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Veterans with PTSD and comorbid substance use disorders: Does single versus poly-substance use disorder affect treatment outcomes?



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ABSTRACT

Introduction: Substance use disorders (SUD) frequently co-occur with posttraumatic stress disorder (PTSD). Little is known, however, about how individuals with a single SUD diagnosis (relating to only one substance) compare to individuals with poly-SUD diagnoses (relating to more than one substance) on substance use and PTSD treatment outcomes. To address this gap in the literature, we utilized data from a larger study investigating a 12-week integrated, exposure-based treatment (i.e., Concurrent Treatment of PTSD and Substance Use Disorders using Prolonged Exposure, or COPE) to examine treatment outcomes by single vs. poly-SUD status.

Method: Participants were 54 Veterans (92.6% male, average age = 39.72) categorized as having single SUD (n = 39) or poly-SUD (n = 15). T-tests characterized group differences in baseline demographics and presenting symptomatology. Multilevel models examined differences in treatment trajectories between participants with single vs. poly-SUD.

Results: Groups did not differ on baseline frequency of substance use, PTSD symptoms, or treatment retention; however, individuals with poly-SUD evidenced greater reductions in percent days using substances than individuals with a single SUD, and individuals with a single SUD had greater reductions in PTSD symptoms than individuals with poly-SUD over the course of treatment.

Discussion: The findings from this exploratory study suggest that Veterans with PTSD and co-occurring poly-SUD, as compared to a single-SUD, may experience greater improvement in substance use but less improvement in PTSD symptoms during integrated treatment. Future research should identify ways to enhance treatment outcomes for individuals with poly-SUD, and to better understand mechanisms of change for this population.

1. Introduction

Substance use disorders (SUD) and posttraumatic stress disorder (PTSD) frequently co-occur, such that individuals with PTSD are significantly more likely to develop SUD than individuals without PTSD (Debell et al., 2014; Grant et al., 2015). This psychiatric comorbidity is particularly prevalent among military Veterans (Petrakis et al., 2011; Teeters et al., 2017). For example, among Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) Veterans utilizing VA healthcare services, 63% of those diagnosed with SUD meet criteria for comorbid PTSD (Seal et al., 2011). Because the concomitance between SUD and PTSD contributes to an increased number of physical and mental health problems, as well as impairment in social and vocational

functioning, it is imperative to identify factors that influence treatment outcomes (Anderson et al., 2017; Mills et al., 2006; Ouimette et al., 2006).

Polysubstance use is one factor that may influence treatment outcomes. Individuals with poly-substance use disorder (poly-SUD) who have been exposed to multiple traumas have a greater risk for medical health complications (e.g., HIV; Mills et al., 2006). Thus, individuals with poly-SUD may present to treatment with more severe symptomatology and have a more complicated course of treatment due to other comorbidities. The current study seeks to explore this theory by examining baseline clinical characteristics and treatment outcomes in dually-diagnosed individuals with poly-SUD.

Several studies have explored whether the type of substance (e.g.,

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alcohol, cocaine, opioids, cannabis) and/or the number of different substances used impacts PTSD symptomatology. Because different substances can be used to stimulate or depress the nervous system, an individuals' substance of choice may be reflective of their PTSD symptomatology, as substances can be used to self-medicate PTSD symptoms (Khantzian, 1985). For example, a recent study by Dworkin and colleagues (Dworkin et al., 2018) investigated how specific and multiple substances were associated with the presentation of PTSD symptoms. They found that individuals with cannabis, cocaine, or opioid use disorders reported the most severe hyperarousal symptoms, and individuals with a sedative/hypnotic/anxiolytic use disorder reported the most severe numbing symptoms (Dworkin et al., 2018). Individuals with alcohol use disorder, or combined alcohol and drug use disorder, reported greater avoidance symptoms than those with any other substance use disorder (Dworkin et al., 2018). These findings highlight the heterogeneity of substance use and PTSD symptomatology among dually-diagnosed individuals. This may have important implications for treatment, such as informing what PTSD symptoms should be targeted based on specific substances or combinations of substances used. To date, however, no one has examined if individuals with poly-SUD report greater overall PTSD severity compared to individuals with single-SUD.

Only a few studies have examined how use of multiple substances impacts treatment outcomes and findings are mixed. Manhapra, Stefanovics, and Rosenheck (2015) found that among individuals admitted to an intensive PTSD program (N = 22,948), those who used only alcohol or only marijuana at intake had lower rates of abstinence at 4-month follow-up, compared to individuals who used cocaine, opioids, and multiple substances. A meta-analysis of cognitive-behavioral interventions for SUD revealed that psychosocial interventions had less efficacy for poly-SUD populations compared to individuals with a single SUD (Dutra et al., 2008). Specifically, individuals with poly-SUD had the lowest percent days abstinence at post-treatment, compared to individuals with a single SUD (Dutra et al., 2008). It has yet to be examined how poly-SUD may be associated with PTSD treatment outcome. Further, previous research has relied on examining abstinence as an indication of substance use frequency, but did not utilize other measures of SUD treatment outcome (e.g., harm reduction).

Given the risks associated with poly-substance use and the considerable number of patients with PTSD/SUD who meet criteria for poly-SUD, it is critical to identify whether and how poly-SUD impacts treatment outcome when comorbid conditions are targeted. The aim of the current exploratory study is to investigate how individuals with PTSD and either single or poly-SUD compare at baseline and over the course of an exposure-based, integrated treatment designed to target both PTSD and SUD severity. It is hypothesized that individuals with poly-SUD would report a greater frequency of substance use and more severe PTSD symptomatology at baseline and throughout treatment as compared to individuals with a single SUD.

2. Materials and methods

2.1. Participants

Participants were U.S. military Veterans enrolled in a larger randomized controlled trial (Back et al., 2019) examining the efficacy of a novel 12-week, exposure-based integrated treatment for comorbid PTSD and SUD (i.e., Concurrent Treatment of PTSD and Substance Use Disorders Using Prolonged Exposure, or COPE; Back et al., 2014) versus Relapse Prevention cognitive behavioral therapy (CBT; Carroll, 1998). This larger study lends evidence to the efficacy of COPE, demonstrating that COPE resulted in significantly greater reductions in PTSD than RP, as well as comparable reductions in SUD during treatment and greater reductions during follow up (Back et al., 2019). All participants met Diagnostic and Statistical Manual of Mental Disorders IV Text Revision

(DSM-IV-TR; American Psychiatric Association, 2000) criteria for current SUD and PTSD.

Only participants randomized to the COPE condition were included in the current analyses (N = 54). Most participants were male (92.6%) with a mean age of 39.72 years (SD = 10.98). Participants primarily identified as Caucasian (68.5%) or African American (29.6%). Participants were recruited through the local Veterans Affairs (VA) Medical Center, flyers posted in the community, and internet and newspaper advertisements. Inclusion criteria were: 1) Veteran, reservist, or member of the National Guard, 2) 18–65 years old, 3) meet DSM-IV criteria for SUD on the Mini International Neuropsychiatric Interview (Sheehan et al., 1997), 4) meet DSM-IV criteria for PTSD on the Clinician Administered PTSD Scale (CAPS; Blake et al., 1995) with a total score \geq 50. Exclusion criteria were: 1) current suicidality and/or homicidality with intent, 2) psychiatric or medical conditions requiring a higher level of care, 3) enrolled in current treatment for PTSD or SUD, and 4) severe cognitive impairment based on the Mini Mental Status Exam, with a cutoff score of 21 (Folstein et al., 1975). Participants who were stabilized on psychotropic medication for at least four weeks were permitted to participate.

2.2. Procedures

Following a baseline assessment to confirm eligibility, participants were randomized to receive 12 sessions of COPE (Back et al., 2014) or Relapse Prevention (Carroll, 1998). The COPE treatment integrates Prolonged Exposure (PE; Foa et al., 2007) for the treatment of PTSD with Relapse Prevention for SUD. Before each therapy session, participants completed measures assessing substance use and PTSD severity since the prior session. Abstinence was not required of participants, although it was strongly encouraged.

2.3. Measures

2.3.1. SUD diagnoses

The MINI (Sheehan et al., 1997), a brief semi-structured interview, was used to assess diagnostic criteria for current alcohol and drug use disorders. Participants were categorized into the single-SUD group if they met current diagnostic criteria for only one type of substance. Participants were categorized into the poly-SUD group if they met current diagnostic criteria for more than one substance use disorder.

2.3.2. Substance use frequency

The Timeline Followback (TLFB; Sobell and Sobell, 1992) is a calendar-based, self-report assessment of alcohol and drug use, which yields high test-retest reliability when compared with self and other reports of substance use (Carey, 1997). Substance use was assessed at baseline (60 days prior) and weekly during treatment. We examined likelihood of use (dichotomous variable: 0 = no use and 1 = use) and percent days used (PDU), a continuous variable. The baseline assessment captured PDU over the 60 days prior to the baseline appointment and the weekly measures captured PDU since the previous appointment.

2.3.3. PTSD diagnosis

The Clinician Administered PTSD Scale (CAPS; Blake et al., 1995) for DSM-IV-TR was used at baseline to assess diagnostic criteria for PTSD. The CAPS assesses the frequency and intensity of 17 DSM-IV-TR symptoms of PTSD. The CAPS is a well-validated measure and demonstrates satisfactory psychometric properties, including good internal consistency, test-retest reliability, and inter-rater reliability (Orsillo, 2002).

2.3.4. PTSD severity

The PTSD Checklist - Military Version (PCL-M; Weathers et al., 1994) is a continuous measure and was used in the current study to

assess PTSD symptom severity at baseline and weekly during treatment. The PCL-M consists of 17 Likert-type scale items rated 1 (“Not at all”) through 5 (“Extremely”), and scores can range from 17 to 85. The PCL-M has good psychometric properties including good internal consistency, convergent validity, test-retest reliability, and temporal stability (Wilkins et al., 2011). In the current sample internal reliability at each assessment time point ranged from good to excellent ($\alpha = 0.88$ to 0.97).

2.4. Data analysis

Group differences (i.e., single vs. poly-SUD) in demographic and baseline characteristics were assessed using chi-square or t-tests, as appropriate. Multilevel models in Mplus v 8.1 (Muthén and Muthén, 1998–2017; Muthén and Muthén, 2017) examined whether the two groups differed in SUD and PTSD severity, independently, across the course of treatment. Substance use was modeled using two-part modeling (Olsen and Schafer, 2001) to capture likelihood of use (0 = no use; 1 = use) over the given week and frequency of use (PDU), conditioned on substance use. Intercepts in each of the models were allowed to vary. The first therapy session was coded as 0 and then session was entered as a fixed effect in the models. Substance use group (single SUD = -1; poly-SUD = 1) and the interaction of group by session were also specified as fixed effects. Prior to entering the SUD group as a predictor, it was examined whether a linear or quadratic effect of session number best fit the data. It was found that a linear model provided the best fit.

3. Results

3.1. Demographic and clinical characteristics

Most individuals in the sample ($n = 39$) met criteria for a single SUD, and the remaining individuals ($n = 15$) met criteria for poly-SUD. Of those in the poly-SUD group, only two participants met criteria for more than 2 SUDs (i.e., met criteria for 3 SUDs). As shown in Table 1, the majority of participants in the single SUD group and all of the participants in the poly-SUD group met criteria for an alcohol use disorder. Single SUD participants did not differ significantly from poly-SUD participants on demographic characteristics, including age ($t(52) = -0.86, p = 0.39$), sex ($\chi^2 = 1.06, p = 0.30$), and race ($\chi^2 = 3.12, p = 0.21$). Both groups reported exposure to a similar number of lifetime traumas ($t(50) = 0.14, p = 0.89$), baseline substance use frequency ($t(20.13) = -0.37, p = 0.72$), and PTSD severity, both according to the CAPS ($t(52) = 1.49, p = 0.14$) and the PCL-M ($t(52) = 0.09, p = 0.93$). Retention was also similar between groups ($t(52) = 0.33, p = 0.74$).

3.2. Substance use frequency over the course of treatment

The number of participants using substances and means of PDU of any substance are provided in Table 2 by SUD group (single vs. poly-SUD) and treatment session. By end of treatment (Session 12), 45.5% of single-SUD participants and 75% of poly-SUD participants reported that they had abstained since the week prior. Among those who were using, single-SUD persons were using 25% of the time, compared to the poly-SUD group who was using 8% of the time. Results of the two-part model suggest that session number significantly predicted likelihood of use and PDU, such that participants in both groups had a lower likelihood and frequency of substance use as therapy progressed (see Table 3). That is, the number of single-SUD individuals and poly-SUD individuals using substances decreased and substance use frequency for both groups decreased as participants advanced through the treatment. SUD group did not predict probability of substance use or PDU but the interaction of session by SUD group predicted PDU, suggesting that individuals with poly-SUD evidenced greater reductions in substance use

Table 1
Demographic and Baseline Clinical Characteristics by SUD Group (N = 54).

Characteristic	Single-SUD (n = 39) M(SD) or N	Poly-SUD (n = 15) M(SD) or N
Age	38.92 (10.05)	41.80 (13.26)
Sex		
Male	37	13
Female	2	2
Race		
White/Caucasian	29	8
Black/African American	9	7
More than one/Other	1	0
Substance Use Diagnosis		
Alcohol	33	15
Opioid	4	5
Cocaine	1	7
Marijuana	1	4
Sedative/Hypnotic/Anxiolytic	0	1
Other	0	1
Baseline Substance Use Frequency (percent days using)	45.68 (32.67)	50.33 (44.35)
Baseline PTSD Severity (CAPS)	79.64 (18.73)	71.53 (15.46)
Baseline PTSD Severity (PCL-M)	61.97 (11.47)	61.67 (10.55)
Average Number of Lifetime Traumatic Events	10.71 (2.92)	10.57 (3.59)
Number of Treatment Sessions Completed	8.95 (4.07)	8.53 (4.37)

Note: SUD = substance use disorder; PTSD = posttraumatic stress disorder; CAPS = Clinician Administered PTSD Scale; PCL-M = PTSD Checklist – Military Version.

frequency over the course of treatment than individuals with a single SUD (Fig. 1).

3.3. PTSD severity over the course of treatment

Average PTSD severity by treatment session and SUD group is also presented in Table 2. Fig. 2 illustrates the findings from the multilevel model, demonstrating that PTSD severity decreased significantly over the course of treatment for single and poly-SUD groups. Session and the interaction of session by SUD group significantly predicted PTSD severity (see Table 3), such that individuals with a single SUD evidenced significantly greater reductions in PTSD severity as compared to individuals with poly SUD.¹

4. Discussion

The frequent co-occurrence of SUD and PTSD among both civilians and military veterans is well-documented (Grant et al., 2015; Teeters et al., 2017). Although research has identified differences in treatment outcomes for single-SUD and poly-SUD individuals in SUD treatment (Dutra et al., 2008; Dworkin et al., 2018; Mills et al., 2006), no research to date has examined the effect of single versus poly-SUD among individuals with comorbid SUD/PTSD receiving integrated treatment. The current exploratory study sought to address this gap in the literature by examining presenting characteristics and response to integrated treatment among veterans with PTSD and single or poly-SUD who participated in an integrated, exposure-based treatment (i.e., COPE).

¹ As all poly-SUD participants, but not all single SUD participants, met criteria for alcohol use disorder, we re-ran models limiting the sample to only poly-SUD participants and single SUD participants who met criteria for alcohol use disorder. This allows us to examine if single SUD individuals with only a drug use disorder drive the effects found in the models. Results from our re-analysis were relatively consistent with the model including the entire sample except that the effect of SUD group by session on substance use trended toward significance ($p = 0.097$).

Table 2

Number of individuals who used substances with means and standard deviations of substance use frequency and PTSD severity across treatment sessions by SUD group.

Session #	Single SUD			Poly-SUD		
	Participants Who Used Any Substance (%)	Substance Use Frequency (Percent Days Used)	PTSD Severity (PCL-M)	Participants Who Used Any Substance (%)	Substance Use Frequency (Percent Days Used)	PTSD Severity (PCL-M)
1	67.6	33.21 (36.91)	58.28 (13.11)	57.1	43.72 (42.72)	58.14 (7.38)
2	66.7	34.20 (36.88)	57.92 (14.14)	53.8	34.61 (40.35)	59.23 (11.74)
3	62.9	30.85 (34.61)	54.09 (13.73)	41.7	28.62 (40.03)	53.17 (9.19)
4	66.7	30.60 (30.91)	51.03 (14.90)	50.0	37.26 (39.82)	57.08 (14.39)
5	51.6	23.44 (31.92)	48.16 (16.19)	53.8	34.32 (40.41)	57.31 (12.61)
6	58.1	22.08 (26.44)	41.70 (14.71)	70.0	16.22 (26.28)	56.73 (13.48)
7	58.6	22.21 (26.14)	41.11 (18.22)	55.6	21.47 (28.64)	52.33 (18.28)
8	60.7	24.69 (31.92)	39.00 (16.16)	25.0	14.75 (29.14)	51.75 (14.06)
9	51.9	24.85 (29.97)	37.73 (17.19)	37.5	13.97 (22.15)	51.89 (13.98)
10	54.2	19.73 (25.05)	35.61 (17.87)	28.6	18.08 (25.51)	52.57 (12.97)
11	50.0	16.70 (23.56)	37.24 (18.61)	28.6	7.66 (12.14)	46.88 (13.87)
12	54.5	25.48 (31.00)	33.86 (16.37)	25.0	7.94 (16.15)	44.89 (15.87)

Note: Percentages calculated with participants with missing data excluded. SUD = substance use disorder; PTSD = posttraumatic stress disorder; PCL-M = PTSD Checklist – Military Version.

Table 3

Fixed Effects of Treatment Session and SUD Group as Predictors of Substance Use and PTSD Severity.

Estimate	B	SE	p	Substance Use		
				B	SE	p
Intercept/Threshold	37.61	5.00	< 0.001	-2.19	1.15	0.057
Session	-1.46	0.25	< 0.001	-0.24	0.06	< 0.001
SUD Group	4.06	5.00	0.417	-0.5	1.06	0.64
Session x SUD Group	-0.55	0.25	0.029	-0.02	0.06	0.789
PTSD Severity						
Intercept/Threshold	58.55	2.10	< 0.001			
Session	-1.62	0.14	< 0.001			
SUD Group	0.37	2.10	0.86			
Session x SUD Group	0.58	0.14	< 0.001			

Note: SUD = substance use disorder; PTSD = posttraumatic stress disorder; PCL-M = PTSD Checklist – Military Version; *p < 0.05.

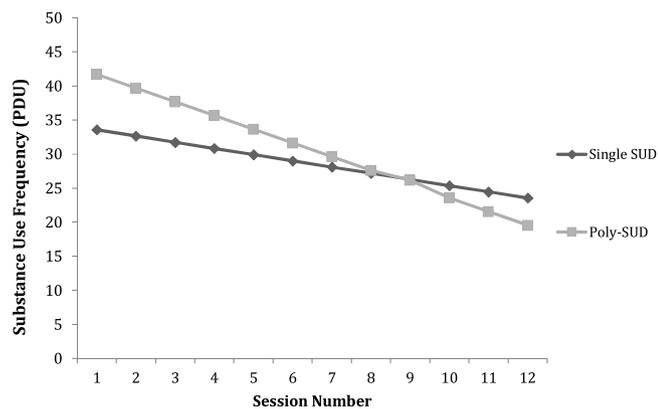


Fig. 1. Estimated Change in Substance Use Frequency from First Treatment Session to End of Treatment by SUD Group.

Note: SUD = Substance use disorder; PDU = Percent days used.

The results from the current study suggest that individuals with poly-SUD did not differ from individuals with single SUD with regard to baseline substance use frequency. By Session 12, the poly-SUD group was using substances approximately 8% of the time and the single SUD group was using approximately 25% of the time (see Table 2). Results of the multilevel model demonstrate that individuals in both groups showed significant reductions in substance use frequency across the course of treatment. Further, individuals with poly-SUD showed greater

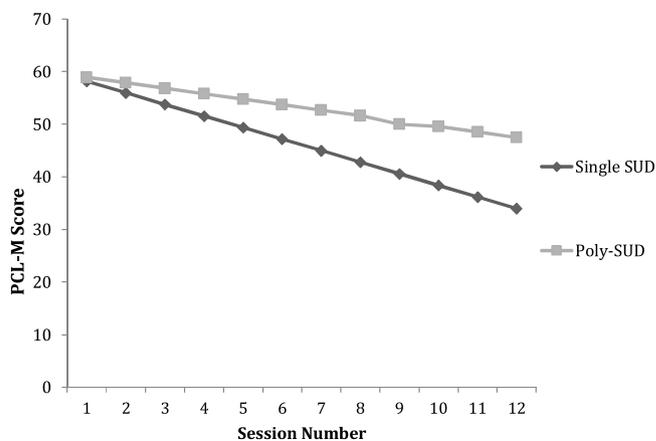


Fig. 2. Estimated Change in PTSD Severity from First Treatment Session to End of Treatment by SUD Group.

Note: SUD = Substance use disorder; PCL-M = PTSD Checklist – Military Version.

reductions than individuals with a single SUD. This finding may have been due to a relatively small sample of poly-SUD individuals and stands in contrast to previous research examining SUD-only populations, which reports worse treatment outcomes for poly-SUD individuals (i.e., lowest post-treatment abstinence, Dutra et al., 2008). The current study's findings may be discrepant from Dutra et al.'s (2008) findings because abstinence was not used as the measure of SUD treatment outcome. Rather, we examined PDU as a measure of SUD treatment outcome because abstinence was encouraged but not required for participants. Trials that require a goal of abstinence may incur greater dropout or retain individuals with more severe SUD than the current study saw. Further, our findings may differ from Dutra and colleagues' (2008) meta-analysis because they focused primarily on illicit substances. In the current sample, the majority of single-SUD participants had alcohol use disorder and most of the poly-SUD participants had an alcohol use disorder as well as a drug use disorder. Future research should examine the effect of single vs. poly-SUD on treatment outcomes among dually-diagnosed individuals with primarily drug use disorders.

Individuals in the poly-SUD group may have adhered to the SUD treatment component of COPE to a greater extent than the single SUD group, thereby demonstrating a greater reduction in substance use. Many individuals with co-occurring SUD and PTSD use alcohol or other substances to self-medicate the discomfort associated with PTSD

symptoms (Khantzian, 1985; Leeies et al., 2010; Ouimette et al., 2010). Previous research with similar samples has demonstrated that reduction in SUD is largely attributable to PTSD symptom change (Badour et al., 2017). Thus, it is possible that because the COPE treatment targets PTSD symptoms concurrently with SUD, and is not specific to a particular substance, participants showed reductions in substance use frequency, particularly if they were diagnosed with multiple SUDs. Motivations for change may have also differed between groups, with the poly-SUD group identifying their behaviors as more risky or dangerous and therefore exhibiting higher motivations to reduce their substance use. Future research should address such group differences as they may prove to be predictors or influencers of treatment outcomes.

Individuals with poly-SUD reported similar levels of PTSD severity as individuals with single SUD at baseline. There were group differences in PTSD symptom severity over the course of treatment, though in the opposite direction of what was found for substance use. That is, individuals with a single SUD showed greater reductions of PTSD severity than individuals with poly-SUD across the course of treatment. Future research is needed to identify mechanisms to help explain why individuals with poly-SUD, despite having comparable reductions in substance use frequency, showed less improvement in PTSD treatment outcomes and how this relates to their substance use frequency. Because individuals in the poly-SUD group demonstrated more prominent reductions in substance use frequency, their PTSD symptoms may be more severe than the single-SUD group because they are no longer self-medicating their PTSD symptoms (Khantzian, 1985). Alternatively, individuals reducing use of multiple substances may be encountering more withdrawal symptoms, relative to individuals with single SUD, which may mimic or exacerbate PTSD symptoms. It may also be that individuals with poly-SUD may be less able to benefit from prolonged exposures perhaps due to a history of chronic use and/or greater neurocognitive impairment (Loeber et al., 2009). As many SUD/PTSD patients have polysubstance use (Mills et al., 2012), it will be important to develop, further adapt, or perhaps lengthen treatment in order to effectively reduce PTSD severity among patients with poly-SUD (Dutra et al., 2008).

The current exploratory study is limited by the relatively small, predominately male, veteran sample. Thus, it is uncertain how the findings might generalize to a more diverse population. The SUD groups were of unequal sizes and had little diversity in the substances being used, which may have impacted the results. We found that when we re-analyzed the data to include only individuals with alcohol use disorder or alcohol use disorder and drug use disorder, the effect of group by session on substance use frequency was no longer significant. It is possible that single SUD individuals with a drug use disorder were driving the effects found for substance use frequency in our main analyses. However, given the sample size, future research should aim to replicate these preliminary findings in larger samples. Further, the sample size was too small to examine the quantity of each substance separately and we did not collect data on whether poly-SUD individuals were using substances in combination or at different times on days in which they used both substances. This information will be important for future studies to collect so that the needs of poly-SUD individuals can be better characterized.

The current study consists of post-hoc analyses; thus caution is advised when considering any causal inferences that might be drawn from the results of this study. In addition, the current study examined self-report measures, which are subject to recall bias. Further, we were unable to examine substance use quantity at a granular level because there is no accurate way to standardize amount of use across substances. Future research should report biological markers of substance use. Additionally, the definition of “polysubstance” is defined ambiguously throughout the literature and not included in the DSM-5 (American Psychiatric Association, 2013). Some researchers define polysubstance use as using three or more substances within the same time period (e.g., Manhapra et al., 2015), whereas others define the

term based on the number of SUD diagnoses a person is ascribed (e.g., Dutra et al., 2008). The outcomes may differ depending on how polysubstance use is defined and the findings should be interpreted with consideration to a given study's definition.

In summary, PTSD patients with both single and poly-SUD evidenced significant reductions in SUD and PTSD severity during the course of an integrated, exposure-based treatment for PTSD/SUD. However, poly-SUD individuals had a greater reduction of substance use frequency and single SUD individuals had a greater reduction in PTSD severity over the course of treatment. The findings contribute to a growing literature on factors that influence treatment efficacy for integrated, exposure-based interventions. In particular, future research should focus on identifying ways to enhance PTSD treatment outcomes for individuals with poly-SUD. This may include incorporating extended treatment protocols for polysubstance users who are more likely to develop serious medical problems associated with drug use or experience re-traumatization (Mills et al., 2006). Future research may focus on developing an integrated treatment for polysubstance users that includes additional sessions targeting PTSD coupled with adjunct medication for SUD and PTSD symptoms.

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Contributors

Sudie E. Back and Therese K. Killeen designed the study and wrote the protocol. Stephanie M. Jeffers and Taylor Laffey wrote the first draft of the manuscript. Stephanie M. Jeffers finalized the manuscript for publication. Amber M. Jarnecke did the data analysis and edited drafts of the manuscript. Julianne C. Flanagan conducted literature searches, provided summaries of previous research studies, and edited drafts of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

All authors declare that they have no conflicts of interest.

References

- American Psychiatric Association (APA), 2000. *Diagnostic and Statistical Manual of Mental Disorders*, fourth ed. American Psychiatric Association, Washington, DC text revision.
- American Psychiatric Association (APA), 2013. *Diagnostic and Statistical Manual of Mental Health Disorders*, fifth ed. American Psychiatric Publishing, Arlington, VA.
- Anderson, R.E., Bonar, E.E., Walton, M.A., Goldstick, J.E., Rauch, S.A.M., Epstein-Ngo, Q.M., Chermack, S.T., 2017. A latent profile analysis of aggression and victimization across relationship types among veterans who use substances. *J. Stud. Alcohol Drugs* 78, 597–607. <https://doi.org/10.15288/jsad.2017.78.597>.
- Back, S.E., Foa, E.B., Killeen, T.K., Mills, K.L., Teesson, M., Dansky Cotton, B., Carroll, K.M., Brady, K.T., 2014. *Concurrent Treatment of PTSD and Substance Use Disorders Using Prolonged Exposure (COPE): Therapist Guide. Treatments That Work. US: Oxford University Press, New York.*
- Back, S.E., Killeen, T., Badour, C.L., Flanagan, J.C., Allan, N.P., Ana, E.S., Lozano, B., Korte, K.J., Foa, E.B., Brady, K.T., 2019. Concurrent treatment of substance use disorders and PTSD using prolonged exposure: a randomized clinical trial in military veterans. *Addict. Behav.* 90, 369–377.
- Badour, C.L., Flanagan, J.C., Gros, D.F., Killeen, T., Pericot-Valverde, I., Korte, K.J., Allan, N.P., Back, S.E., 2017. Habituation of distress and craving during treatment as predictors of change in PTSD symptoms and substance use severity. *J. Consult. Clin. Psychol.* 85, 274.
- Blake, D.D., Weathers, F.W., Nagy, L.M., Kaloupek, D.G., Gusman, F.D., Charney, D.S., Keane, T.M., 1995. The development of a clinician-administered PTSD scale. *J.*

- Trauma. *Stress* 8, 75–90.
- Carey, K.B., 1997. Reliability and validity of the time-line follow-back interview among psychiatric outpatients: a preliminary report. *Psychol. Addict. Behav.* 11, 26.
- Carroll, K.M., 1998. Treating drug dependence: recent advances and old truths. In: Miller, W.R., Heather, N. (Eds.), *Applied Clinical Psychology. Treating Addictive Behaviors*. US: Plenum Press, New York, pp. 217–229.
- Debell, F., Fear, N.T., Head, M., Batt-Rawden, S., Greenberg, N., Wessely, S., Goodwin, L., 2014. A systematic review of the comorbidity between PTSD and alcohol misuse. *Soc. Psychiatry Psychiatr. Epidemiol.* 49, 1401–1425. <https://doi.org/10.1007/s00127-014-0855-7>.
- Dutra, L., Stathopoulou, G., Basden, S.L., Leyro, T.M., Powers, M.B., Otto, M.W., 2008. A meta-analytic review of psychosocial interventions for substance use disorders. *Am. J. Psychiatry* 165, 179–187.
- Dworkin, E.R., Wanklyn, S., Stasiewicz, P.R., Coffey, S.F., 2018. PTSD symptom presentation among people with alcohol and drug use disorders: comparisons by substance of abuse. *Addict. Behav.* 76, 188–194.
- Foa, E., Hembree, E., Rothbaum, B., 2007. *Prolonged Exposure Therapy for PTSD*. Oxford University, New York.
- Folstein, M.F., Folstein, S.E., McHugh, P.R., 1975. “Mini-Mental State”: a practical method for grading the cognitive state of patients for the clinician. *J. Psychiatr. Res.* 12, 189–198.
- Grant, B.F., Goldstein, R.B., Saha, T.D., Chou, S.P., Jung, J., Zhang, H., Pickering, R.P., Ruan, W.J., Smith, S.M., Huang, B., Hasin, D.S., 2015. Epidemiology of DSM-5 alcohol use disorder: results from the national epidemiologic survey on alcohol and related conditions III. *JAMA Psychiatry* 72, 757–766. <https://doi.org/10.1001/jamapsychiatry.2015.0584>.
- Khantzian, E.J., 1985. The self-medication hypothesis of addictive disorders: focus on heroin and cocaine dependence. *Am. J. Psychiatry* 142, 1259–1264. <https://doi.org/10.1176/ajp.142.11.1259>.
- Leeies, M., Pagura, J., Sareen, J., Bolton, J.M., 2010. The use of alcohol and drugs to self-medicate symptoms of posttraumatic stress disorder. *Depress. Anxiety* 27, 731–736.
- Loeber, S., Vollstadt-Klein, S., von der Goltz, C., Flor, H., Mann, K., Kiefer, F., 2009. Attentional bias in alcohol-dependent patients: the role of chronicity and executive functioning. *Addict. Biol.* 14, 194–203. <https://doi.org/10.1111/j.1369-1600.2009.00146.x>.
- Manhapa, A., Stefanovics, E., Rosenheck, R., 2015. Treatment outcomes for veterans with PTSD and substance use: impact of specific substances and achievement of abstinence. *Drug Alcohol Depend.* 156, 70–77.
- Mills, K.L., Teesson, M., Ross, J., Peters, L., 2006. Trauma, PTSD, and substance use disorders: findings from the Australian national survey of mental health and well-being. *Am. J. Psychiatry* 163, 652–658.
- Mills, K.L., Teesson, M., Back, S.E., Brady, K.T., Baker, A.L., Hopwood, S., Sannibale, C., Barrett, E.L., Merz, S., Rosenfeld, J., Ewer, P.L., 2012. Integrated exposure-based therapy for co-occurring posttraumatic stress disorder and substance dependence: A randomized controlled trial. *JAMA* 308, 690–699.
- Muthén, L.K., Muthén, B.O., 2017. *Mplus User's Guide*, eighth ed. Muthén and Muthén, California.
- Olsen, M.K., Schafer, J.L., 2001. A two-part random-effects model for semicontinuous longitudinal data. *J. Am. Stat. Assoc.* 96, 730–745. <https://doi.org/10.1198/016214501753168389>.
- Orsillo, S.M., 2002. Measures for acute stress disorder and posttraumatic stress disorder. In: Antony, M.M., Orsillo, S.M., Roemer, L. (Eds.), *Practitioner's Guide to Empirically Based Measures of Anxiety*. AABT Clinical Assessment Series. Springer, Massachusetts, pp. 255–307.
- Quimette, P., Goodwin, E., Brown, P.J., 2006. Health and well being of substance use disorder patients with and without posttraumatic stress disorder. *Addict. Behav.* 31, 1415–1423. <https://doi.org/10.1016/j.addbeh.2005.11.010>.
- Quimette, P., Read, J.P., Wade, M., Tirone, V., 2010. Modeling associations between posttraumatic stress symptoms and substance use. *Addict. Behav.* 35, 64–67. <https://doi.org/10.1016/j.addbeh.2009.08.009>.
- Petrakis, I.L., Rosenheck, R., Desai, R., 2011. Substance use comorbidity among veterans with posttraumatic stress disorder and other psychiatric illness. *Am. J. Addict.* 20, 185–189.
- Seal, K.H., Cohen, G., Waldrop, A., Cohen, B.E., Maguen, S., Ren, L., 2011. Substance use disorders in Iraq and Afghanistan veterans in VA healthcare, 2001–2010: implications for screening, diagnosis and treatment. *Drug Alcohol Depend.* 116, 93–101.
- Sheehan, D., Lecrubier, Y., Sheehan, K.H., Janavs, J., Weiller, E., Keskiner, A., Schinka, J., Knapp, E., Sheehan, M.F., Dunbar, G.C., 1997. The validity of the Mini International Neuropsychiatric Interview (MINI) according to the SCID-P and its reliability. *Eur. Psychiatry* 12, 232–241.
- Sobell, L.C., Sobell, M.B., 1992. Timeline follow-back. In: Litten, R.Z., Allen, J.P. (Eds.), *Measuring Alcohol Consumption*. Humana Press, New Jersey, pp. 41–72.
- Teeters, J.B., Lancaster, C.L., Brown, D.G., Back, S.E., 2017. Substance use disorders in military veterans: prevalence and treatment challenges. *Subst. Abuse Rehabil.* 8, 69.
- Weathers, F., Litz, B., Herman, D., Huska, J., Keane, T., 1994. PTSD Checklist - Military Version for DSM-IV (Accessed April 4, 2019) Available at. https://deploymentpsych.org/system/files/member_resource/4-PCL-M.pdf.
- Wilkins, K.C., Lang, A.J., Norman, S.B., 2011. Synthesis of the psychometric properties of the PTSD checklist (PCL) military, civilian, and specific versions. *Depress. Anxiety* 28, 596–606.