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Psychedelic Treatment for Trauma-Related Psychological and Cognitive Impairment Among US Special Operations Forces Veterans

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Abstract

Background: U.S. Special Operations Forces Veterans are at increased risk for a variety of mental health problems and cognitive impairment associated with military service. Current treatments are lacking in effectiveness and adherence. Therefore, this study examined psychedelic treatment with ibogaine and 5-methoxy-N,N-dimethyltryptamine for trauma-related psychological and cognitive impairment among U.S. Special Operations Forces Veterans.

Method: We conducted a survey of Veterans who completed a specific psychedelic clinical program in Mexico between 2017 and 2019. Questions probed retrospective reports of mental health and cognitive functioning during the 30 days before and 30 days after treatment. A total of 65 people completed treatment during this time frame and were eligible for contact. Of these, 51 (78%) completed the survey and were included in data analyses (mean age = 40; male = 96%; married = 55%; Caucasian/White = 92%; Operation Enduring Freedom/Operation Iraqi Freedom Service = 96%).

Results: Results indicated significant and very large reductions in retrospective report of suicidal ideation ($p < .001$; $d = -1.9$), cognitive impairment ($p < .001$; $d = -2.8$), and symptoms of posttraumatic stress disorder ($p < .001$; $d = -3.6$), depression ($p < .001$; $d = -3.7$), and anxiety ($p < .001$; $d = -3.1$). Results also showed a significant and large increase in retrospective report of psychological flexibility ($p < .001$; $d = 2.9$) from before-to-after the psychedelic treatment. Increases in the retrospective report of psychological flexibility were strongly associated with retrospective report of reductions in cognitive impairment, and symptoms of posttraumatic stress disorder, depression, and anxiety (rs range −0.61 to −0.75; $p < .001$). Additionally, most participants rated the psychedelic experiences as one of the top five personally meaningful (84%), spiritually significant (88%), and psychologically insightful (86%) experiences of their lives.

Limitations: Several limitations should be considered including the retrospective, self-report, survey design of the study, and the lack of randomization and blinding, thus making these finding preliminary.

Conclusion: U.S. Special Operations Forces Veterans may have unique treatment needs because of the sequela of problems associated with repeated trauma exposure and the nature of the exposure. Psychedelic-assisted therapy with these under-researched psychedelics may hold unique promise for this population. However, controlled studies are needed to determine whether this treatment is efficacious in relieving mental health and cognitive impairment among U.S. Special Operations Forces Veterans.

Keywords

special operations, veterans, ibogaine, 5-methoxy-N,N-dimethyltryptamine, trauma, cognitive impairment

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Introduction

Special Operations Forces (SOF) personnel constitute the most elite members of the military; they were selected based upon indicators of superior physical and psychological resilience and trained to endure the challenges of combat.[1,2] The group cohesion among elite SOF

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members is a protective factor against posttraumatic stress disorder (PTSD) and other mental health issues.[2] Despite inherent resiliencies and specialized training, SOF personnel are often exposed to a greater number of deployments and intense combat which are associated with increased prevalence of PTSD.[2,3] Although SOF Veterans exhibit PTSD symptoms at rates comparable to conventional forces Veterans,[3,4] they may be more reluctant to seek mental health treatment.[3] There is growing concern of a mental health crisis and an alarming increase in the incidence of suicides in SOF members highlighting limited effective treatment methods for this unique population.[3,4]

Combat Veterans with PTSD frequently demonstrate a complex spectrum of co-morbid psychological and neuropsychiatric symptoms.[5] One of the signature injuries of the recent conflicts in Iraq and Afghanistan is traumatic brain injury (TBI)—largely attributed to exposure to improvised explosive devices and increased survival from life-threatening injuries. Veterans who have sustained a TBI are more likely to have comorbid psychological and neuropsychiatric issues including PTSD, depression, anxiety, cognitive impairment, and suicidal behaviors.[5]

Currently available treatments demonstrate limited efficacy in addressing the unique and complex spectrum of psychiatric symptoms in SOF members and Veterans.[6] Currently approved psychotherapies aim to address troubling memories (e.g., cognitive processing therapy, prolonged exposure, eye movement desensitization, and reprocessing), and although these therapies are the most effective treatments currently available, they do not work for all Veterans.[7] Pharmacotherapies (e.g., Selective serotonin reuptake inhibitors, selective norepinephrine reuptake inhibitors tricyclic antidepressants, mood stabilizers, antipsychotics, or psychostimulants) are prescribed to reduce persistent physiological arousal, mood symptoms, or mitigate cognitive deficits.[8,9] However, current pharmacotherapies also have limited efficacy for many individuals with PTSD, have unwanted side effects, and require long-term use.[7,10,11] Therefore, it is essential that novel and potentially curative treatment approaches are developed that can address the underlying etiology and spectrum of symptoms in the Veteran population. Given the comorbid presentations associated with PTSD (depression, anxiety, etc.), there is need to develop transdiagnostic treatments that can simultaneously address PTSD and its common overlapping comorbities.[12,13]

Psychedelic drugs demonstrate potential as transdiagnostic treatment approaches for the Veteran population. Psilocybin, lysergic acid diethylamide (LSD), and 3,4-methylenodloxymethamphetanine (MDMA) are the most widely researched psychedelic-assisted therapies. These substances exhibit preliminary efficacy as transdiagnostic treatments in numerous psychiatric conditions including depression and anxiety associated with life-threatening diseases,[14,15] treatment-resistant depression,[16] substance use disorders,[17,18] and in Veterans with PTSD.[19,20] Although none of these treatments are as yet approved by the Food and Drug Administration, the therapeutic efficacy of these substances is broadly hypothesized to occur in part through pharmacological action on serotonergic functioning, stimulation of neurotrophic growth factors and neuroplastic changes,[17,21] and through psychological mechanisms such as reprocessing of traumatic content, emotional breakthroughs, mystical-type experiences, and fostering adaptive changes in personality.[19,20,22,23] Ibogaine and 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT) are lesser researched psychedelic substances which may be of particular relevance for addressing the symptom clusters experienced by SOF Veterans.

Ibogaine

Ibogaine is a psychoactive indole alkaloid which is extracted from the *Tabernanthe iboga* rainforest shrub and has been used for centuries in Central Africa for initiatory rituals.[24] Ibogaine was used in France for over 30 years as an anti-depressant and a stimulant until the mid-1960s.[25] Ibogaine treatment is reported to alleviate a spectrum of mood and anxiety symptoms[25–28] and is associated with self-reported improvements in cognitive functioning in individuals with substance use disorders.[29–31] During treatment, ibogaine allows the evocation and reprocessing of traumatic memories and occasions therapeutic and meaningful visions of spiritual and autobiographical content,[26,29,30,32] which are of central relevance in addressing PTSD-related psychological content. The benefits of ibogaine may be associated with its effects on serotonin and dopamine transporters, sigma, N-methyl-d-aspartate, nicotinic acetylcholine, and opioid receptors,[29,33,34] and the production of glial-derived neurotrophic factors[35] and brain-derived neurotropic factor[36] which are identified sites of interest in the treatment of cognitive impairment in neuropsychiatric disorders.[37–42] The primary adverse effects of ibogaine include cardiovascular effects (e.g., Q-wave/T-wave interval prolongation, bradycardia, arrythmias, and in rare cases, sudden cardiac death),[43] ataxia, nausea, and vomiting,[44] and psychological effects (e.g., auditory and visual hallucinations, re-experiencing traumatic memories, acute fear, distress, or guilt).[31,45]

5-Methoxy-N,N-Dimethyltryptamine

5-MeO-DMT is a psychedelic tryptamine found in plant species[46] and notably in the venomous secretions of the Sonoran Desert/Colorado River toad.[47] In observational

studies, 5-MeO-DMT demonstrates therapeutic potential across a variety of psychiatric symptoms that correspond with common sequelae in Veteran populations. For example, in individuals who received vaporized 5-MeO-DMT in a group naturalistic setting, approximately 80% of those who reported a diagnosis of depression (n = 149) or anxiety (n = 173) endorsed improvements in these conditions following 5-MeO-DMT use.[48] In an epidemiological survey of 515 individuals, participants who endorsed having psychiatric diagnoses indicated that their symptoms improved following 5-MeO-DMT use, including PTSD (79%)[49] and depression (77%), and anxiety (69%).[50] In a recent prospective study, a single administration of vaporized 5-MeO-DMT from toad secretion was associated with reductions in symptoms of depression, anxiety, and stress as well as increased life satisfaction and mindfulness-related capacities.[51] The observed psychotherapeutic effects of 5-MeO-DMT may occur in part through occasioning mystical-type experiences[52] or experiences of ego dissolution[51] similar to other classical psychedelics such as psilocybin[53,54] and LSD.[55] 5-MeO-DMT also demonstrates neuroprotective, regenerative, and anti-inflammatory properties which may prove therapeutic in addressing the underlying etiology of cognitive impairment and PTSD.[56–58] The primary adverse effects of 5-MeO-DMT include physical effects such as alterations in blood pressure and heart rate,[59] heart palpitations, chest pressure, and physical shaking/trembling as well as psychological effects including feelings of acute fear, anxiety, sadness, grief, guilt, and near-death type experiences.[50,60]

Current Study

Collectively, these recent findings suggest psychedelics, in particular ibogaine and 5-MeO-DMT, may be promising transdiagnostic tools for treating the spectrum of neuropsychiatric symptoms in SOF Veterans. However, because ibogaine and 5-MeO-DMT are illegal in the United States, many people, including Veterans,[29] seek these treatments in countries where they are not illegal (e.g., unscheduled in Mexico).[50] The primary aim of the current study was to examine the outcomes of a multimodal clinical psychedelic program on mental health functioning among U.S. SOF Veterans. Given the prior studies among people who have received ibogaine or 5-MeO-DMT have reported positive clinical outcomes associated with multiple mental health problems (e.g., depression, anxiety, PTSD, substance use), we hypothesized that participants would report reductions in symptom severity across multiple mental health domains. Furthermore, because studies have shown that psychedelics can occasion experiences that are often described as personally meaningful, spiritually significant, and contribute to life satisfaction and well-being, we hypothesized that the participants would report acute and enduring positive effects of these treatment experiences.

Method

Clinical Program

All participants were English-speaking U.S. SOF Veterans and received treatment at a clinical psychedelic program in Mexico between 2017 and 2019 (time since treatment varied between one month and two years), which involved psychedelic-assisted therapy with ibogaine and 5-MeO-DMT. Prior to enrolling in the clinical program, participants were referred by word of mouth and then completed an initial medical screening with a program physician. During the screening, participants were asked about their medication history, past and present medical conditions, Veterans Administration disability rating, treatment history, and history of TBI. Individuals using contraindicated medications or medications that interact with 5-MeO-DMT or ibogaine could only proceed if they adhered to a tapering schedule designed by the program's pharmacist. Individuals that passed the initial medical screening were referred to a clinician for psychological intake and screening. Individuals are excluded from treatment if they present with current eating disorders, current, or past psychotic spectrum disorders or bipolar I disorder, or symptoms of impaired reality testing. Lastly, all individuals were required to undergo laboratory tests that consisted of a complete blood count with differential, metabolic panel, urine drug screen, and a 12-lead electrocardiogram. Patients that were obese or over the age of 55 were required to undergo a stress test.

The clinical program occurred in a residential setting in Mexico over a period of three days. On Day 1, a program therapist hosted a group psychedelic preparation session, during which the therapist explained the range of effects one may experience while under the influence of ibogaine, advised participants to practice mindfulness techniques if necessary, and identify their intentions for the experience. Participants were then administered urine toxicology screen and alcohol tests to confirm no contraindicated substances were detected and, if passed, were administered a single oral dose (10 mg/kg) of ibogaine hydrochloride (99% purity) in a group setting with four to five participants. All participants laid on a bed in a supine position and received continuous cardiac monitoring, intravenous fluids, and medical monitoring throughout the ibogaine session. On Day 2, participants were encouraged to spend the day processing or integrating their ibogaine experience (e.g., talking about their experience, writing/journaling). Much of the integration

was introspective; however, participants could also integrate by speaking with others. Psychological support was provided by clinical psychedelic program staff via one-on-one meetings, and optional group integration sessions (e.g., talking about their experience with other patients) were also offered. On Day 3, participants attended preparation sessions for their upcoming 5-MeO-DMT experience and afterwards were each administered 5-MeO-DMT one at a time. Participants received at least three doses: 5 mg, 15 mg, and 30 mg for a total of 50 mg of inhaled 5-MeO-DMT (amount of 5-MeO-DMT estimated at 15%, which is a common concentration when excreted from bufo alvarius).[52,61] Participants that did not reach observed peak effects (i.e., altered state of consciousness or emotional catharsis) were administered a fourth dose of 30 mg, and possibly a fifth dose up to 45 mg. After acute effects had subsided for each participant, they were invited to integrate their experience both individually and via group activities.

Recruitment Procedure for Retrospective Survey

From April 2019 to September 2019, recruitment emails were sent to individuals who previously participated in the clinical program. Initial emails were sent weekly for four weeks. All recruitment emails included a link to a secure anonymous survey (hosted by Survey Gizmo), as well as a brief statement of the purpose, study risks and privacy statement, and the study eligibility criteria. No personally identifying information was collected in the survey, and all procedures were approved by an independent human subject's review board at Solutions Institutional Review Board. To meet inclusion criteria for the study, participants had to be between the ages of 18 to 64 years; have participated in the clinical psychedelic program; and be able to read, write, and understand the English language. After providing informed consent, study participants completed a battery of measures that assessed PTSD, substance use, depression, anxiety, cognitive problems, and suicidal thoughts and behaviors (see description or measures below). Measures asking sensitive questions (i.e., PTSD symptoms and suicidal ideation) included a "trigger warning," and the participant would only see the questions on that measure if they agreed to proceed. If a participant said they did not want to answer those questions they were able to proceed on to the next set of survey items, effectively leaving that specific questionnaire unanswered. Additionally, because some questions may have been distressing to some individuals, participants were given the option to select "prefer not to answer" to skip any individual item in a survey. Participants were also provided contact information for the director of clinical psychedelic program and the National Suicide Prevention Hotline for assistance coping with any distress. Participants did not receive compensation for their participation in the study.

Measures

PTSD Symptoms. The PTSD checklist (PCL-5) is a 21-item measure that assesses each of the 21 Diagnostic and Statistical Manual of Mental Disorders (5th edition) symptoms of PTSD.[62] Respondents were asked to rate how bothersome (0 = "not at all" to 4 = "extremely") each of the symptoms were one month before and one month after participating in the treatment program.

Depression Symptoms. The Patient Health Questionnaire-2 is a two-item survey used as an initial assessment for depressed mood and anhedonia.[63] Respondents reported how often (0 = "not at all" to 3 = "nearly every day") they experienced the symptoms one month before and one month after participating in the treatment program. Scores higher than three points are often suggestive of major depressive disorder.

Anxiety Symptoms. The Generalized Anxiety Disorder 2-item is used to assess presence of anxiety symptoms.[64,65] Respondents reported the frequency (0 = "not at all" to 3 = "nearly every day") at which they experienced feeling anxious or worried one month before and one month after participating in the treatment program. Generally, a cut off score of three points is used to identify further diagnostic evaluation for generalized anxiety disorder.

Suicidal Ideation. The Depressive Symptom Index Suicidality Subscale is a brief four-item screening tool for suicidality.[66,67] Respondents were asked to select a statement that best describes them one month before and one month after participating in the treatment program. Each of the four items were rated on a four-point scale (0–3).

Cognitive Functioning. The Medical Outcomes Study—Cognitive Functioning (MOS-CF) subscale was utilized for the present study. The MOS-CF is comprised of 6 items and assesses the amount of time an individual has become confused or had difficulties with reaction time, reasoning, memory, attention and concentration.[68] Respondents were asked to rate the frequency (0 = "none of the time" to 5 = "all of the time") at which they experienced each symptom one month before and one month after participating in the treatment program.

Psychological Flexibility. The Acceptance and Action Questionnaire II (AAQ-II) is a one-factor, seven-item measure used to assess psychological inflexibility or experiential avoidance.[69] In the present study, the degree of

psychological flexibility was assessed by asking respondents to provide retrospective ratings one month before and one month after participating in the treatment program. Respondents rated each item on a seven-point scale (1 = "never true to 7 = "always true"), and lower scores were indicative of higher levels of psychological flexibility.

Military History. The 11-item measure used in the present study was developed to assess military history. Items on this measure were modified from the National Survey of Veterans, Section A[70] and assessed the military status, military branch, number of deployments, and military occupation.

Treatment History. The treatment history measure is an eight-item measure developed to assess the clinical psychedelic program. Participants provided information on the conditions for which they are seeking treatment (e.g., depression, anxiety, TBI, PTSD, drug/alcohol misuse), treatments they have attempted prior to participating in this clinical psychedelic program (e.g., psychotherapy, 12-Step programs, psychiatric medications, psychedelic-assisted therapies, transcranial magnetic stimulation), and an evaluation of the clinical psychedelic program (i.e., satisfaction level, likelihood for recommendation to others, and comparison to past treatments).

Demographics. Respondents were asked nine items that evaluated basic demographic information including age, sex, ethnicity, educational attainment, marital status, state of residence, and employment status.

Analysis

Descriptive analyses of demographic, background, and treatment history characteristics for all study variables were calculated. Regarding primary outcomes, a series of t-tests were calculated examining mean differences in retrospective reports of mental health symptoms (e.g., PTSD, depression, anxiety), cognitive functioning, suicidal ideation, and psychological flexibility from before-to-after the psychedelic treatment. Change scores were then calculated by subtracting the retrospective reports of one month *after* treatment scores from the retrospective reports of one month *before* treatment scores on all primary outcome measures (PTSD, depression, anxiety, suicidal ideation, cognitive impairment, and psychological flexibility). A correlation analysis was then used to examine the relationship between changes in retrospective reports of psychological flexibility and mental health symptoms, cognitive functioning, and suicidal ideation. Effect sizes for the paired samples t-tests were calculated using the Cohen's d statistic. Descriptive analyses also assessed treatment satisfaction (e.g., how satisfied participants were with the clinical program, how likely they were to recommend the program to others, and whether the treatment was better or worse than ones they tried previously). Proportions were then used to characterize the number of participants reporting positive enduring effects (e.g., how much the treatment contributed to enduring changes in their sense of self, mood, behaviors, attitudes), and the degree to which they believed the program was personally meaningful, spiritually significant, psychologically insightful, and psychologically challenging. Analyses were conducted using SPSS version 25.[71]

Results

Respondent Characteristics

Sample demographics are provided in Table 1. The sample (n = 51) was comprised primarily of adult (*M* age = 40.4, standard deviation = 5.6), Caucasian/White (94%), non-Hispanic (92%) men (96%). Approximately three-quarters (76%) of the sample reported having a bachelor's, master's, or advanced graduate college degree, and one-half (55%) were married and living with their spouse. Participants reported serving in various branches of the military including Army (18%), Navy (75%), and Marine Corps (6%), and most (96%) reported serving in Operation Enduring Freedom or Operation Iraqi Freedom. Overall, most participants (59%) reported serving in five or more deployments (range 1–18). Self-reported vocation/occupation in the military varied (e.g., Army Ranger, Green Beret, Special Operations Medic), but most participants (63%) reported a designation of Navy's Seal, Air, and Land Forces (SEALs). Over three-quarters (82%) reported having sustained head injuries during a military deployment, with 57% reporting between 1 and 10 head injuries total, and 18% reporting between 1 and 20 blast exposures.

Treatment History

Many participants reported engaging in several psychosocial and other treatments in the years prior to their involvement with the clinical psychedelic treatment program. For example, most participants had tried nutritional/dietary changes (59%), yoga (55%), psychotherapy (43%), cannabis (43%), or psychiatric medications (41%).

Primary Outcomes: Mental Health Symptoms, Suicidal Ideation, and Cognitive Functioning

As shown in Table 2, there were significant and very large reductions in retrospective reports of suicidal ideation ($p < .001$; $d = -1.9$), cognitive impairment ($p < .001$; $d = -2.8$), and symptoms of PTSD ($p < .001$; $d = -3.6$), depression ($p < .001$; $d = -3.7$), and anxiety

Table 1. Demographic and background characteristics of the sample (N = 51).

Characteristic	% or mean (standard deviation)
Age	40.4 (5.6)
Sex (male)	96%
Race	
Caucasian/White	92%
Mixed race	4%
Asian	2%
Hispanic (no)	94%
Education	
Less than bachelor's	24%
Bachelor's degree	41%
Master's degree	28%
Advanced degree	8%
Marital status	
Married and living with spouse	55%
Divorced or separated	24%
Never married	16%
Living with partner	6%
Military branch (could select more than one)	
Army	18%
Navy	75%
Marine Corps	6%
Service era (could select more than one)	
September 2001 or later	90%
August 1990 to August 2001	29%
May 1975 to July 1990	4%
Operation enduring freedom/Iraqi freedom (yes)	96%
Number of deployments	
1–5	55%
6–10	29%
11–18	16%

($p < .001$; $d = -3.1$) from before-to-after the clinical psychedelic treatment program. Notably, the retrospective reports of decreases in symptoms were substantial, such that participants reported that they were no longer elevated above clinical cutoffs on these symptom measures after the psychedelic therapy. Results also showed a significant and large increase in retrospective reports of psychological flexibility ($p < .001$; $d = 2.9$) from before-to-after the psychedelic treatment and increases in retrospective reports of psychological flexibility were strongly associated with retrospective reports of reductions in cognitive impairment, and symptoms of PTSD, depression, and anxiety (rs range 0.61–0.75; $ps < .001$).

Treatment Satisfaction

Participants reported an overwhelmingly high degree of satisfaction with the clinical psychedelic program. Specifically, 80% of participants stated that they were either very (28%) or completely (53%) satisfied with the program. Overall, 92% of the participants reported that they were "very likely" to recommend this clinical psychedelic treatment program to others. Almost all (96%) of the participants reported that this program was "much better" than prior treatment they had attempted in the past.

Enduring Effects

Participants in this study reported that the clinical psychedelic treatment program was one of the top five most personally meaningful (84%), spiritually significant (88%), psychologically insightful (86%), and psychologically challenging (69%) experiences of their entire lives. Furthermore, participants reported strong positive and desirable changes in their sense of personal well-being or life satisfaction (77%), life's purpose (75%), life's meaning (73%), social relationships (73%), attitudes about life (74%), attitudes about self (72%), mood (59%), behavior (63%), attitudes about death (56%), how spiritual they are (65%), relationship to nature (57%), and their views regarding the true nature of reality and the universe (69%).

Discussion

A panel of experts have recently noted in a consensus statement that there is a "crisis" regarding the limited number of effective therapies available for those suffering from PTSD.[72] Preliminary results from our study suggest that ibogaine and 5-MeO-DMT treatments may offer a novel, rapid-acting and potentially cost-effective treatment for people suffering from PTSD. Participants in this study received a single dose of ibogaine and three to five doses of 5-MeO-DMT over the course of three days. When surveyed about their symptoms after treatment, participants reported significant and large reductions in PTSD ($d = -3.6$), depression ($d = -3.7$), and anxiety symptoms ($d = -3.1$), suicidal ideation ($d = -1.9$), and cognitive impairment ($d = -2.8$). Importantly, these improvements occurred over a short period of time and after a limited number of exposures to ibogaine and 5-MeO-DMT.

Another important finding from this study was that participants reported increased psychological flexibility ($d = 2.9$) following their ibogaine and 5-MeO-DMT treatment, and these increases were strongly associated with reductions in cognitive impairment, and symptoms of PTSD, depression, and anxiety. Interestingly, researchers have begun to examine the relationship between psychological flexibility and therapeutic outcomes after using psychedelics.[73,74] Consistent with the current findings, a recent study showed significant increases in psychological flexibility after using a

Table 2. Comparison of retrospective ratings (means and standard deviations) of mental health symptoms, suicidal ideation, and psychological flexibility in the 30-days before and 30-days after the clinical psychedelic treatment program.

Variable (N)[a,b]	Before treatment M (SD)	After treatment M (SD)	Change score M (SD)	t-test	Effect size (Cohen's d)[c]
PTSD symptoms (38)	46.2 (18.8)	12.0 (11.6)	−34.2 (19.3)	10.90***	−3.6
Depression symptoms (51)	4.1 (1.7)	0.9 (1.1)	−3.2 (1.8)	13.00***	−3.7
Anxiety symptoms (51)	4.0 (2.1)	1.1 (1.3)	−2.9 (1.9)	10.85***	−3.1
Cognitive impairment (51)	2.4 (1.2)	1.0 (0.6)	−1.5 (1.0)	10.03***	−2.8
Suicidal ideation (41)	2.7 (2.8)	0.4 (1.0)	−2.3 (2.5)	5.94***	−1.9
Psychological flexibility[d] (51)	3.3 (1.7)	1.0 (0.8)	2.3 (1.6)	10.27***	2.9

Note: Analyses are based on retrospective reports of symptoms in the one month before and one month after psychedelic therapy treatment. Therefore, effect size estimates are based on retrospective report of changes in mental health functioning. PTSD: posttraumatic stress disorder; SD: standard deviation.
***$p < .001$.

[a]N's varied because measures asking sensitive questions (PTSD symptoms and suicidal ideation) included a "trigger warning." If a participant said they did not want to answer those questions they were able to proceed on to the next set of survey items, effectively leaving that specific questionnaire unanswered. Additionally, because some questions may have been distressing to some individuals, participants were given the option to select "prefer not to answer" to skip any individual item in a survey.

[b]Score range for each measure: PTSD symptoms (0–80; scores above 31–33 suggest need for PTSD treatment; decrease of 10 or more considered clinically meaningful)[48]; depression symptoms (0–6; score above 3 suggests major depressive disorder likely)[49]; anxiety symptoms (0–6; score above 3 suggests generalized anxiety disorder likely)[50,51]; cognitive impairment (0–5)[54]; suicidal ideation (0–12)[52,53]; psychological flexibility (1–7).[57]

[c]Effect sizes are approximately 2 to 4 times greater than what would be considered a "large" effect (i.e., >.80).

[d]This measure is reversed scored; the lower the score the greater one's psychological flexibility.

psychedelic substance in nonclinical settings, and these increases in psychological flexibility mediated the relationship between the acute effects of psychedelics and decreases in depression and anxiety.[73] Furthermore, increased cognitive flexibility has been associated with decreased PTSD symptom severity[75] as well as being a positive predictor of treatment outcomes.[76] It is possible that psychedelic-assisted therapy may promote change by increasing psychological flexibility more rapidly than traditional psychotherapy.[74]

Limitations

Ibogaine and 5-MeO-DMT are currently Schedule I substances, which significantly hampers the ability of researchers to effectively study the risks and potential benefits of their administration.[77] To circumvent these barriers, we employed a quasi-experimental one-group pretest/posttest design using "then-test" items to assess pretreatment symptoms one month prior to and one month after treatment. This design has several limitations, including recall bias when using "then-test" questions, wherein participants may have recalled their baseline symptoms as worse than they actually were due to their improved present state—a phenomenon researchers call the "present state effect."[78] Additionally, "then-test" questions have the potential to influence posttest responses when used in close proximity to posttest questions.[79]

Second, the study lacked gold standard clinician administered clinical assessments for mental health or cognitive impairment which makes it impossible to confirm clinical diagnoses and it is possible that some participants did not meet criteria for PTSD or other psychiatric disorders. Instead, we relied on perceived changes in mental health and cognitive functioning which may have been influenced by a variety of factors including a more optimistic or less critical view of their functioning. The study is also limited in that we did not assess for expectancy effects nor is there any way to account for the placebo effect in a retrospective uncontrolled study. Furthermore, the study is limited due to selection bias and lack of a control group, randomization, or blinding. This study is also limited in generalizability to the population of predominately white, non-Hispanic, male U.S. SOF Veterans seeking psychedelic therapy with ibogaine and 5-MeO-DMT.

Conclusions

This is the first study to report on the effects of ibogaine and 5-MeO-DMT used as a treatment for SOF Veterans suffering from psychological and cognitive impairment. Our preliminary results suggest that ibogaine and 5-MeO-DMT may offer a rapid and robust, and well-tolerated, treatment option for those suffering from a variety of psychiatric and cognitive symptoms. However, further research is needed to support this preliminary evidence. Our results suggest that randomized, double blind, placebo-controlled trials are warranted in order to determine the safety and efficacy of ibogaine and 5-MeO-DMT in treating Veterans with psychiatric and cognitive impairment. Our study did not assess adverse effects or side effects of ibogaine and 5-MeO-

DMT which should be investigated in future research. Future research should also explore the unique effects of ibogaine and 5-MeO-DMT individually in the treatment of psychiatric disorders.

Given the significant number of Veterans suffering from PTSD and other psychiatric problems and the overwhelming rates of suicide among military and Veteran populations, investigation into novel pharmacotherapies such as ibogaine and 5-MeO-DMT are needed. Furthermore, because of the promising trial results of MDMA-assisted psychotherapy,[20,23] it is also possible that these novel therapies could be paired with trauma-focused psychotherapy to increase adherence and outcomes. This would be an advantage, especially in light of the fact that a significant portion of Veterans consistently demonstrate high levels of nonresponse and drop-out rates for conventional therapies[80,81] as well as limited confidence in the perceived efficacy of VA mental health treatment.[82] Despite the need for more research, results from this study provide a signal that ibogaine and 5-MeO-DMT may offer a robust and rapid acting treatment option for Veterans suffering from PTSD.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: A. K. D., J. P. B., and L. A. A. are board members of Source Research Foundation. L. A. A. is an associate editor for *Chronic Stress*, a scientific journal published by Sage.

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