

Research paper

Mystical experiences during magnesium-Ibogaine are associated with improvements in PTSD symptoms in veterans

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ABSTRACT

Ibogaine is an atypical psychedelic that evokes unique subjective effects, including mystical experiences. Mystical experiences have shown a mediating effect on clinical improvements following treatment with several psychedelic substances; however, the relationship between mystical experiences and clinical outcomes following ibogaine remains unclear. We examined the association between mystical experiences during ibogaine and subsequent changes in PTSD severity. We also explored the relationship between mystical experiences and several electroencephalography (EEG) measures found to underlie some of ibogaine's therapeutic effects. Our study included 30 male Veterans with traumatic brain injury from repeated blast/combat exposures who underwent magnesium-ibogaine therapy. We assessed mystical experiences post-treatment using the Mystical Experiences Questionnaire (MEQ30). PTSD severity and resting-state EEG assessments occurred at baseline and immediately and 1-month post-treatment. In linear mixed models, we used the time by MEQ30 interaction to assess the relationship between MEQ30 and changes in PTSD severity and EEG measures after treatment. Participants reporting greater intensity of mystical experiences following magnesium-ibogaine exhibited larger reductions in PTSD both immediately and one month after treatment (time by MEQ30 interaction for change from baseline: immediate post-treatment $B_{adj} = -5.89$, $p_{adj} < 0.001$; 1-month post-treatment $B_{adj} = -4.45$, $p_{adj} = 0.007$). Greater intensity of mystical experiences was also associated with larger reductions in peak alpha frequency one month after treatment ($B_{adj} = -0.38$, $p_{adj} = 0.006$). These findings suggest that mystical experiences may contribute to improvements in PTSD following magnesium-ibogaine. Greater mystical experiences during ibogaine treatment may also be related to persisting decreases in peak alpha frequency.

1. Introduction

1.1. PTSD and psychedelic treatment

Posttraumatic stress disorder (PTSD) is highly prevalent, particularly among combat-exposed veterans. In veterans who served in Iraq and Afghanistan, the prevalence of PTSD and traumatic brain injury (TBI)

are estimated at 23 % and 9–28 %, respectively (Fulton et al., 2015; Reger et al., 2022). Yet, there have been few advancements in pharmacological treatment for the past 20–30 years (Krediet et al., 2020; Krystal et al., 2017). Combat-related PTSD and PTSD in the presence of TBI are also associated with poorer outcomes after conventional treatment (Koek et al., 2016; Lindquist et al., 2017; Sayer et al., 2009; Vasterling et al., 2018). To address the need for better treatment, there

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¹ Dr. Nolan Williams passed away on October 8, 2025. All other authors affirm that Dr. Nolan Williams made significant contributions to the conception, design, and interpretation of the work and that this submission is consistent with his intentions. This work is dedicated to his memory.

has been a recent resurgence of research into psychedelic and related compounds as a treatment option. Most studies of psychedelics for PTSD have used MDMA or ketamine in the context of psychedelic-assisted therapy (Krediet et al., 2020; Varker et al., 2021). Overall, outcomes from trials of MDMA and ketamine for PTSD are promising, showing superior effects as compared with placebo (Krediet et al., 2020; Varker et al., 2021). A recent open-label study of the psychedelic ibogaine, coupled with magnesium to protect against cardiotoxicity, also showed significant improvements in PTSD after a single session in combat-exposed veterans with traumatic brain injury (Cherian et al., 2024). Outcomes of this trial are encouraging given that it involved 1) large effects despite application in a population at high risk for treatment failure (combat-exposed veterans with traumatic brain injury), and 2) a rapid-acting treatment (protocol involved only one psychedelic session). However, the cognitive and neurobiological mechanisms by which magnesium-ibogaine may exert its therapeutic effects are largely unknown.

1.2. Magnesium-ibogaine - origins and effects

Ibogaine is classified as an atypical psychedelic derived from the root bark of the *Tabernanthe iboga* plant, historically used in religious, spiritual, and healing ceremonies among several cultures in Africa (Köck et al., 2022). While the effects of ibogaine show some overlap with those of other psychedelic substances, there are also key differences in ibogaine's molecular and subjective effects (Vorobyeva and Kozlova, 2022; Waters, 2021). For example, ibogaine has been particularly associated with experiences of a vivid dream-like state and immersion in one's memories (Kohek et al., 2020; Schenberg et al., 2017). A qualitative analysis of subjective experiences during the recent magnesium-ibogaine trial (Cherian et al., 2024) corroborated this literature, with veterans reporting intense effects that frequently involved elements of their traumatic experiences (Olash et al., 2025, manuscript under review). It has proven challenging to quantitatively measure subjective experiences associated with psychedelics, as these experiences are often described as "ineffable" (Ko et al., 2022; Reiff et al., 2020). However, "mystical experiences" have emerged as a potentially useful construct for this purpose.

1.3. Mystical experiences and clinical outcomes

Mysticism broadly refers to the direct experience of a higher spiritual power. In psychology and neuroscience literatures on psychedelics, understandings of mystical experiences have centered around Walter Stace's conceptual framework, in which mystical experiences encompass the following: internal unity, external unity, nontemporal/nonspatial quality, inner subjectivity, objectivity and reality, sacredness, deeply felt peace and joy, paradoxicality, and ineffability (Ko et al., 2022; Mosur-injohn et al., 2023; Pahnke and Richards, 1966; Stace, 1960). Several instruments have been developed to quantify mystical experiences, such as the Hood Mysticism Scale, Mystical Experiences Questionnaire (MEQ), and 5 Dimensional Altered State of Consciousness Scale (Barrett et al., 2015; Dittrich, 1998; Hood Jr. et al., 2001; Ko et al., 2022; Mosur-injohn et al., 2023). These instruments have been used in several trials of psychedelics for psychiatric symptoms. For example, a recent review of 12 studies found that more intense mystical experiences during psychedelic use (psilocybin, ayahuasca, or ketamine) were associated with greater improvements in depression, cancer-related distress, and substance use (Ko et al., 2022). However, to our knowledge, the relationship between mystical experiences during psychedelic use and improvements in PTSD-related sequelae of TBI has not yet been examined. Additionally, the relationship between mystical experiences induced by ibogaine and clinical improvements remains underexplored.

1.4. Biological bases of mystical experience

Following from our hypothesis that mystical experiences may contribute to the potent clinical benefits observed following ibogaine treatment, we also explored whether mystical experiences may contribute to the modulation of neurophysiological mechanisms after ibogaine treatment that are thought to underlie those clinical benefits. Previous electroencephalography (EEG) and magnetoencephalography (MEG) studies of other psychedelics (including LSD, psilocybin, DMT, and ayahuasca) have reported moderate associations between stronger mystical-like subjective experiences and changes in a range of EEG measures of brain function, such as decreases in alpha power (Carhart-Harris et al., 2016; Muthukumaraswamy et al., 2013; Timmermann et al., 2023). We previously identified unique changes in specific neurophysiological indices after ibogaine treatment, some of which correlated with clinical outcomes (Lissemore et al., 2025). For example, peak alpha frequency (PAF) was significantly lowered after ibogaine treatment, which persisted at one-month follow-up, and correlated with improvements in PTSD symptoms. However, the neural correlates of mystical experiences induced by ibogaine have not yet been studied.

1.5. Study aims and hypotheses

The present study examined whether the intensity of mystical experiences during magnesium-ibogaine treatment was associated with changes in PTSD severity among combat-exposed veterans with TBI. We registered the following primary hypothesis on Open Science Framework (OSF): higher intensity of mystical experience, as measured by the MEQ30 total score, will be associated with greater improvement in PTSD severity immediately post-treatment. The following hypotheses were registered as secondary: higher MEQ30 subscale scores will be associated with greater improvement in PTSD severity immediately post-treatment, higher MEQ30 total scores will be associated with greater improvement in depression severity immediately post-treatment, and higher MEQ30 total scores will be associated with greater improvement in PTSD severity 1-month post-treatment. Exploratory analyses examined the association between MEQ30 total scores and change in anxiety severity and functional disability. We also explored whether mystical experiences were associated with changes in EEG markers previously linked to ibogaine's clinical effects.

2. Method

2.1. Study design

The current study involved a secondary analysis of data collected for the first prospective, open-label investigation of the safety and clinical efficacy of Magnesium-Ibogaine: the Stanford Traumatic Injury to the CNS (MISTIC; Cherian et al., 2024). A series of psychiatric, neuro-cognitive, and neurobiological assessments were conducted at Stanford University for 30 participants who had independently enrolled in the MISTIC treatment at Ambio Life Sciences in Mexico. In-person assessments were performed 2–3 days preceding treatment, 3.5–5 days after ibogaine administration, and 1-month following treatment.

Magnesium-ibogaine treatment took place over 5 days and involved a maximum of 5 participants per session. Day 1 included arrival, medical assessment, and preparatory ceremonial activities. Dosing took place on the evening of Day 2. Participants underwent continued monitoring for 72 h following dosing, as ibogaine's effects can persist throughout this time frame. Prior to dosing, participants undertook an 8-h period of fasting, an intravenous infusion of 1 g magnesium sulfate, and ingested an oral gastrointestinal protective agent (1–2 h preceding ibogaine). Ibogaine administration began with a test dose of 2–3 mg/kg. After approximately 40 min, additional doses were administered across a 2-h period, with the total dose administered not exceeding 14 mg/kg. One participant received an additional dose of 4 mg/kg 12 h following the

primary dose; this occurred at the discretion of clinic personnel due to insufficient treatment intensity. The ibogaine was synthesized in South Africa by Cape Analytical Service Laboratories (ibogaine hydrochloride, 98 % pure). Twelve hours following the final ibogaine dose, participants received an intravenous dose of magnesium sulfate, oral and intravenous antioxidants, and metabolic supporting agents. Ibogaine administration took place in a large room with mats spread on the floor. Although administered in a common space, the ibogaine treatment was largely an individual experience; participants spent the majority of the treatment session lying prone on a mat with eyeshades. Medical staff were available at a 1:2 ratio of staff to patients for monitoring and management, but no specific coaching or psychological support was provided during the magnesium-ibogaine dosing period. Participants undertook integration activities on Day 4, which included group or individual sessions with coaches to process the psychedelic experience, as well as the option to engage in the following wellness activities available at the Ambio Clinic: sweat lodge, massage, yoga, reiki, breath work, and meditation. Participants returned to Stanford University on Day 5.

Participants were also paired by VETS, Inc. with licensed therapists with experience coaching patients undergoing psychedelic therapy. Interaction with therapists included virtual pretreatment preparatory sessions (coaching on intention-setting, treatment expectations, and managing anxiety) and posttreatment integration sessions (processing emotions and integrating insights).

See Cherian et al. (2024) for more details regarding study procedures (NCT04313712). Primary and secondary hypotheses were registered on [osf.io](https://osf.io/syvv2) (<https://osf.io/syvv2>). Written informed consent was obtained from all participants, and all research procedures were approved by the Stanford University Institutional Review Board. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation.

2.2. Participants

Thirty male Special Operations Veterans participated. All veterans were evaluated for safety to participate in the MISTIC protocol as part of the Ambio Life Sciences screening process, including bloodwork, electrocardiogram, and medication review and adjustment for prevention of medication interactions. Study inclusion criteria were age of 18–70 years, ability to provide informed consent, history of head trauma (evaluated using the Ohio State University Screening for TBI exposure and the Department of Defense TBI classification; Corrigan and Bogner, 2007; Fortier et al., 2014), and history of combat or blast exposure. Exclusion criteria included contraindication to magnetic resonance imaging, history of neurological disorder (excluding sequelae of TBI), history of psychotic symptoms, clinical abnormalities that could affect participant safety or study integrity, concurrent participation in another clinical trial, and risk for suicidal behavior during the study.

2.3. Assessment instruments

Psychiatric diagnoses were determined using the Mini International Neurodiagnostic Interview (MINI; American Psychiatric Association, 2013; Sheehan et al., 1998). Combat exposure stress and number of TBIs sustained were measured using the Combat Exposure Scale (CES) and Boston Assessment for Traumatic Brain Injury (BAT-L), respectively (Fortier et al., 2014; Keane et al., 1989). PTSD severity was assessed using the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5; Weathers et al., 2018). Depression and anxiety were assessed using the Montgomery-Åsberg Depression Rating Scale (MADRS) and structured interview guide for the Hamilton Anxiety Rating Scale (SIGH-A), respectively (Hamilton, 1959; Montgomery and Åsberg, 1979; Shear et al., 2001). The severity of functional disability was assessed using the WHO Disability Assessment Schedule - 2.0 (WHODAS; Ustun et al., 2010). See Cherian et al. (2024) for further details.

Mystical experiences were assessed using the revised Mystical Experiences Questionnaire (MEQ30; Barrett et al., 2015), a 30-item self-report questionnaire designed to assess the intensity and dimensions of experiences associated with the use of psychedelics. The MEQ30 uses a 0–5 Likert scale from 0 “none; not at all” to 5 “extreme (more than any other time in my life and stronger than 4)”. We administered the MEQ30 via online questionnaire at the immediate post-treatment time point. Three participants completed the MEQ30 between 34 and 35 days following ibogaine-magnesium dosing. Potential impacts of delayed survey completion were examined using a sensitivity analysis, excluding those participants. MEQ30 subscales include: mystical (15 items), positive mood (6 items), transcendence of space and time (6 items), and ineffability (3 items).

2.4. EEG data acquisition and processing

Six minutes of eyes-open resting-state EEG recordings were performed at baseline ($N = 30$), immediate-post ($N = 30$), and 1-month post time points ($n = 27$). EEG data were recorded with 64 Ag-AgCl channels (actiCAP slim EEG cap; Brain Products GmbH, Germany; sampling rate: 10 kHz), using an acti64CHamp Amplifier and Cz as an online reference. Data were preprocessed offline using the EEGLAB toolbox, which included: (1) downsampling to 1 kHz, (2) application of 60 Hz notch, 1 Hz high-pass, and 50 Hz low-pass filters, (3) trimming to remove edge effects, (4) rejection of noisy channels using ARTIST code in MATLAB and visual inspection, (5) rejection of 2-s epochs with excessive noise, (6) average re-referencing, (7) independent component analysis to remove ocular and muscular artifacts, and (8) average re-referencing (Delorme and Makeig, 2004; Wu et al., 2018). See Lissemore et al. (2025) for further details.

EEG measures previously found to be modulated by ibogaine were of interest, including spectral power in predefined canonical frequency bands (delta 1–4 Hz, theta 4–8 Hz, alpha 8–13 Hz, beta 13–30 Hz, and gamma 30–50 Hz) normalized to broadband power, theta/beta ratio, PAF, and Lempel-Ziv complexity (LZc). Spectra were computed using Welch's method (2-s Hamming windows, 50 % overlap), and analyses of power and theta/beta ratio were restricted to two regions of interest in which we previously identified neurophysiological changes after ibogaine (medial frontal: AFz, F1, Fz, F2; medial posterior: CP1, CPz, CP2, P1, Pz, P2, POz). Global PAF was computed as the local maximum frequency (7–14 Hz) for each channel and then averaged across all channels. For global LZc, a 30 Hz low-pass filter was applied prior to computing the envelope of the signal via Hilbert transform, to ensure that LZc was not influenced by muscle activity. LZc was computed on the mean thresholded binarized envelope and normalized to a randomly shuffled time series, as described in detail elsewhere (Lissemore et al., 2025).

2.5. Statistical analysis

Our primary aim was assessed with a linear mixed model. To investigate the relationship between MEQ30 total score and change in CAPS-5 across treatment, our model used a dependent variable of the CAPS-5 score (at baseline, immediate-post, and 1-month post), independent variables (included as fixed effects) of MEQ30 total score, time point (as a factor), and the MEQ30 by time point interaction. Our model also included a random intercept for each participant. Age, CES total, and number of TBIs were included a priori as independent variables due to anticipated association with our primary outcome measure (Cherian et al., 2024). Our parameters of interest from this model are the MEQ30 by time point interaction coefficients for baseline to immediate post (primary hypothesis) and baseline to 1-month post (secondary hypothesis). We assessed significance by estimating the 95 % confidence interval.

Additional analyses used the same format as described above, replacing the dependent variable (CAPS-5) or key predictors (MEQ30

and MEQ30 by time point interaction terms) with the appropriate variables (e.g., PAF as the dependent variable, or MEQ30 subscale score replacing MEQ30 total). To facilitate the interpretability of model coefficients, MEQ30 total score and subscale scores were entered as averages rather than sums (i.e., MEQ30 total scores for each participant ranged from 0 to 5). We maintained a significance level of $p < .05$ for interpreting the outcomes of our secondary and exploratory analyses. We did not implement an alpha adjustment as our inferences all focused on individual null hypotheses. As described by [García-Pérez \(2023\)](#) and [Rubin \(2024\)](#), use of alpha adjustment is most appropriate in the case of an omnibus hypothesis, which is examined by testing a set of sub-hypotheses and then accepting or rejecting the omnibus hypothesis on the basis of their intersecting outcomes. Although alpha adjustments are frequently applied in an attempt to control the “family-wise error rate”, when applied in the context of interpreting individual hypotheses, this has the superficial effect of shifting the alpha level for all hypotheses from α to α^* and an associated inflation of the Type II error rate.

We also used a linear mixed model to examine the relationship between endorsement of a complete mystical experience (as defined by [Barrett et al., 2015](#)) and change in CAPS-5 (exploratory analysis). These outcomes are presented in the supplementary materials.

Assumptions for the linear mixed models were checked through the inspection of residual distributions for outliers, deviations from normality, and heteroscedasticity. Linear mixed models are known to be relatively robust to deviations from these assumptions; no major violations of assumptions were apparent. Spearman correlations were also obtained between MEQ30 score and change in PTSD severity or PAF after treatment. Analyses were conducted using R and SPSS ([IBM SPSS Statistics \[Version 30.0\], 2024](#); [R Core Team, 2024](#)).

3. Results

3.1. Descriptives

All thirty participants completed baseline and post-treatment clinical assessments. As determined by the MINI, 23 participants met criteria for a diagnosis of PTSD at baseline. The number of TBIs ranged from three to “in the thousands”; therefore, the number of TBIs for these participants was imputed to be 5 standard deviations above the mean. Please see [Table 1](#) for additional demographic data and scores at baseline for the MEQ30 and clinical outcomes. Distribution of ratings for each MEQ30 item is presented in Fig. S1.

3.2. Relationship between mystical experiences and PTSD severity

For our primary outcome of change in PTSD severity, we found a significant MEQ30 by time point interaction of $B_{adj} = -5.89$ ($F(1,56) = 13.65$, $p < .001$, 95 % CI $[-9.08, -2.70]$, [Table 2](#)) for baseline to immediate-post. In other words, for every 1 pt. increase in MEQ30 total (corresponding to a 30 pt. increase in raw score), there is an expected 5.89 reduction in CAPS-5 score from baseline to immediate-post. This is also consistent with a significant correlation between MEQ30 total score and change in CAPS-5 severity score from baseline to immediate-post ($\rho = -0.53$, $p = .003$, 95 % CI $[-0.75, -0.20]$, [Fig. 1A](#)).

For the relationship between MEQ30 total score and change in PTSD severity from baseline to 1-month post, our model yielded an unstandardized coefficient for the interaction term of -4.45 ($F(1,56) = 7.79$, $p = .007$, 95 % CI $[-7.64, -1.26]$, [Table 2](#)). Similarly, MEQ30 total score correlated significantly with change in CAPS-5 severity score from baseline to 1-month post ($\rho = -0.49$, $p = .007$, 95 % CI $[-0.73, -0.14]$, [Fig. 1B](#)). In summary, higher intensity of mystical experiences was associated with greater reductions in PTSD severity at both immediate-post and 1-month post-treatment.

Table 1
Demographic characteristics and baseline clinical scores for study sample (N = 30).

Variables	Mean (SD)	Diagnosis according to MINI DSM-5	n
Age	44.9 (7.5)	PTSD	23
CES	29.6 (5.2)	Major Depressive Disorder	15
nTBI	64.8 (94.1) ^a	Anxiety disorder ^b	14
CAPS-5	31.7 (12.5)	Alcohol use disorder	15
MADRS	25.5 (8.8)	Other SUD ^c	6
SIGH-A	20.8 (8.5)		
WHODAS-2.0	30.2 (14.7)		
MEQ30			
Full scale	3.29 (1.1)		
Mystical subscale	3.18 (1.4)		
Positive mood subscale	3.24 (1.2)		
Transcendence subscale	3.27 (1.3)		
Ineffability subscale	4.00 (1.1)		

Note. CAPS-5, Clinician-Administered PTSD Scale for DSM-5; CES, Combat Exposure Scale; DSM-5, Diagnostic and Statistical Manual of Mental Disorders, 5th edn.; MADRS, Montgomery-Åsberg Depression Rating Scale; MINI, Mini International Neuropsychiatric Interview; nTBI, number of TBIs as assessed using the Boston Assessment of Traumatic Brain Injury-Lifetime; SIGH-A, structured interview guide for the Hamilton Anxiety Rating Scale; SUD, substance use disorder; WHODAS-2.0, WHO Disability Assessment Schedule - 2.0.

^a The data presented for nTBI include imputed scores for three participants; these participants estimated sustaining more than one thousand TBIs. As these three estimates were orders of magnitude higher than the estimates provided by the remaining 27 participants (range: 3–207), at the recommendation of a statistician, we entered an imputed value of five times the standard deviation (300.74) for these datapoints.

^b Includes generalized anxiety disorder ($n = 8$), panic disorder ($n = 6$), agoraphobia ($n = 4$), and social anxiety disorder ($n = 3$). Four participants had >1 anxiety disorder.

^c Includes pain medication ($n = 1$), stimulants ($n = 3$) and cannabis ($n = 2$).

3.3. Relationship between MEQ30 subscales and PTSD severity

Model coefficients for MEQ30 subscales are presented in [Table 2](#). Both immediately and 1-month post-treatment, the 95 % confidence intervals for the MEQ30 subscale by time point interactions were largely overlapping. Significant interactions at $p < .05$ were identified for all subscale-by-time-point relationships, with the exclusion of ineffability by time point for the baseline to 1-month post contrast. These outcomes suggest that the association between the four MEQ30 subscale scores and decreases in CAPS-5 were similar, with no compelling indication of a particular subscale having an outsize impact on reducing PTSD severity.

3.4. Relationship between mystical experiences and secondary clinical measures

Outcomes from models examining the relationship between MEQ30 total score and change in severity of depression, anxiety, and functional disability are presented in [Table 3](#). Models predicting depression and anxiety severity yielded significant interaction terms with MEQ30 total score, whereas the model predicting functional disability did not. This indicates that participants endorsing more intense mystical experiences during ibogaine showed larger decreases in the severity of depression and anxiety at both follow-up time points. The intensity of mystical experience was not associated with pre- to post-treatment changes in functional disability.

3.5. Relationship between mystical experiences and neurophysiological effects

Beyond clinical outcomes, we also examined neurophysiological effects associated with mystical experience intensity. For global PAF, our

Table 2
Mixed models predicting CAPS-5 scores for MEQ30 total and subscales.

Predictor Parameter	MEQ30 Total		Mystical subscale		Positive mood subscale		Transcendence subscale		Ineffability subscale	
	<i>B_{adj}</i> (95 % CI)	<i>p_{adj}</i>	<i>B_{adj}</i> (95 % CI)	<i>p_{adj}</i>	<i>B_{adj}</i> (95 % CI)	<i>p_{adj}</i>	<i>B_{adj}</i> (95 % CI)	<i>p_{adj}</i>	<i>B_{adj}</i> (95 % CI)	<i>p_{adj}</i>
Baseline to immediate post MEQ _{predictor} x Time point	-5.89 (-9.08, -2.70)	<0.001	-3.68 (-6.25, -1.12)	0.006	-3.56 (-6.49, -0.63)	0.018	-4.95 (-7.66, -2.24)	<0.001	-4.46 (-7.87, -1.05)	0.011
Baseline to 1-month post MEQ _{predictor} x Time point	-4.45 (-7.64, -1.26)	0.007	-2.78 (-5.34, -0.21)	0.034	-3.05 (-5.98, -0.13)	0.041	-3.60 (-6.31, -0.89)	0.01	-2.83 (-6.24, 0.58)	0.10
Num obs	90		90		90		90		90	
R2 Marg.	0.714		0.703		0.706		0.712		0.700	
R2 Cond.	0.834		0.819		0.813		0.832		0.813	
ICC Adj.	0.419		0.390		0.362		0.419		0.378	
ICC Cond.	0.120		0.116		0.106		0.121		0.114	

Note. MEQ_{predictor} represents the key independent variable of interest for each of the five models (i.e., for the five LME models presented above, MEQ_{predictor} stands for MEQ30 full scale, mystical subscale, positive mood subscale, transcendence subscale, and ineffability subscale, respectively). All models were adjusted for age, CES, and number of TBIs. Model format: CAPS-5 = MEQ_{predictor} + time point (as factor), MEQ_{predictor} x time point, age, CES, number of TBIs, random intercept. Parameters are provided for interaction terms only and are presented as unstandardized coefficients: *B_{adj}* (95 % CI). Interaction terms (MEQ_{predictor} x time point) are interpretable as follows: for every 1 pt. increase in MEQ_{predictor} total there is an expected *B_{adj}* increase in the magnitude of change in CAPS-5 severity from baseline to respective time point (baseline or 1-month post). Regarding parameters not presented in the table, MEQ_{predictor} coefficients were significant for the models with MEQ30 total, mystical, positive mood, and transcendence subscale. The MEQ_{predictor} coefficient was not significant for the model predicting CAPS-5 from the ineffability subscale. Time point coefficients (baseline to immediate-post and baseline to 1-month post; indicating main effect of time) were significant across all models. Coefficients for age, CES, and number of TBIs were not significant in any of the models.

Significant *p*-values (<0.05) are highlighted in bold.

mixed model included a sample size of $n = 26$ for baseline to immediate-post, and $n = 23$ for baseline to 1-month post. Four participants from the initial $N = 30$ were excluded because no alpha peak was identified in >20 % of channels, and three participants did not undergo EEG measurements at 1-month for logistical reasons. The unstandardized coefficient for the MEQ30 by time point interaction term for the baseline to immediate-post contrast was -0.098 ($F(1,45) = 0.561$, $p = .46$, 95 % CI $[-0.36, 0.17]$), and for the baseline to 1-month follow-up contrast was -0.38 ($F(1,45) = 8.15$, $p = .006$, 95 % CI $[-0.65, -0.11]$). These results indicate that more intense mystical experiences were associated with larger decreases in PAF one month after magnesium-ibogaine treatment, but not at immediate post-treatment. These model results are consistent with a significant Spearman correlation between MEQ30 total score and change in PAF from baseline to 1-month post ($rho = -0.49$, $p = .019$, 95 % CI $[-0.75, -0.09]$; Fig. 2). No significant interactions between time point and MEQ30 total score were observed for the other EEG measures of interest.

3.6. Sensitivity analysis

Three participants completed the MEQ30 more than one week following immediate-post (MEQ30 completed at 34–35 days following ibogaine-magnesium dose). To explore the potential impact of this, we ran sensitivity analyses excluding those three participants. We also conducted a correlation between MEQ30 scores and the length of delay between immediate-post and survey completion. These analyses did not indicate an effect of the length of delay to survey completion on MEQ30 ratings (see supplemental analyses). We also investigated dose (ibogaine/kg) as a potential confound by correlating dose and MEQ30, as well as rerunning our primary analyses with dose included as a fixed effect. These analyses did not indicate a significant effect of dose on outcomes (see supplemental analyses).

4. Discussion

4.1. Relationship between mystical experience and PTSD severity

In this study, higher scores on the MEQ30 were associated with larger reductions in PTSD severity from baseline to immediate post-treatment. The point estimate for the effect size of this association was moderate ($rho = 0.53$), but the margin of error spanned a range from weak to strong effect size (Akoglu, 2018). The effect persisted one month after treatment, although it was slightly weaker. These results suggest that the more intense the mystical experiences during magnesium-ibogaine treatment, the greater the capacity for improvement in PTSD symptoms after ibogaine treatment, both immediately and one month after treatment.

Why might mystical experiences alleviate PTSD symptoms? People who have had mystical experiences often report feelings of profound connection to a higher spiritual power, creating a safe context in which they can reprocess their trauma without the typical fear response (Henner et al., 2022). By radically altering a person's sense of self (the phenomenon of “ego death”), mystical experiences can revise rigid, maladaptive beliefs that stem from their trauma, e.g., “I am broken” or “I will never be safe” (Buchborn et al., 2023). Feelings of extraordinary interconnectedness reported during mystical experiences can also ameliorate dissociation and a sense of disconnection, which are common in PTSD (Armour et al., 2014; Henner et al., 2022).

Our analysis was correlational and therefore cannot provide causal evidence regarding the role of mystical experience in the observed clinical effects. Although there is some theoretical and qualitative evidence to support a connection between mystical experiences and clinical benefit (Ko et al., 2022; Kohek et al., 2020), it is also possible that mystical experiences are an epiphenomenon (Olson et al., 2020; Yaden et al., 2024). A few recent studies in mouse models found that non-hallucinogenic analogues of ibogaine and LSD still produced

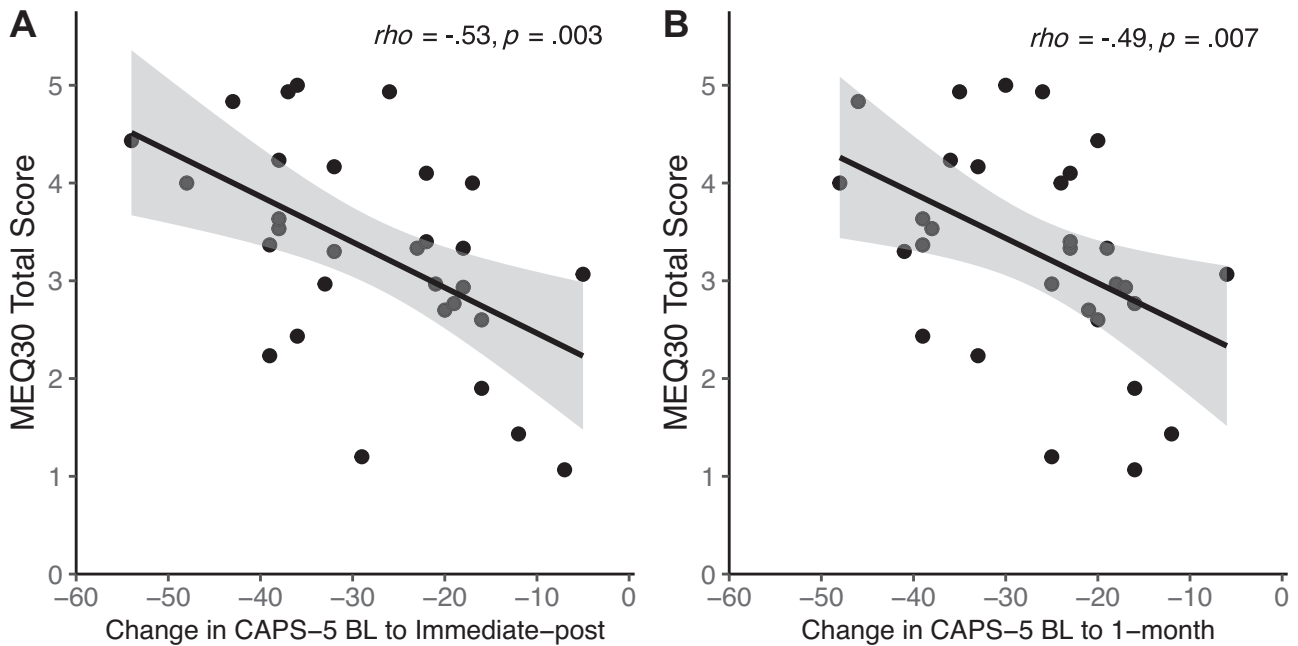


Fig. 1. Scatterplots of MEQ30 total and change in CAPS-5 from baseline to follow-up time points

Note. Higher intensity of mystical experiences were associated with larger decreases in PTSD severity (CAPS-5) at both immediate-post and 1-month post treatment. A. Scatterplot of MEQ30 total score and change in CAPS-5 from baseline (BL) to immediate-post for $N = 30$ including line of fit (simple linear regression) and 95 % confidence interval for visualization purposes. B. Scatterplot of MEQ30 total score and change in CAPS-5 from BL to 1-month post for $N = 30$ including line of fit (simple linear regression) and 95 % confidence interval for visualization purposes.

Table 3

Mixed models predicting secondary clinical assessment outcomes.

Outcome measure	MADRS		SIGH-A		WHODAS	
Parameter	B_{adj} (95 % CI)	P_{adj}	B_{adj} (95 % CI)	P_{adj}	B_{adj} (95 % CI)	P_{adj}
Baseline to Immediate post						
MEQ30 x Time point	-2.95 (-5.43, -0.47)	0.021	-3.51 (-5.78, -1.23)	0.003	-1.36 (-5.97, 3.26)	0.558
Baseline to 1-month post						
MEQ30 x Time point	-2.77 (-5.26, -0.29)	0.029	-3.34 (-5.61, -1.07)	0.005	-2.42 (-7.39, 2.54)	0.332
Num obs	90		90		86	
R2 Marg.	0.741		0.673		0.449	
R2 Cond.	0.835		0.792		0.716	
ICC Adj.	0.363		0.363		0.485	
ICC Cond.	0.094		0.119		0.267	

Note. All models are adjusted for age, CES, and number of TBIs. Model format: Clinical outcome (e.g., MADRS) = MEQ30 + time point (as factor), MEQ30 x time point, age, CES, number of TBIs, random intercept. Parameters are provided for interaction terms only and presented as unstandardized coefficient (95 % CI). Interaction terms (MEQ30 x time point) are interpretable as follows: for every 1 pt. increase in MEQ30 total there is an expected B_{adj} increase in the magnitude of change in outcome measure (e.g., MADRS) severity from baseline to respective follow-up time point (baseline or one-month-post). Regarding parameters not presented in the table, the MEQ30 coefficient was significant for the model predicting SIGH-A but was not significant for the models predicting MADRS or WHODAS. Time point coefficients (baseline to immediate-post and baseline to 1-month post; indicating main effect of time) were significant across all models. Coefficients for age, CES, and number of TBIs were not significant in any of the models.

Significant p -values (<0.05) are highlighted in bold.

behavioral responses consistent with antidepressant and anti-stress effects (Cameron et al., 2021; Lewis et al., 2023). Thus, the hallucinogenic, e.g., mystical, quality of psychedelic experiences may not be necessary for their therapeutic effects. However, to our knowledge, there have not been studies of non-hallucinogenic analogues of psychedelics in humans to date.

4.2. MEQ30 subscales

The only MEQ30 subscale that did not show a significant interaction with time was the ineffability subscale at 1-month post-treatment. We suspect the lack of a statistically significant effect may be attributable to reduced reliability of the composite (ineffability only includes 3 items),

as lower reliability for a measure decreases statistical power (Kanyongo et al., 2007). Overall, none of the MEQ subscales showed exceptionally stronger or weaker associations with PTSD severity. This is consistent with the findings of Barrett et al. (2015)'s psychometric study, which established the MEQ30 as a unidimensional scale.

4.3. Relationship between mystical experiences and anxiety, depression, and functional disability

Our analyses identified significant associations between the intensity of mystical experiences and reductions in anxiety and depression, but not functional disability. The observed relationships are consistent with outcomes from several previous studies of non-ibogaine psychedelic

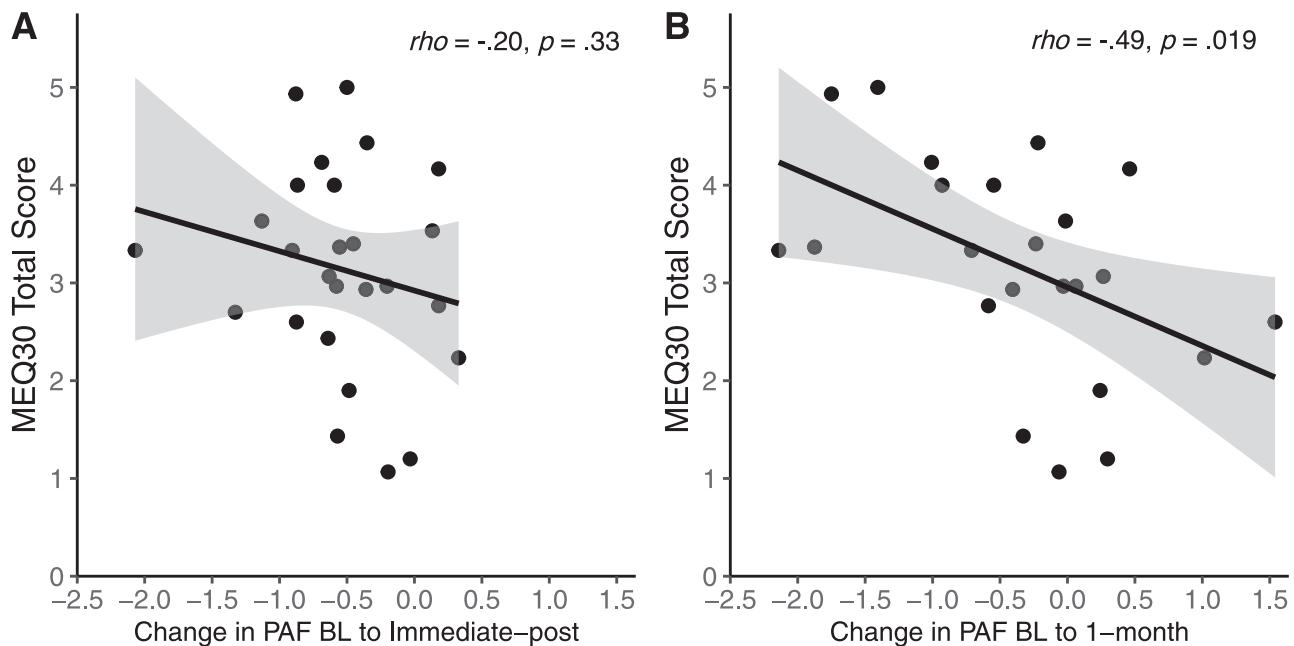


Fig. 2. Scatterplots of MEQ30 total and change in PAF from baseline to follow-up time points

Note. Higher intensity of mystical experiences was associated with larger decreases in peak alpha frequency (PAF) at 1-month post-treatment but not at immediate post-treatment. A. Scatterplot of MEQ30 total score and change in PAF from baseline (BL) to immediate-post for $N = 26$ including line of fit (simple linear regression) and 95 % confidence interval for visualization purposes. B. Scatterplot of MEQ30 total score and change in PAF from BL to 1-month post for $N = 23$ including line of fit (simple linear regression) and 95 % confidence interval for visualization purposes.

substances; these studies were also conducted in clinical populations and found associations between greater mystical experiences and improvements in depression and anxiety (Bogenschutz et al., 2015; Carhart-Harris et al., 2018; Dakwar et al., 2018; Garcia-Romeu et al., 2015; Hendricks, 2018; Johnson et al., 2017; Ko et al., 2022; Palhano-Fontes et al., 2019; Roseman et al., 2018; Ross et al., 2016; Rothberg et al., 2021). A recent psychometric study suggested that the WHODAS-2.0 may be less sensitive for persons with mild as opposed to moderate or severe disability (Herrold et al., 2021). This is likely relevant for the current analysis, as the average disability at baseline ($M = 30.2$, $SD = 14.7$) fell within the WHODAS-2.0 criteria for mild (mild disability: 20–39). Additionally, the relationship between mystical experiences and magnesium-ibogaine's beneficial effects may be specific to psychiatric symptoms. As a combined measure of physical and psychological disability, the WHODAS may be less sensitive to changes in psychological distress and disability as compared with the MADRS and SIGH-A (Marx et al., 2015).

4.4. Relationship between mystical experiences and peak alpha frequency

More intense mystical experiences during magnesium-ibogaine were associated with greater sustained reductions in PAF one month after treatment. This slowing of PAF was previously found to be associated with greater improvements in PTSD symptoms after magnesium-ibogaine treatment, particularly in arousal and reactivity symptoms (Lissemore et al., 2025). These prior findings suggest that PAF reductions may serve as a neurophysiological marker of reduced hyperarousal following magnesium-ibogaine. Accordingly, higher PAF has been associated with worse PTSD symptom severity and hyperarousal symptoms in veterans (Wahbeh and Oken, 2013), states of higher arousal (Gutmann et al., 2015), and greater activation of brain regions involved in arousal and attention (Jann et al., 2010). Taken together, these results raise the possibility that more intense mystical experiences during magnesium-ibogaine enable larger, persisting shifts in the neural mechanisms underlying hyperarousal in PTSD. Notably, mystical experience intensity was specifically associated with PAF reductions one

month after treatment; although PAF reductions immediately post-treatment showed a similar direction of association, that association was non-significant. Mystical experiences observed during magnesium-ibogaine treatment may therefore relate more strongly to enduring neural adaptations than to transient acute effects. This long-term shift in oscillatory activity induced by neuroplastic effects of magnesium-ibogaine is in line with delayed EEG spectral changes following ketamine observed by Anijärvi et al. (2023).

The neural mechanisms linking PAF changes to mystical experiences remain unclear. One possible framework comes from the RELaxed Beliefs Under pSychedelics (REBUS) model, which proposes that psychedelics relax top-down constraints encoded in the brain's predictive priors (Carhart-Harris and Friston, 2019). Broadly speaking, the brain becomes less restricted by its own predictions, and bottom-up, sensory information about the environment has a greater capacity to influence perception. Alpha oscillations are thought to mediate top-down inhibition of perception (Jensen, 2024; Klimesch et al., 2007), and slower PAF has been associated with reduced top-down modulation of perceptual processing (Wutz et al., 2018). Accordingly, long-term reductions in PAF following ibogaine might reflect a lasting relaxation of top-down control over sensory or perceptual systems. While it is unclear whether similar mechanisms extend to higher-order belief systems, such as those engaged during mystical experiences, this possible link warrants further investigation.

4.5. Strengths & limitations

The current study has several strengths, the most notable being that this is the first study to examine the relationship between mystical experiences during magnesium ibogaine and clinical improvements in persons with TBI and symptoms of PTSD. The use of a validated clinician-administered assessment of PTSD (CAPS-5) combined with a structured assessment of mystical experience (MEQ30) and EEG measures of related neural mechanisms enables this study to uniquely contribute to understanding the potential applications of magnesium-ibogaine for human health.

The current study also has several limitations, including its open-label design. The absence of a control condition prevents us from disentangling the effects of magnesium-ibogaine from expectancy effects. However, the observed clinical effects appeared much stronger than would be expected from a placebo response (Cherian et al., 2024). Additionally, this study did not include more comprehensive assessments of psychedelic experience, such as the 5- Dimensional Altered States of Consciousness Scale or Hallucinogen Rating Scale (Dittrich, 1998; Strassman et al., 1994). The acute effects of psychedelics assessed by the MEQ30 are highly correlated with other acute effects (Liechti et al., 2017), rendering the specificity of the association between mystical experience and clinical change unclear; for example, overall positive emotional effects (Holze et al., 2023) may similarly predict outcomes following ibogaine-magnesium. Another limitation is that the MEQ30 lacks a measure of “connectedness,” which may mediate the therapeutic benefits of psychedelics (Stocker et al., 2024). The MEQ30 is also biased towards collecting information about positive experiences elicited by psychedelics and neglects potentially important information about negative, uncomfortable, or even terrifying experiences (Greyson and Evans Bush, 1992; Lukoff, 1985; Pahnke and Richards, 1966). Inclusion of more comprehensive scales in future studies is recommended to address some of these unanswered questions. Finally, the majority of participants completed the MEQ30 at 3–7 days post-dosing and underwent an integration session before completing the questionnaire; these factors may have influenced participants' recollection of their ibogaine experience and associated responses on the MEQ30.

4.6. Future directions

The outcomes presented in this paper suggest several valuable directions for future research. First, it will be important to explore the durability of the observed impacts of MISTIC on TBI sequelae and how the intensity of mystical experiences relates to effects beyond 1-month post-treatment. Follow-up randomized trials including a control condition or various doses may help address the limitations related to the current trial's open-label design. Additionally, replication studies including larger and more diverse samples will clarify the generalizability of our findings. Exploration of biological mechanisms underlying mystical experience could be deepened by the acquisition of EEG during the MISTIC dosing session. Future psychometric studies of the MEQ30 after ibogaine, as well as alternative measures of mystical experience in ibogaine studies, would help distinguish the true association between mystical experiences and clinical outcomes from questionnaire-related biases. Research on the relationship between subjective experiences and clinical outcomes of MISTIC may also benefit from assessment of other phenomenological constructs that appear related yet distinct from mystical experience, such as emotional breakthrough and psychological insight (Peill et al., 2022; Roseman et al., 2019).

Author note

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jad.2025.120722>.

Data availability

Owing to the sensitivity of psychiatric patient data, our IRB requires individualized review before data sharing. We have produced anonymized data related to the present findings for sharing with all scientists with research and data safeguarding plans that comport with Stanford University guidelines. Please contact corresponding author Randi Brown at rbrown@paloalto.edu for any data-sharing requests.

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