Psychedelic treatment for co-occurring alcohol misuse and post-traumatic stress symptoms among United States Special Operations Forces Veterans

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ABSTRACT

Background & aims: Special Operations Forces Veterans (SOFV) have unique treatment needs stemming from multiple repeated forms of combat exposure resulting in a complex sequela of problems including alcohol misuse and post-traumatic stress symptoms. Current approved pharmacologic treatments for alcohol misuse and PTSD are lacking in adherence and efficacy, warranting novel treatment development. The current study examined the correlations between psychedelic treatment and changes in alcohol misuse among trauma exposed United States SOFV.

Method: An anonymous internet-based survey was conducted among SOFV who completed a specific psychedelic clinical program in Mexico. Retrospective questions probed alcohol use and post-traumatic stress symptoms during the 30-days before and 30-days after the psychedelic treatment. A total of 65 SOFV completed treatment and were eligible for contact. Of these, 51 (78%) completed the survey, and 27 (42%) reported alcohol misuse (≥4 on the AUDIT-C) in the 30 days prior to treatment and were included in analyses (Mean Age 540; male 96%; Caucasian/White 96%).

Results: There were significant and very large reductions in retrospective reports of alcohol use (P < 0.001; d = –2.4) and post-traumatic stress symptoms (P < 0.001; d = –2.8) and a significant and large increase in psychological flexibility (P < 0.001; d = –1.8), from before-to-after the psychedelic treatment. In the 30 days after treatment, 85% reduced their alcohol consumption to non-risky levels (33% abstinent; 52% non-risky drinking). Increases in psychological flexibility were strongly associated with reductions in alcohol use and post-traumatic stress symptoms (rs range 0.38–0.90; ps < 0.05).

Conclusion: Rigorous longitudinal studies should be conducted to determine whether psychedelic-assisted therapy holds promise as an intervention in this population.

KEYWORDS

psychedelics, veterans, special operations, treatment, alcohol misuse, post-traumatic stress

INTRODUCTION

Special Operations Forces (SOF) constitute the most elite members of the United States military, selected for their superior physical and psychological resilience, and trained to endure the many challenges related to combat (Bartone, Valdes, & Sandvik, 2016; Hanwell & de Silva, 2012).
The group cohesion experienced among SOF personnel has been identified as a protective factor against mental health problems (Hanwella & de Silva, 2012). However, despite their resilience and specialized training, they are often exposed to a greater number of deployments and intense combat episodes, correlating with increased prevalence of mental health problems (Hanwella & de Silva, 2012; Hing, Cabrera, Barstow, & Forsten, 2012). Compounding this issue, SOF Veterans (SOFV) are reluctant to seek mental health treatment (Hing et al., 2012), and there is growing concern of a rise in mental health problems and an alarming increase in the incidence of suicides in this population, highlighting the limited effective treatment methods (Hing et al., 2012; Rocklein Kemplin, Paun, Godbee, & Brandon, 2019).

One primary concern is that alcohol misuse is pervasive among US Veterans, with 32% of Veterans meeting criteria for a diagnosis of alcohol use disorder (AUD) (Lance et al., 2016). Heavy episodic drinking is similarly widespread and one of the most prevalent types of substance misuse among Veterans (Hoggatt, Lehavot, Krenek, Schweizer, & Simpson, 2017; Wagner et al., 2007). Young male Veterans (18–25 years of age) are the most susceptible to alcohol misuse with 1 in 4 meeting criteria for AUD and 56% reporting heavy drinking (Hoggatt et al., 2017). Furthermore, Veterans suffer significant deleterious effects from alcohol misuse that spans physical, cognitive, and social domains. For example, Veterans with AUD are at an increased risk for all-cause mortality, including suicidality (Norman, Haller, Hamblen, Southwick, & Pietrzak, 2018), while heavy drinking is associated with work performance problems, alcohol-impaired driving, and criminal justice problems (Chwastiak, Rosenheck, Desai, & Kazis, 2010; Stahre, Brewer, Fonseca, & Naimi, 2009).

The high rates of alcohol misuse among Veterans can be attributed to the direct impact of traumatic experiences, such as combat exposure and military sexual assault, as well as secondary to mental health illness (Fillo, Heavye, Homish, & Homish, 2018; Jacobson et al., 2008). The relationship between alcohol misuse and trauma is complex, but the prevailing self-medication hypothesis proposes that alcohol use is an attempt to regulate difficult emotions and suppress post-traumatic psychiatric symptoms (Boyd-Ball, Manson, Noonan, & Beals, 2006; Forbes et al., 2015; Schum & Chard, 2012). Studies among Veterans demonstrated a diagnosis of post-traumatic stress disorder (PTSD) doubled one’s risk of alcohol misuse compared to those without a diagnosis (Jakupcak et al., 2010).

Beyond the harmful impacts on the individual, the Department of Defense reports alcohol misuse costs approximately 1.1 billion dollars per year, in part due to the limited efficacy of current treatments (Harwood, Zhang, Dall, Olaia, & Fagan, 2009; Hoggatt et al., 2017). The US Food and Drug Administration have approved three pharmacologic drugs for the treatment of AUD: disulfiram, naltrexone, and acamprosate (Kranzler & Soyka, 2018). However, naltrexone is the only drug robustly studied in Veterans with AUD (Krystal, Cramer, Krol, Kirk, & Rosenheck, 2001), demonstrating that compared to placebo, naltrexone did not show any benefit in reducing relapse, amount of alcohol consumed, or days spent drinking (Krystal et al., 2001). Compounding the problems of limited effective treatments for AUD, a similar urgent need for effective treatments for PTSD exists (Krystal et al., 2017).

Taken together, current pharmacologic treatments are lacking in efficacy, highlighting the importance of research exploring novel pharmacologic drugs for this vulnerable population. Therefore, the primary aim of this observational study is to assess whether psychedelic treatment with ibogaine and 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT) is associated with reductions in alcohol use and PTSD symptoms among SOFV engaged in high-risk drinking.

METHODS

Recruitment procedure for retrospective survey

Data for this study are comprised of data from a previously published survey of SOFV who engaged in ibogaine and 5-MeO-DMT treatment in Mexico between 2017 and 2019 (Davis, Averill, Sepeda, Barsuglia, & Amoroso, 2020). Recruitment occurred from April to September 2019. Recruitment emails were sent to individuals who previously participated in this clinical program (65 eligible patients) and were sent weekly for four weeks. All emails included a link to a secure anonymous survey as well as information about the purpose of the study, the risks involved, and the protections for privacy and eligibility criteria. No personally identifying information was collected and all procedures were approved by a human subject’s review board (Solutions IRB). After providing informed consent, respondents completed questionnaires assessing PTSD, alcohol use, psychological flexibility, and demographics (see description of measures in published study, Davis et al., 2020). No compensation was provided for participation in this study. A total of 51 SOFV (78% of all SOFV treated at this clinic) participated in the parent study. Respondents included in this new analysis included any participant who reported alcohol misuse in the month prior to treatment. As such, the sample was reduced (N = 27; 53% of respondents in the parent study), and all analyses included in this manuscript are based on this subsample.

Clinical program

A full description of the clinical psychedelic program that the SOFV took part is published elsewhere (Davis et al., 2020). Briefly, patients were referred to this program by word of mouth and completed an initial medical and psychological screening (exclusion criteria provided in published report; Davis et al., 2020). The clinical program occurred over 3 days in a residential setting in Mexico. On the first day a therapist facilitated a group therapy session, wherein the therapist explained the range of psychedelic effects one may experience, advised patients to use mindfulness techniques if necessary, and helped them identify their goals or primary objectives for the treatment for the session. Next, patients were administered a urine toxicology screen and alcohol breathalyzer to confirm no
psychological flexibility. The Acceptance and Action Questionnaire (AAQII) is a 7-item measure used to assess psychological inflexibility (Bond et al., 2011). In the present study, the degree of psychological flexibility was assessed by respondents providing retrospective ratings 30 days prior to and 30 days following treatment. A change score was calculated by subtracting the mean of the total PCL-5 after treatment score from the total PCL-5 before treatment score.

**Psychological flexibility.** The Acceptance and Action Questionnaire (AAQII) is a 7-item measure used to assess psychological inflexibility (Bond et al., 2011). In the present study, the degree of psychological flexibility was assessed by respondents providing retrospective ratings 30 days prior to and 30 days following treatment. Respondents rated each item on a 7-point scale (0 = "Never true to 6 = "Always true"). A change score was calculated by subtracting the mean of the psychological flexibility after treatment score from the psychological flexibility before treatment score. Lower, and decreasing, scores on this measure are associated with greater psychological flexibility.

**Military history.** An 11-item measure was developed to assess military history using items modified from Section A of the National Survey of Veterans (Westat, 2010). Items assessed the military status, military branch, and number of deployments.

**Demographics.** Respondents were asked items assessing their basic demographics including age, sex, education, military service, ethnicity, marital status, employment status, and state of residence.

**RESULTS**

**Respondent characteristics**

The sample was comprised of SOFV who retrospectively reported a positive screen for alcohol misuse on the AUDIT-C (≥4 on the AUDIT-C; N = 27) prior to treatment. Of these respondents, 30% screened positive for moderate risk drinking (N = 8; AUDIT-C = 4–5), 26% for high-risk drinking (N = 7; AUDIT-C = 6–7), and 44% for severe risk drinking (N = 12; AUDIT-C = 8–12) prior to treatment. Respondents were primarily middle-aged (M = 40, SD = 5.5) men (96%). The largest proportion of respondents reported having a bachelor’s degree (48%) and were married, living with their spouse (67%). Although most of the sample served in the Navy (74%), smaller proportions served in the Army (11%) and Marine Corps (7%). Notably, most respondents reported their service occurred beginning in September 2001 or later (89%) with the vast majority also having served in Operations Enduring Freedom/Iraqi Freedom/New Dawn (93%). The number of deployments ranged between 1 and 18 with approximately one-half (56%) reporting 1–5, 37% reporting 6–10, and 7% reporting 11-18 deployments.

**Change in alcohol misuse, PTSD symptoms, and psychological flexibility**

Following their psychedelic treatment, most of the sample retrospectively reported they were either completely abstinent (N = 9; 33%; AUDIT-C = 0) or engaging in low-risk drinking (N = 14; 52%; AUDIT-C = 1–3) in the month following treatment. However, 4% (N = 1) remained drinking at the severe risk level (AUDIT-C = 8–12). Overall, Table 1 shows that patients retrospectively reported large decreases in alcohol use (P < 0.001; d = –2.4), PTSD symptoms (P < 0.001; d = –2.8), and a large increase in psychological flexibility (P < 0.001; d = –1.8) from before-to-after psychedelic treatment. The results of Pearson correlations indicated that increases in psychological flexibility (decreasing scores indicate greater psychological flexibility) were moderately correlated with decreases in alcohol use (r = 0.38, P = 0.049) and strongly correlated with decreases in PTSD symptoms (r = 0.90, P < 0.001).

**DISCUSSION**

The present findings demonstrated that psychedelic treatment with ibogaine and 5-MeO-DMT are associated with
Table 1. Change in symptom severity before and after treatment among respondents who screened positively on the AUDIT-C.

<table>
<thead>
<tr>
<th>Measure (N*)</th>
<th>Before treatment M (SD)</th>
<th>After treatment M (SD)</th>
<th>Change Score M (SD)</th>
<th>t-test</th>
<th>df</th>
<th>Effect Size (Cohen’s d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol use (27)</td>
<td>7.1 (2.4)</td>
<td>1.9 (2.1)</td>
<td>−5.18 (3.25)</td>
<td>−8.30***</td>
<td>26</td>
<td>−2.4</td>
</tr>
<tr>
<td>PTSD symptoms (20)</td>
<td>50.6 (18.4)</td>
<td>10.7 (8.4)</td>
<td>−39.95 (18.40)</td>
<td>−9.71***</td>
<td>19</td>
<td>−2.8</td>
</tr>
<tr>
<td>Psychological Flexibility (27)</td>
<td>3.4 (1.7)</td>
<td>0.9 (0.8)</td>
<td>−2.47 (1.59)</td>
<td>−8.06***</td>
<td>26</td>
<td>−1.8</td>
</tr>
</tbody>
</table>

Note. This table compares symptom severity in patients that screened positively on the AUDIT-C (score ≥ 4). N’s may vary as respondents had the option to avoid answering measures with sensitive or triggering questions (PTSD symptoms).

* Scale score interpretation: Alcohol use (AUDIT-C: range 0–12, higher scores indicate greater alcohol misuse); PTSD Symptoms (range 0–80; scores greater than 31–33 indicate need for PTSD treatment and a score reduction ≥ 10 indicates clinically significant improvement); Psychological flexibility (AAQII: range 0–6, a reduction in this scale means that there is an improvement in in psychological inflexibility). ***P < 0.001.

retrospective reports of rapid and significant decreases in alcohol use and PTSD symptoms among a clinical sample of SOVF. These findings are consistent with prior studies showing that MDMA, a serotonergic psychedelic, has been shown to produce significant PTSD symptom reduction (O’Carroll G et al., 2018). Additionally, animal studies have shown that ibogaine was effective in reducing alcohol consumption in alcohol-preferring rats (Rezvani, Overstreet, & Leef, 1995), and a case report documented the reduction of alcohol use following ibogaine and 5-MeO-DMT treatment in Mexico (Barsuglia et al., 2018). Moreover, a substantial amount of survey data has shown that psychedelics, in particular 5-MeO-DMT, has been associated with improvements in mental health, affect, cognition, and substance use in non-clinical samples (Barbosa et al., 2018; Davis, Barsuglia, Lancelotta, Grant, & Renn, 2018; Davis, So, Lancelotta, Barsuglia, & Griffiths, 2019; Garcia-Romeu et al., 2020; Garcia-Romeu et al., 2019; Uthaug et al., 2019; Uthaug et al., 2020). The current study extends this body of research by demonstrating the retrospectively reported utility of sequential administration of ibogaine and 5-MeO-DMT treatment in a clinical setting among an at-risk population of SOVF.

Findings from this study also showed that retrospectively reported decreases in alcohol use and PTSD symptoms were both correlated with increases in psychological flexibility attributed to the psychedelic treatment. Consistent with prior studies, psychological inflexibility has been implicated in a variety of pathologic mental states (Levin et al., 2014), in particular those suffering from PTSD and AUD (Grosso et al., 2014; Meyer, Morissette, Kimbrel, Kruse, & Gulliver, 2013), and therapies designed to enhance psychological flexibility (i.e., Acceptance and Commitment Therapy) have been shown to reduce symptom severity in patients with comorbid PTSD and AUD (Meyer et al., 2018). However, the effect sizes found in this study are approximately 2–3 times greater than the effect sizes found in prior studies (prior study: \( d = 0.91 \) to \( d = 0.98 \) versus current study: \( d = -1.8 \) to \( -2.8 \)). Furthermore, prior studies implemented at least 10 therapy sessions to produce benefits (Meyer et al., 2018). In contrast, ibogaine and 5-MeO-DMT treatment is associated with rapid (over the course of 3 days) improvement in symptoms. The rapid onset of symptom improvement highlights a potential breakthrough in therapeutics for this difficult to treat population that has high treatment dropout rates (Odenwald & Semrau, 2013; Watts et al., 2014), but future controlled studies are needed to ascertain the clinical efficacy of this treatment.

Although the neurophysiologic effects of psychedelics are complex, there are proposed mechanisms that could explain the reductions in alcohol use and PTSD symptoms reported in this study. In animal models, ibogaine induced expression of glial-derived neurotrophic factor (GDNF) expression in the ventral tegmental area (VTA), a neurologic locus in the addiction pathway, and resulted in reductions in ethanol self-administration (Carnicella, He, Yowell, Glick, & Ron, 2010). Additionally, 5-MeO-DMT is an agonist at the 5-HT2A receptor, which reduces mesolimbic dopamine levels in the addiction pathway, potentially impairing the reward stimulus and the synaptic maintenance of this circuit in response to ethanol (Liester & Prickett, 2012). It is possible that these two substances modulate synapse formation and dopaminergic transmission in this pathway, leading to their anti-addictive effects. With respect to PTSD, psychedelics are thought to mediate improvements in these symptoms through memory reconsolidation and fear extinction via inhibition of the amygdala and excitation of the hippocampus (Thal & Lommen, 2018).

Although the results of this study are promising, there are limitations to consider. First, the sample was subject to selection bias, as respondents were those who personally sought treatment with ibogaine and 5-MeO-DMT for their symptoms. Similarly, it is possible that those who chose not to participate or were not able to respond to the survey recruitment may also have experienced neutral or negative outcomes associated with treatment. As this study used a cross-sectional retrospective report design, respondents may have also overestimated their improvement due to recall bias and future studies should incorporate a longitudinal design with clinician-rated measures. As such, these three factors may have resulted in anticipated and greater self-reported benefits. Further limits to generalizability were due to the demographic homogeneity of the largely Caucasian, middle-aged, male sample with prior military experience, representing a small percentage of the general population and may or may not be representative of the larger Veteran population that were not SOF. In addition, two different substances with varying doses were administered in
succession, making it challenging to parse out differential benefits. Due to the classifications of ibogaine and 5-MeO-DMT as schedule I drugs, our study design was restricted, leading to a lack of randomization, blinding, and use of a control group ultimately preventing determinations of causality.

Future studies should work to elucidate whether there are heterogenous benefits provided by ibogaine or 5-MeO-DMT compared to placebo, utilizing clinician-rated outcomes as opposed to self-report to increase the validity of symptom improvement. Furthermore, although our study showed rapid benefits, we did not assess the extent these changes persisted in the long-term. Nevertheless, findings suggest that these psychedelic therapies offer potential alternative approaches to the debilitating mental health and substance misuse problems plaguing the Veteran communities. More research, with adequate control conditions and laboratory drug administration, is urgently needed to explore the clinical safety of this intervention and to determine whether this approach is sufficient to maintain the clinical benefits in the long-term.

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**REFERENCES**


