veterans with PTSD and alcohol dependence [64]. Participants were randomized to receive 1 or the other primary drug in conjunction with either naltrexone (for alcohol dependence) or a placebo. Individuals on both paroxetine and desipramine evidenced significant decreases in PTSD symptoms during the trial; however, the 2 conditions did not differ from one another. Furthermore, given that there was no placebo control condition, it is hard to interpret the significant declines in symptoms. With regard to alcohol use, individuals on desipramine reported fewer heavy drinking days. There was no effect for naltrexone on any study outcomes.

Taken together, efforts to examine pharmacological approaches to treating PTSD-SUD have been limited, with no replication of significant results being conducted to our knowledge. Future efforts in this area might consider investigating common underlying neurobiology between PTSD and SUD, as identified in a recent review by Norman and colleagues [65•].

Conclusion

Considering the above literature on the treatment of cooccurring PTSD and SUD, continued investigation of exposure-based treatments for PTSD that are delivered in conjunction with SUD treatment is likely the most promising. However, it may be unrealistic to assume that providers in SUD treatment centers, who have varied training backgrounds, will be willing or able to incorporate PE in their treatment approaches. Therefore, 2 integrated treatment approaches currently under investigation are attempting to provide concurrent PTSD and SUD treatment that is conducted by separate therapists. First, Foa and colleagues are examining concurrent treatment of PTSD and alcohol dependence by pairing PE for PTSD with naltrexone for alcohol dependence. Participants will receive PE or no PE, in combination with naltrexone or a placebo. Preliminary results (n=70) are promising, with participants showing reductions in PTSD and alcohol dependence symptoms over the course of the study, including maintenance at 3- and 6-months post-treatment [66].

Second, Coffey and colleagues are currently investigating PE concurrent with residential SUD treatment in a community treatment facility. Here, PE has been slightly modified to fit within the 60-minute treatment sessions of standard community treatment, with 9–12 twice-weekly sessions occurring for 50–60 minutes each. PE is being compared with a healthy lifestyles (HLS) control condition, which focuses on increasing healthy behaviors (eg, sleep, eating). Preliminary data (n=51) are promising, with individuals in both conditions showing lasting treatment gains in PTSD and alcohol use at 3- and 6-months post-treatment, and those in the PE condition evidencing significantly greater improvements. Specifically, preliminary data indicate individuals in the PE condition have evidenced a 72 % PTSD symptom reduction at 6 months compared with 46 % symptom reduction in the HLS condition [67]. PE also has not evidenced negative outcomes in terms of treatment drop-out (69 % completed all sessions) or alcohol use (90 % abstinent at 6-months compared with 88

% in the control intervention and 50 % at baseline), indicating that it is well tolerated in this population.

Although there is promising emerging data on the utility of exposure-based interventions for PTSD-SUD, there is still a great need for further work in this field. Specifically, there is a pressing need to test established PTSD treatments with patients who have both PTSD and SUD. For example, the two PTSD interventions that have the greatest empirical support in the literature are PE [51•] and cognitive processing therapy (CPT) [68]. Unfortunately, to date, only PE has been tested with substance abusing clients. It is important that both of these well-established PTSD interventions are tested with substance abusing clients so that practitioners and clients have choices when making treatment decisions. It is also important that we test both of these interventions rather than continue to attempt to develop new interventions, essentially from scratch. A far better approach would be to build on the existing research literature and test these established PTSD treatments with patients suffering from co-occurring PTSD-SUD. If well-designed clinical trials do not support the use of PE or CPT, then the development of new interventions for co-occurring PTSD-SUD would be warranted.

When testing established PTSD treatments, such as PE or CPT, or when attempting to develop new interventions for co-occurring PTSD-SUD, it is important to note that a simple within-group improvement on either PTSD or SUD symptoms should not constitute evidence to support the effectiveness of the intervention. There is now clear evidence that abstinence from alcohol and drugs can lead to statistically significant improvements in PTSD symptoms in the absence of an intervention directed at PTSD [38, 44•, 45]. Therefore, demonstrating within-group improvements from a PTSD intervention that does not outperform a control condition is not terribly meaningful. Future studies should not be satisfied with simple within-group improvement on either PTSD or SUD symptoms and should strive to outperform a control condition.

Lastly, there is a strong need for further testing of medications to treat co-occurring PTSD-SUD. Despite the fact that psychosocial interventions, such as PE and CPT, have been shown to be effective since the early 1990s, finding a therapist proficient in these interventions can still be challenging for some patients. Medications that effectively treat co-occurring PTSD-SUD could provide relief to patients unable to find a therapist proficient in empirically supported treatments for PTSD. However, similar to the benchmark needed for the tests of psychosocial interventions (ie, within-group improvements does not necessarily constitute evidence that the treatment is effective), well-designed medication studies must involve a placebo control condition to demonstrate that a medication produces a substantially larger decrease in symptoms than simple abstinence from alcohol and drugs.

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Table 1

Summary of psychosocial treatment studies for PTSD-SUD

Citation	Sample	*n*	Treatment	Control group	Main findings
Boden et al. [47]	Male veterans in VA SUD clinic	98	Seeking safety plus treatment as Usual	Treatment as usual	- No group differences in PTSD or alcohol use - Seeking safety group decreased illicit drug use
Brady et al. [56]	Treatment-seeking individuals	39	Concurrent treatment of PTSD and cocaine dependence	None	- Treatment gains in PTSD and cocaine use that were maintained at 6-months post-treatment
Donovan et al. [48]	Male veterans	46	Transcend	None	- Improvements in PTSD and SUD outcomes
Hien et al. [45]	Women recruited from community and clinical settings	107	Seeking safety	Relapse prevention	- Equal improvements in both conditions
Hien et al. [44•]	Women in community SUD treatment programs	353	Seeking safety	Women's health education	- Equal improvements in both conditions
Lynch et al. [43]	Incarcerated women	114	Seeking safety	Waitlist	- Seeking safety related to improvement in PTSD and depressive symptoms
McGovern et al. [50]	Individuals receiving intensive outpatient SUD treatment	53	Integrated cognitive-behavioral therapy (I-CBT)	Individual addiction counseling	- I-CBT related to greater improvements in PTSD and SUD outcomes - PTSD symptoms severity did not differ between groups at 6-month follow-up
Najavits et al. [58]	Male community sample	5	Seeking safety plus exposure therapy	None	- Improvements in PTSD and SUD - Exposure rated as most useful treatment component by patients
Norman et al. [42]	Male OIF/OEF veterans	9	Seeking safety	None	- Seeking safety related to improvement in PTSD and depressive symptoms - 5 participants decreased number of drinking days
Triffleman [54]	Primarily cocaine-abusing patients	12	Substance dependence PTSD therapy	12-Step facilitation	- PTSD symptoms decreased during treatment for both groups - Substance use decreased over follow-up
Zlotnick et al. [46]	Incarcerated women	49	Seeking safety plus Treatment as usual	Treatment as usual	- Equal improvements in both conditions

Table 2

Summary of medication trials for PTSD-SUD

Authors	Sample	*n*	Active group (s)	Control group	Main findings
Alderman et al. [63]	Male combat veterans	43	Topiramate	None	- Significant reduction in PTSD symptoms
					- No reduction in drinking behavior
Brady et al. [61]	Individuals recruited through the community and outpatient SUD treatment	94	Sertraline	Placebo	- No significant group differences in alcohol consumption or PTSD symptoms
Petrakis et al. [62]	Veterans attending outpatient VA clinics	93	(1) Naltrexone + placebo	Placebo	- Active conditions related to equal improvements in SUD outcomes (fewer drinking days, longer abstinence)
			(2) Disulfiram + placebo		- Active conditions related to improvements in PTSD symptoms
			(3) Naltrexone + disulfiram		- Disulfiram and naltrexone less effective for PTSD when administered in combination with one another
Petrakis et al. [64]	Primarily male veterans	88	(1) Paroxetine + naltrexone	No inactive control condition	- Paroxetine and desipramine related to equivalent reductions in PTSD symptoms
			(2) Paroxetine + placebo		- Desipramine related to fewer heavy drinking days
			(3) Desipramine + naltrexone		- No effect observed for naltrexone
			(4) Desipramine + placebo		