Original Paper

Enhancing mindfulness and compassion through an ayahuasca-inspired formulation containing N,N-DMT and harmine: A randomized controlled trial in healthy subjects

Journal of Psychopharmacology
1–11

DOI: 10.1177/02698811251344689
journals.sagepub.com/home/jop

Helena D Aicher[1,2,3*], Ilhui A Wicki[1*], Daniel Meling[1,4], Michael J Mueller[1,3,5], Dario A Dornbierer[1,6] and Milan Scheidegger[1,3]

Abstract

Background: Mindfulness and compassion are therapeutically relevant and can be increased through different forms of meditation practices. However, meditation practice needs time and commitment. These resources are often limited in patients with mood disorders. Therefore, efficacious remedies that increase mindfulness and compassion could provide therapeutic options. This study aimed to investigate the relationship between psychedelic experiences induced by an ayahuasca-inspired N,N-dimethyltryptamine (DMT)/harmine formulation on mindfulness and compassion in healthy subjects.
Methods: This study applies a randomized, double-blind, placebo-controlled within-subjects design in a laboratory setting with 31 healthy participants. Each subject received a formulation comprising DMT + harmine, harmine + placebo, and placebo only on three different study days. Primary outcomes were mindfulness (MINDSENS) and compassion (SOCS).
Results: A significant effect of the drug on mindfulness ($p < 0.05$, $F = 3.41$), self-compassion (SOCS-S; $p < 0.01$, $F = 7.53$), and compassion with others (SOCS-O; $p < 0.05$, $F = 3.37$) 1 day post-treatment was found. Significant differences between the high- and low-sensitivity groups were found for mindfulness ($p < 0.05$, $F = 6.54$), self-compassion ($p < 0.05$, $F = 4.21$), and compassion with others ($p < 0.05$, $F = 4.42$).
Conclusions: In line with previous studies on traditional botanical ayahuasca, our findings support the notion that the DMT/harmine formulation might have therapeutic potential through its ability to acutely enhance mindfulness and compassion. Continuing studies in therapeutic settings are needed to further elucidate the mechanisms of action of ayahuasca-inspired formulations.

Keywords
N,N-DMT, harmine, ayahuasca, mindfulness, compassion

Background

Improvement of mindfulness- and compassion-related capabilities through different forms of meditation practices can lead to better psychological well-being (Brown and Ryan, 2003; Coffey et al., 2010; Goldberg et al., 2022; Khoury et al., 2013; Reangsing et al., 2021). Meditation practice needs time, commitment, and motivation, which is often limited in patients with mood disorders (e.g., depression, bipolar disorder, anxiety, and addiction disorders). Therefore, rapid-acting, safe, and efficacious therapies that increase mindfulness could help patients to better deal with those mental disorders. From a psychotherapeutic perspective, meditation and mindfulness practice became a central element of the so-called third wave of cognitive behavioral therapies. Programs like acceptance and commitment therapy, mindfulness-based cognitive therapy (MBCT), mindfulness-based stress reduction, or compassion-focused therapy (CFT) facilitate competences like observing, non-reacting, decentering, and self-compassion (see methods) and are promising approaches for the treatment of anxiety, depression, and pain (Goyal et al., 2014; Pots and Chakhssi, 2022).

The recent resurgence of psychedelic research (Tullis, 2021) has brought forth promising results in the treatment of mood and anxiety disorders (Carhart-Harris et al., 2016, 2021; Gasser et al., 2015; Gukasyan et al., 2022; von Rotz et al., 2023). Several systematic reviews and meta-analyses have been conducted, showing the promising potential of psychedelic-assisted therapies

[1]Psychedelic Research and Therapy Development, Adult Psychiatry and Psychotherapy, Psychiatric University Hospital Zurich, University of Zurich, Zurich, Switzerland
[2]Department of Psychology, University of Zurich, Zurich, Switzerland
[3]Neuroscience Center Zurich, University of Zurich, Zurich, Switzerland
[4]Faculty of Medicine, Department of Psychosomatic Medicine and Psychotherapy, Medical Center – University of Freiburg, Freiburg, Germany
[5]Department of Health Science and Technology, ETH Zurich, Zurich, Switzerland
[6]Institute of Pharmacology and Toxicology, University of Zurich, Zurich, Switzerland

*These authors contributed equally to this work and share first authorship.

Corresponding author:
HD Aicher, Psychedelic Research and Therapy Development, Adult Psychiatry and Psychotherapy, Psychiatric University Hospital Zurich, University of Zurich, Lenggstrasse 31, P.O. Box 363, Zurich CH-8032, Switzerland.
Email: helena.aicher@uzh.ch

(Andersen et al., 2021; Ko et al., 2023; Luoma et al., 2020; Reiff et al., 2020; Romeo et al., 2021). Notably, the indigenous plant medicine ayahuasca shows a rapid antidepressant action in patients with treatment-resistant depression in placebo-controlled trials (Palhano-Fontes et al., 2019; Zeifman et al., 2019). General improvement of mental health is frequently reported by experienced ayahuasca users (Sarris et al., 2021), especially enhancement of emotional empathy due to both pharmacological and non-pharmacological (e.g., ceremonial setting) factors (Uthaug et al., 2021). Improved outcome measures in clinically depressed patients (van Oorsouw et al., 2022) as well as increased mindfulness-related and self-compassion capabilities in healthy subjects (Domínguez-Clavé et al., 2016; Soler et al., 2016) after ingestion of ayahuasca or ayahuasca analogues have been found. These findings are well in line with other serotonergic psychedelics that showed potential to enhance mindfulness, alongside positive effects on prosocial behaviors and empathy for others (Jungaberle et al., 2018).

The molecule N,N-dimethyltryptamine (DMT) is the main psychoactive compound in ayahuasca and shares a structural similarity with the 5-HT2A receptor agonist psilocybin (O-phosphoryl-4-hydroxy-N,N-dimethyltryptamine) and the endogenous neurotransmitter serotonin (5-hydroxytryptamine). Unlike other psychedelics, DMT has been found in the brain of rats (Dean et al., 2019) and seems to be endogenously produced in humans (Barker, 2022; Barker et al., 2012; Franzen and Gross, 1965; Kärkkäinen et al., 2005). However, it is still unclear what the physiological role of DMT is (e.g., under which circumstances it is being produced) and if it reaches sufficient brain concentrations to produce any subjective effects in humans. Nonetheless, DMT is widely spread throughout nature in around 60 identified plants, for example, in *Psychotria viridis, Diplopterys cabrerana*, or *Mimosa hostilis/tenuiflora*, which are part of the indigenous plant medicine ayahuasca and have been used in rituals and ceremonies for centuries (Frecska et al., 2016). As DMT is quickly degraded by the enzyme monoamine oxidase A (MAO-A) when orally administered, only the presence of an MAO-inhibitor (MAO-I) leads to intensified lasting effects. *Banisteriopsis caapi*, known as "vine of the souls," is the plant in ayahuasca containing MAO-inhibiting beta-carbolines like harmine, harmaline, and tetrahydroharmine. Their names derive from the plant *Peganum harmala*, which also contains beta-carbolines and is postulated to be the main ingredient of the Eurasian concoction *Soma* or *Hoama* (Clark, 2019; Flattery and Schwartz, 1989), which also has been used on the Eurasian continent for millennia (Glennon, 1981; Sanches et al., 2016; Youdim et al., 2006). Harmine has, like many other MAO-I inhibitors, some nonspecific serotonergic effects by elevating serotonin levels in the synaptic cleft (Herraiz et al., 2010). Notably, MAO-I such as iproniazid and moclobemide were used as the first medication treatments for depression since the 1950s (López-Muñoz et al., 2007).

The pharmacological and non-pharmacological mechanisms of action of ayahuasca and DMT-based formulations remain poorly understood. The ingestion of ayahuasca induces an altered state of consciousness (lasting 2–5 h) that shares a similarity to dream-like states with elevated introspective awareness (Riba et al., 2001) and changed perspectives on thoughts and feelings comparable to mindfulness-based training outcomes (Baer et al., 2006). This, in turn, may support certain forms of detachment from maladaptive thoughts or emotions, also called "decentering," which is a core feature of the therapeutic potential of mindfulness practices (Fresco et al., 2007).

According to Grossman, 2008 (2011) and Van Dam et al. (2018), mindfulness is a complex construct and difficult to measure (low reliability). It is therefore suggested that the measurement of compassion could be more accurate, precise, and reliable (Gu et al., 2020). Compassion in this work is clearly defined by five subdimensions, namely recognizing suffering, understanding the universality of suffering, feeling for the person suffering, tolerating uncomfortable feelings, and motivation to act/acting to alleviate suffering (see methods). CFT (Gilbert, 2014; Pots and Chakhssi, 2022) is a recently developed therapeutic approach that is particularly suited for individuals characterized by the tendency to negatively evaluate and judge aspects of the self. Several meta-analyses demonstrate efficacy for compassion-based interventions in various (non)-clinical populations with moderate to large effects on depression and well-being (Kirby et al., 2017; Millard et al., 2023; Wakelin et al., 2022; Wilson et al., 2019). Hence, self-compassion and compassion with others may provide a valuable resource to cope with difficult emotions and thoughts during psychedelic experiences and to reduce suffering in clinical populations.

This study aimed to evaluate mindfulness- and compassion-related capabilities after the intake of an ayahuasca-inspired formulation containing intranasal DMT and sublingual harmine (DMT/HAR) compared to harmine alone (HAR) and placebo (PLA) in healthy subjects using a double-blind, placebo-controlled, randomized trial design. We expected to find a significant increase in mindfulness (MINDSENS), self-compassion (SOCS-S), and compassion with others (SOCS-O) after the DMT/HAR intervention, with less pronounced effects in the HAR condition compared to PLA. We expected these effects to be stronger for high versus low responders to DMT/HAR (high- vs low-sensitivity group).

Methods

Study design

The trial applied a double-blind, randomized, placebo-controlled, within-subjects study design in 31 healthy subjects with three conditions: (1) DMT + harmine (DMT/HAR), (2) placebo + harmine (HAR), and (3) placebo + placebo (PLA). An overview of the study design with the timepoints, interventions, and assessments relevant for this publication is shown in Figure 1.

Setting

The study was conducted during the daytime in the rooms of the Human Sleep Laboratories. The soundproof and temperature-controlled rooms were set up in a comfortable living room atmosphere and equipped with dimmable lights and a sound system (see Supplemental Figure 4). Technical monitoring and measuring devices were installed. Throughout all study days, a standardized playlist containing non-stimulating background music was played to provide a feeling of comfort and relaxation. It was an individual setting with one participant in the room. A medically

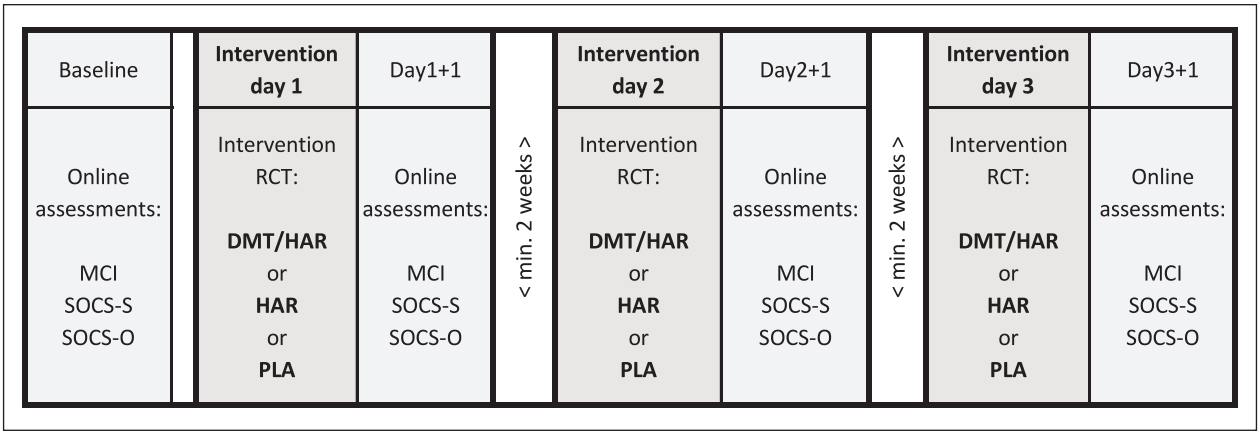

Figure 1. Study plan overview.
Overview of the double-blind crossover RCT study design with the timepoints, interventions, and assessments. Each participant got all three interventions, DMT/HAR (DMT + harmine), HAR (harmine + placebo), and PLA (placebo + placebo), on three different intervention days in a randomized order. The washout period between intervention days was at least 2 weeks. The main outcome measures (MCI, SOCS-S, and SOCS-O) were assessed at baseline and 1 day after each intervention day.
MCI: MINDSENS composite index (mindfulness); SOCS-S: Sussex Oxford compassion scale (self-compassion subscale); SOCS-O: Sussex Oxford compassion scale (compassion with others subscale).

trained experimenter was present all the time to supervise the participants.

Study drug

We explored novel parenteral administration routes and delivery mechanisms, specifically designed to deliver purified forms of harmine and DMT, extracted from the plant *Mimosa hostilis/tenuiflora*. DMT in combination with harmine or other pharmacological MAO inhibitors is commonly called *ayahuasca-analogue* or *pharmahuasca*. To bypass the shortcomings of oral administration, like nausea and vomiting, harmine was provided as orodispersible tablets (ODTs) for buccal delivery, whereas DMT was formulated as an intranasal spray solution to enable an incremental dosing of the psychotropic compound and to standardize the bioavailability (Dornbierer et al., 2023). Analogous placebo formulations (ODT and intranasal spray with comparable texture and taste) were administered.

Thirty minutes after administration of harmine HCl (100 mg; mg/kg body weight: $M = 1.298$, 1.075–1.667; this is below maximum tolerated dose found in Ables et al., 2024 for oral harmine) or placebo, respectively, the repeated intermittent dosing of DMT or placebo was initiated with a total of 100 mg DMT in intervals of 15 min (10 mg each timepoint) over a period of 150 min. Overall, this was experienced as a moderate dose (Aicher et al., 2024). In case of tolerability issues, participants had the possibility to discontinue DMT administration and potentially continue at the next time point. The option to skip a dose was chosen only twice over the full study. Only a few and small side effects were observed and are reported in Mueller, Aicher and Dornbierer et al. (2025).

Participants and permissions

A total of 37 healthy male participants were recruited after a thorough medical and psychological screening day. Six dropped out (four before the first intervention day, two after the first intervention day; they decided not to participate further because of the time commitment); drop-outs were replaced. In all, 31 participants (25.39 ± 4.21 years) completed all three intervention days and were considered for the analysis. The following criteria were required for inclusion: (i) age 20–40, (ii) BMI 18.5–30, (iii) male sex to avoid the potential impact of menstrual cycle on blood chemistry—because of blood chemistry analyses reported elsewhere (Mueller, Aicher and Dornbierer, 2025), (iv) no current or previous history of somatic, neurological, or psychiatric disorder, assessed during medical and psychiatric screening, (v) no family history of psychosis, bipolar, or other severe psychiatric disorders, (vi) no acute or chronic medication intake that could interact with the study drug, and (vii) no current or regular drug intake. A detailed overview of the demographics of participants, including their previous drug experience and their motivation to participate in the study, can be found in Supplemental Tables 1–4. Participants received monetary compensation (320.- CHF ≅ € total, or 60.- CHF ≅ € per completed intervention day). All participants provided written informed consent according to the Declaration of Helsinki.

Outcome measures

The following questionnaires were applied:

The MINDSENS Composite Index (MCI; Soler et al., 2014) consists of 10 items of the Five Facet Mindfulness Questionnaire (FFMQ) (Baer et al., 2006) and nine items of the Experiences Questionnaire (EQ; Fresco et al., 2007). The 19 items of the FFMQ and EQ that discriminated best between daily meditation practitioners and non-meditators were selected for the MINDSENS Composite Index. Examples of the subgroups are as follows: *observing* "I pay attention to how my emotions affect my thoughts and behavior," *non-reacting* "When I have distressing thoughts or images, I am able just to notice them without reacting," and *decentering* "I have the sense that I am fully aware of what is going on around me and inside me." Decentering is defined as the capacity to step outside one's personal perspective

Table 1. Mindfulness (MCI) and compassion (SOCS) by drug condition and sensitivity to the drug.

Scale	Subscale	Drug condition main effect		Sensitivity main effect		Drug condition* sensitivity interaction	
		F-value	*p*-Value	*F*-value	*p*-Value	*F*-value	*p*-Value
MINDSENS	Global score	3.41	0.040	6.54	0.016	7.87	<0.001
	Observe	0.68	0.512	6.08	0.020	1.14	0.326
	Non-react	8.85	<0.001	3.11	0.088	5.85	0.005
	Decentering	2.01	0.144	5.5	0.026	9.11	<0.001
SOCS-S	Global score	7.53	0.001	4.21	0.049	4.58	0.014
	RS	0.16	0.849	4.25	0.048	0.80	0.456
	UUS	3.47	0.038	0.82	0.374	0.07	0.937
	FPS	5.11	0.009	2.55	0.121	0.10	0.908
	TUF	6.28	0.003	3.15	0.086	3.66	0.032
	AMA	3.36	0.042	2.77	0.107	6.56	0.003
SOCS-O	Global score	3.37	0.042	4.42	0.044	1.66	0.199
	RS	2.72	0.075	5.38	0.028	0.31	0.737
	UUS	1.25	0.294	2.02	0.166	0.23	0.792
	FPS	1.01	0.372	5.75	0.023	1.62	0.208
	TUF	1.27	0.288	1.79	0.191	0.83	0.442
	AMA	6.14	0.004	0.99	0.329	1.70	0.192

Note. $N = 31$. Main effects of drug condition (DMT + harmine vs harmine vs placebo), main effect of sensitivity to the drug (high- vs low-sensitive group of participants separated by median split of the maximum subjective intensity rating), and interaction effect of drug and sensitivity on mindfulness (MINDSENS), self-compassion (SOCS-S), and compassion with others (SOCS-O) are shown.
MCI: MINDSENS composite index; SOCS-S: Sussex Oxford compassion scale self; SOCS-O: Sussex Oxford compassion scale others; RS: recognizing suffering; UUS: understanding the universality of suffering; FPS: feeling for the person suffering; TUF: tolerating uncomfortable feelings; AMA: acting or being motivated to act to alleviate suffering.

of a lived experience and to disidentify from the content of thoughts.

The Sussex Oxford Compassion Scale (SOCS; Gu et al., 2020) defines compassion through five dimensions: (a) *Recognizing suffering*, (b) *understanding the universality of suffering*, (c) *feeling for the person suffering*, (d) *tolerating uncomfortable feelings*, and (e) *motivation to act/acting to alleviate suffering*.

The questionnaire consists of a 20-item scale for others (SOCS-O) and a 20-item scale for self (SOCS-S). Scores on both scales show adequate internal consistency, interpretability, floor/ceiling effects, and convergent and discriminant validity. The items are scored on a 5-point Likert-type scale, ranging from *never* to *all the time*. Time points were baseline, 24 h after the experience, 1-month follow-up, and 4-month follow-up.

Statistical analyses

The data were analyzed with R Studio version 2021.09.2+382 (RStudio Team, 2019). The main subjective outcome measures were mindfulness (measured with the MCI), self-compassion (measured with the SOCS-S), and compassion with others (measured with the SOCS-O). According to a median split of the maximum subjective intensity ratings in the DMT/HAR conditions, participants were grouped into low versus high sensitivity to the study drug. For our hypotheses concerning the main subjective outcome measures, (generalized) linear mixed models (estimated using REML and nloptwrap optimizer) were fitted with the R lme4 package (Bates et al., 2015) to predict the outcome measures with drug condition (DMT/HAR, HAR, PLA) and sensitivity (high vs low) and the interaction of drug and sensitivity. By fitting the models on a standardized version of the dataset, standardized parameters were obtained. A type III repeated measures analysis of variance with Satterthwaite's method table was produced to detect the main and interaction effects. Post hoc pairwise analyses to explore the significant effects were performed using the emmeans package (Lenth et al., 2021). Degrees of freedom (*df*) were calculated with the Kenward–Roger method. The significance level was set to 0.05. Benjamini–Hochberg correction for multiple comparisons was applied.

Results

Mindfulness per condition

Results on the MCI global score and all subscales are shown in Table 1. In the following subsection, the results for the global score are described. The results of the global score by drug condition, grouped by sensitivity to the drug, are visualized in Figure 2. A notable number of observations ($n = 91$, groups: P, 31) were modeled. Visualization of results for the subscales (observing, nonreacting, decentering) can be found in Supplemental Figure 1.

MCI global score

The model's total explanatory power was substantial (conditional $R^2 = 0.86$), and the part related to the fixed effects alone (marginal R^2) was 0.19. A significant main effect of drug ($F(2, 56.19) = 3.41$, $p = 0.04$), a significant main effect of sensitivity ($F(1, 29.08) = 6.54$, $p = 0.016$), and a significant interaction of drug and sensitivity ($F(2, 56.19) = 7.87$, $p < 0.001$) were found.

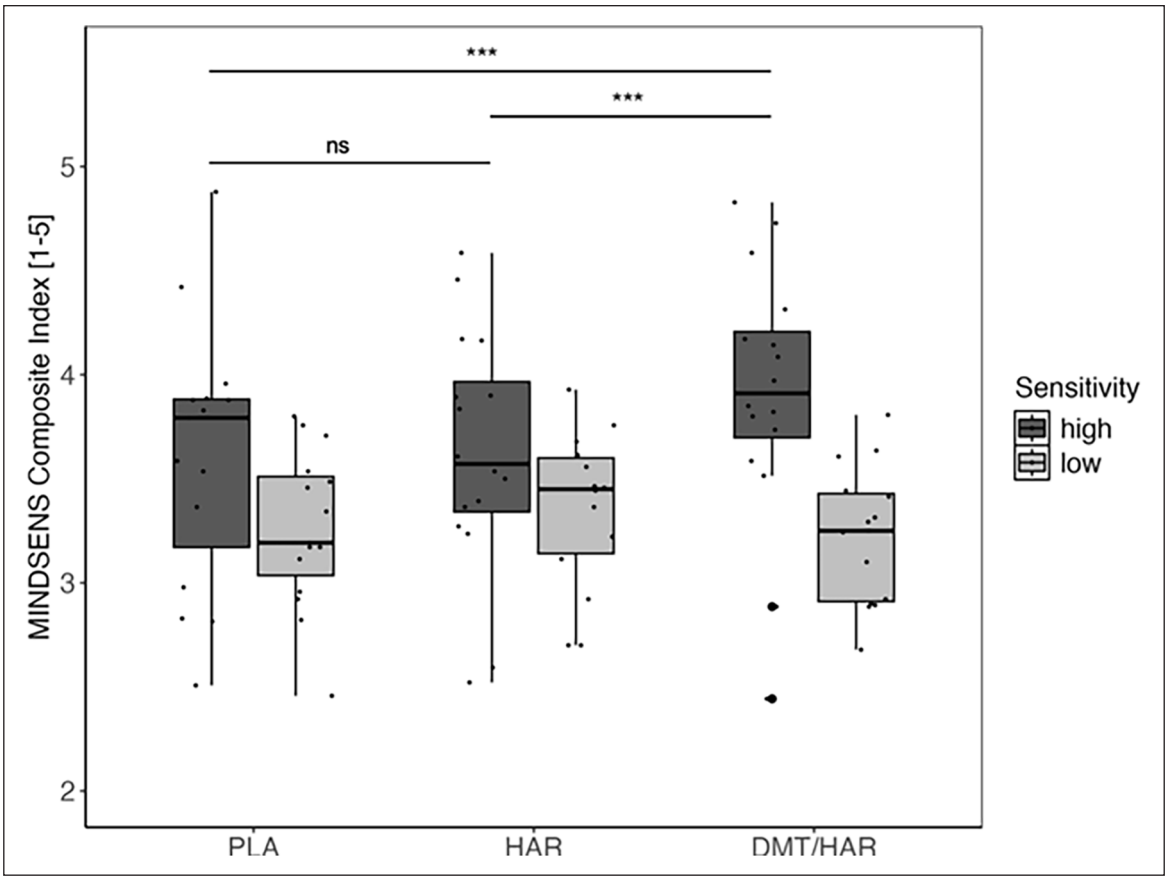

Figure 2. MCI global scores by drug condition and grouped by sensitivity to the drug.
Note. Boxplots with subjective ratings on mindfulness (MCI global score) by drug condition (DMT/HAR, HAR, PLA) and by sensitivity to the drug (high- vs low-sensitive group of participants separated by median split of the maximum subjective intensity rating) are shown. The bigger dots indicate statistical outliers. Minimum possible value: 1; maximum possible value: 5.
MCI: MINDSENS composite index; SOCS-S: Sussex Oxford compassion scale self; SOCS-O: Sussex Oxford compassion scale others; ns: not significant.
*$p < 0.1$. **$p < 0.05$. ***$p < 0.01$.

Post hoc tests revealed that participants showed significantly higher levels of MCI in DMT/HAR compared to PLA (*Mean difference* (*Mdiff*) = 0.14, SE = 0.05, *df* = 56.1, *t*.ratio = 2.58, $p = 0.04$). There was no significant difference in MCI between DMT/HAR and the HAR ($p = 0.17$), nor between HAR and PLA condition ($p = 0.35$). Post hoc tests revealed significantly higher MCI in the high- versus the low-sensitivity group (*Mdiff* = 0.44, SE = 0.17, *df* = 29, *t*.ratio = 2.56, $p = 0.02$).

While the differences between the drug conditions were not different in the low-sensitivity group (DMT/HAR − HAR: $p = 0.54$; DMT/HAR − PLA: $p = 0.66$; HAR − PLA: $p = 0.54$), participants in the high-sensitivity group reported higher levels of MCI in DMT/HAR compared to HAR (*Mdiff* = 0.28, SE = 0.07, *df* = 56.0, *t*.ratio = 3.8, $p < 0.001$), and in DMT/HAR compared to placebo (*Mdiff* = 0.31, SE = 0.07, *df* = 56.2, *t*.ratio = 4.16, $p < 0.001$), but no difference in MCI in HAR compared to PLA ($p = 0.69$). That is, the high-sensitivity group, but not the low-sensitivity group, showed significantly greater MCI in DMT/HAR than in HAR and PLA.

Compassion per condition

Results on the global score and subscales of SOCS-S and SOCS-O are shown in Table 1. In the following subsection, the results of the global score for both scales are described. The results of the global score by drug condition grouped by sensitivity are visualized in Figures 3 and 4. A notable number of observations ($n = 91$, groups: P, 31) were modeled. Visualization of results for the subscales (recognizing suffering, understanding the universality of suffering, feeling for the person suffering, tolerating uncomfortable feelings, acting, or being motivated to act to alleviate suffering) are shown in Supplemental Figures 2 and 3.

SOCS-S global score

The model's total explanatory power was substantial (conditional $R^2 = 0.90$), and the part related to the fixed effects alone (marginal R^2) was 0.14. A significant main effect of drug ($F(2, 56.04) = 7.53$, $p = 0.001$), a significant main effect of sensitivity ($F(1, 28.96) = 4.21$, $p = 0.05$), and a significant interaction of drug and sensitivity ($F(2, 56.04) = 4.58$, $p = 0.014$) were found.

Post hoc tests revealed that participants showed significantly higher levels of SOCS-S in DMT/HAR (*Mdiff* = 2.83, SE = 0.84, *df* = 56.1, *t*.ratio = 3.39, $p < 0.01$) as well as in HAR (*Mdiff* = 2.82, SE = 0.85, *df* = 56.1, *t*.ratio = 3.34, $p < 0.01$) compared to PLA. There was no significant difference in SOCS-S between the DMT + harmine and HAR ($p = 0.99$). Post hoc tests revealed

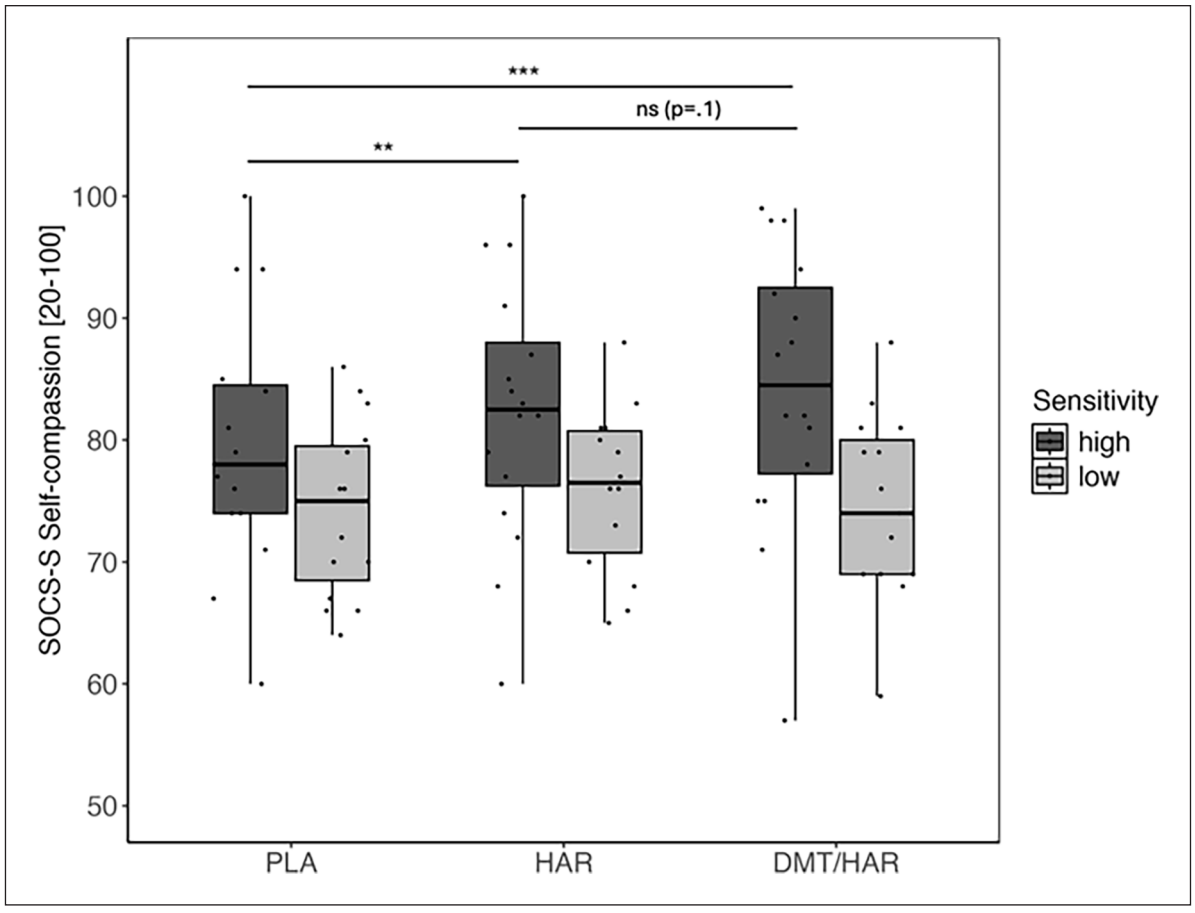

Figure 3. SOCS-S global scores by drug condition and grouped by sensitivity to the drug.
Note. Boxplots with subjective ratings on self-compassion (SOCS-S global score) by drug condition (DMT/HAR, HAR, PLA) and by sensitivity to the drug (high- vs low-sensitive group of participants separated by median split of the maximum subjective intensity rating) are shown. Minimum possible value: 20; maximum possible value: 100.
SOCS-S: Sussex Oxford compassion scale self; ns: not significant.
*$p < 0.1$. **$p < 0.05$. ***$p < 0.01$.

significantly higher SOCS-S in the high- versus the low-sensitivity group (*Mdiff* = 6.59, SE = 3.21, *df* = 29, *t*.ratio = 2.05, $p = 0.05$).

While the differences between the drug conditions were not different in the low-sensitivity group (DMT/HAR − HAR: $p = 0.18$; DMT/HAR − PLA: $p = 0.70$; HAR − PLA: $p = 0.16$), participants in the high-sensitivity group reported higher levels of SOCS-S in DMT/HAR compared to placebo (*Mdiff* = 5.19, SE = 1.18, *df* = 56.1, *t*.ratio = 4.42, $p < 0.001$), and in HAR compared to PLA (*Mdiff* = 3.26, SE = 1.18, *df* = 56.1, *t*.ratio = 2.77, $p = 0.01$), but no difference in SOCS-S between the DMT + HAR and HAR ($p = 0.10$). That is, the high-sensitivity group, but not the low-sensitivity group, showed significantly greater SOCS-S both in DMT/HAR and in HAR than in PLA.

SOCS-O global score

The model's total explanatory power was substantial (conditional $R^2 = 0.88$), and the part related to the fixed effects alone (marginal R^2) was 0.13. A significant main effect of drug ($F(2, 56.14) = 3.37$, $p = 0.042$) and a significant main effect of sensitivity ($F(1, 29.05) = 4.42$, $p = 0.04$) were found. The interaction effect of drug and sensitivity was statistically not significant ($F(2, 56.14) = 1.66$, $p = 0.20$).

Post hoc tests revealed that participants showed significantly higher levels of SOCS-O in DMT/HAR compared to PLA (*Mdiff* = 2.28, SE = 0.88, *df* = 56.1, *t*.ratio = 2.59, $p = 0.04$), and compared to HAR (*Mdiff* = 1.03, SE = 0.88, *df* = 56.1, *t*.ratio = 1.17, $p = 0.25$), but not in HAR compared to PLA (*Mdiff* = 1.25, SE = 0.88, *df* = 56.1, *t*.ratio = 1.41, $p = 0.25$). Post hoc tests revealed significantly higher SOCS-O in the high- versus the low-sensitivity group (*Mdiff* = 6.56, SE = 3.12, *df* = 29, *t*.ratio = 2.10, $p = 0.04$).

While the differences between the drug conditions were not different in the low-sensitivity group (DMT/HAR − HAR: $p = 0.80$; DMT/HAR − PLA: $p = 0.73$; HAR − PLA: $p = 0.73$), participants in the high-sensitivity group reported higher levels of compassion with others in DMT/HAR compared to PLA (*Mdiff* = 3.69, SE = 1.24, *df* = 56.1, *t*.ratio = 2.98, $p = 0.01$), but no differences for the contrasts DMT/HAR − HAR ($p = 0.08$), nor for HAR − PLA ($p = 0.29$). That is, the high-sensitivity group, but not the low-sensitivity group, reported higher levels of compassion with others in DMT/HAR compared to PLA.

Discussion

This randomized, placebo-controlled, double-blinded study aimed to evaluate mindfulness- and compassion-related capabilities after

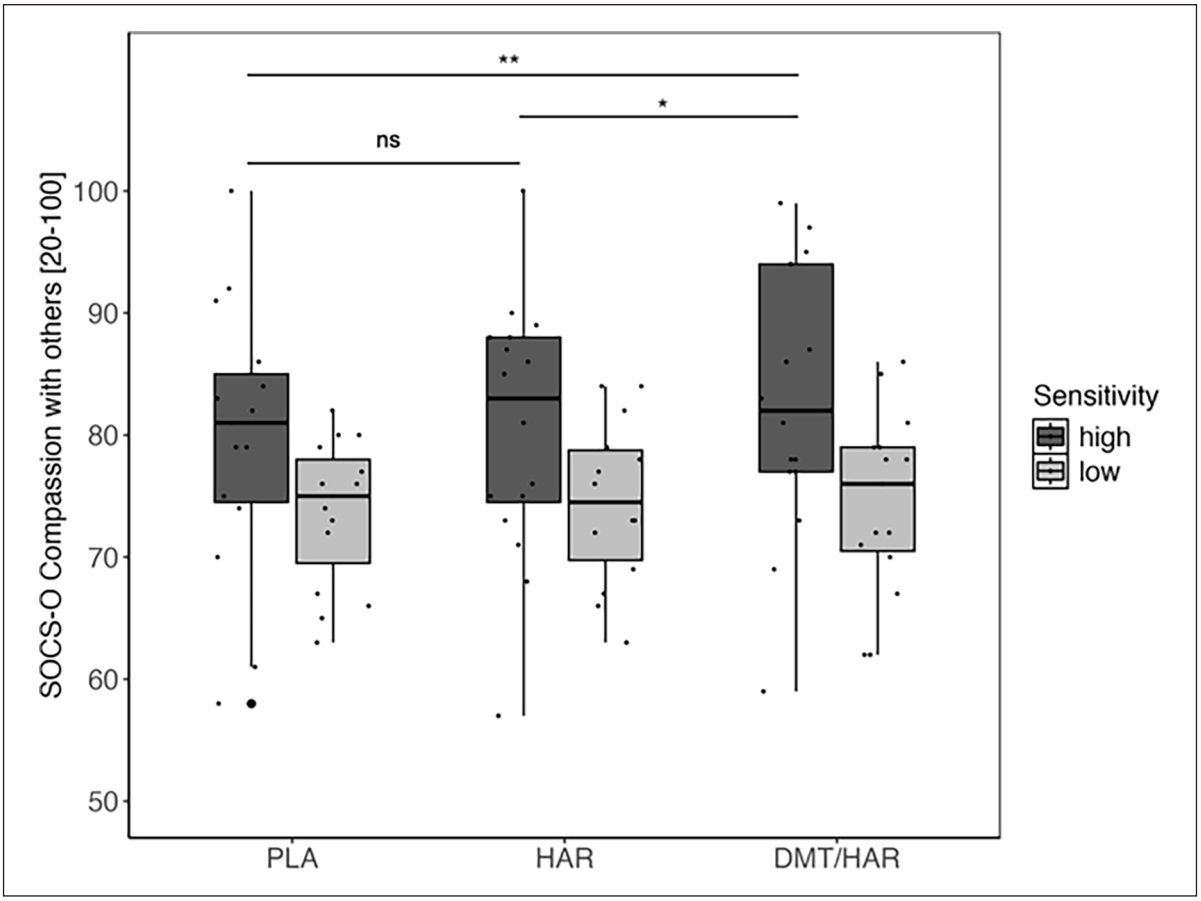

Figure 4. SOCS-O global scores by drug condition and grouped by sensitivity to the drug.
Note.Boxplots with subjective ratings on compassion with others (SOCS-O global score) by drug condition (DMT/HAR, HAR, PLA) and by sensitivity to the drug (high- vs low-sensitive group of participants separated by median split of the maximum subjective intensity rating) are shown. Minimum possible value: 20; maximum possible value: 100.
SOCS-O: Sussex Oxford compassion scale others; ns: not significant.
$^{*}p < 0.1$. $^{**}p < 0.05$. $^{***}p < 0.01$.

the intake of an innovative ayahuasca-inspired formulation (containing DMT and MAO-inhibitor harmine; DMT/HAR) and harmine (HAR) against placebo (PLA) in healthy subjects to explore potential therapeutic change mechanisms. Our findings indicate an acute increase in mindfulness- and compassion-based outcome measures, comparable to changes in meditation practitioners, since the MCI was originally developed to assess the effects of long-term meditation practice. Our study indicates that short-term enhancement in mindfulness abilities can be reached not only by meditation practice, but also by a pharmacological intervention with DMT/HAR in a controlled laboratory setting, even without concomitant mindfulness training. Following our initial hypothesis, we found a significant drug effect with specifically higher mindfulness and compassion scores in DMT/HAR and less pronounced effects in HAR, compared to PLA. Significant effects for HAR could only be found for self-compassion. Participants from the high-sensitivity group were more likely to report differences in mindfulness, self-compassion, and compassion with others when DMT/HAR was compared to HAR or PLA, but not participants from the low-sensitivity group. No lasting effects in the 1-month and 4-month follow-up were found.

Regarding the specific mindfulness subscales, decentering and observing abilities were increased in the high-sensitivity group, and a highly significant drug effect was found for non-reacting. Non-reacting describes a state of mind in which one allows thoughts and feelings to come and go without getting caught up in them, which, in turn, is therapeutically valuable (Baer et al., 2006; Thomas et al., 2013). Decentering on the other hand is defined as the capacity to step outside one's personal perspective of a lived experience and to disidentify from the content of thoughts (Fresco et al., 2007) or in other more specific words it is the capacity to recognize one's thoughts and emotions as temporary events of the mind (Soler et al., 2014). This allows patients to consider thoughts and emotions in a detached manner rather than statements that are necessarily true (Fresco et al., 2007). Hence, increased decentering abilities could explain the therapeutic effect of interventions with psychedelics like ayahuasca in depression (de Osório et al., 2015; Domínguez-Clavé et al., 2016; Sampedro et al., 2017; Sanches et al., 2016; Soler et al., 2016), a disorder that is associated with impaired decentering abilities, in other work also called reduced metacognitive awareness (Teasdale et al., 2002).

Regarding the SOCS-O (compassion with others) subscales, recognizing suffering and feeling for the person suffering were also significantly increased in the high-sensitivity group. In the SOCS-S (self-compassion) subscales, only the recognizing suffering subscale was significantly increased in the high-sensitivity group. Testing for drug effects, most of the subscales of SOCS-S (four out of five) were significantly increased, which indicates that DMT/HAR has a stronger effect on self-compassion compared to compassion with others and mindfulness. Interestingly, self-compassion increased in both the DMT/HAR and HAR conditions. This finding could be explained via the nonspecific serotonergic stimulation effects that are described for the MAO-A inhibitor harmine (Herraiz et al., 2010). Moderately elevated levels of serotonin in the synaptic cleft may reduce anxiety/stress and promote general feelings of empathy and tenderness toward oneself. Comparable findings of adaptive self-attitudes such as increased emotional empathy and self-compassion were observed after ingestion of nonspecific serotonergic substances such as MDMA (Kamboj et al., 2018). Cultivating self-compassion brings understanding toward oneself in instances of perceived inadequacy or suffering (Neff, 2003) and is an important mediator of the positive effects of MBCT interventions on depressive symptoms (Kuyken et al., 2010). Therefore, augmenting CFT with pharmacological interventions that enhance compassion and social connection could be especially suitable for people who have a compromised capacity for experiencing and expressing affiliative motives and emotions, that is, those with high levels of self-criticism and shame (Pots and Chakhssi, 2022). Ayahuasca-inspired formulations might be particularly well suited to support attitudes of openness and acceptance toward physical and mental discomfort by enhancing compassion for self and others, which is a valuable skill set for navigating physical and mental crises and coping with stress in everyday life.

It is possible that the sensitivity to the substance and experiential aspects depends on certain predispositions, such as personality traits. For instance, the trait of absorption, which refers to an individual's openness to a variety of cognitive, perceptual, and imagistic experiences, was found to strongly predict several experiences measured in previous studies (Studerus et al., 2012). Interestingly, trait absorption was not only associated with the ability to reach peak experiences but also found to be elevated in meditation practitioners (Garcia-Campayo et al., 2022). Hence, further research examining personality traits and their influence on the ability to reach intense psychedelic experiences and their association with outcome measures, such as mindfulness, is essential.

Furthermore, depression or other psychiatric disorders (or also somatic diseases) may impact an individual's sensitivity to both mindfulness-based interventions and the pharmacological treatment with DMT/HAR. Depression and also anti-depressive medication might alter neurobiological mechanisms and increase or decrease sensitivity to the DMT/HAR. Further clinical trials with patients are necessary to explore effective doses for patients with mood disorders or other indications. Based on these doses, further studies should investigate whether patients experience effects on mindfulness, compassion, or other therapy-relevant mechanisms induced by DMT/HAR.

In summary, our results provide an explanatory mechanism that could contribute to similar benefits reported in prior studies for ayahuasca in the treatment of addiction and depression (de Osório et al., 2015; Thomas et al., 2013). It is worth mentioning that prior studies showing benefits associated with long-term ayahuasca use could be confounded by participants being members of a religious group or taking ayahuasca in a ceremonial context (Bouso et al., 2012; Fábregas et al., 2010). The present results obtained in a non-ceremonial, controlled laboratory setting, where participants engaged in neurobehavioral tasks, support the notion that ayahuasca-inspired pharmacological formulations, such as those containing DMT and harmine, may transiently increase mindfulness- and compassion-related capabilities independent of context. Despite these significant acute drug effects, we could not find any long-term effects, which may be due to the fact that the study was not embedded in a therapeutic or mindfulness-based setting. Psychedelic-induced states of enhanced mindfulness tend to be short-lived and strongly support the notion of concomitant training and integration to stabilize and maintain more adaptive mental states in everyday life (Scheidegger, 2021a).

Limitations and future research

Our study has some limitations that need to be considered. First, the participant sample was quite homogeneous with regard to gender (male only), age (25 ± 4), educational status (highly educated), and ethnicity, which limits generalization of the findings. There is limited transferability to therapeutic contexts as the study was conducted in a laboratory setting with healthy participants. This study shows a transient increase in mindfulness and compassion in a non-meditation context that was not focused on mindfulness and compassion. It remains an open question for future research to investigate the magnitude and duration of DMT/HAR-induced mindfulness and compassion in a meditation context with meditation practitioners of various expertise levels (which we did in a follow-up study, see Meling et al., 2024). Moreover, the chosen dose range for DMT and harmine was moderate, as participants were expected to repeatedly participate in neurobehavioral tasks during the dosing session, which may have confounded and diminished the overall effects on mindfulness and compassion due to a high level of distraction. Further dose–response studies with higher dose ranges in appropriate settings would be informative to evaluate the therapeutic properties of ayahuasca-inspired formulations. Furthermore, the intensity of the subjective effects of the study drug might, in many cases, lead to an unblinding, at least in the high-sensitivity group, which can be considered another limitation of this work, as it may enhance expectation, respectively, placebo effects. This is a common issue in psychedelic research in general (Muthukumaraswamy et al., 2021). Blinding efficacy was not assessed in this study, which is a limitation.

To conclude, this study shows further evidence supporting that ayahuasca-inspired formulations like DMT/HAR may have the potential to induce acute increases in mindfulness and compassion. The adaptive effects of ayahuasca on psychological functioning are particularly aligned with mindfulness-based approaches that aim to increase compassion, awareness, and psychological flexibility in the service of achieving core life values. Ayahuasca-assisted therapy might work as a catalyst to support such transformative learning processes in the framework of a process-oriented psychotherapy (Mithoefer et al., 2021; Scheidegger, 2018, 2021b; Wheeler and Dyer, 2020). Further research in psychiatric populations is needed to corroborate the prevailing results.

Acknowledgements

We thank Dila Suay, Luzia Caflisch, Alexandra Hempe, and Camilla Steinhart for their help with the study conduction; Claudius Elsner and Jovin Mueller for their medical supervision of the participants during the study days. We thank Hanspeter Landolt for providing the research facility and infrastructure. And we thank our study participants.

Author contributions

HDA: conception and design of the study, study management, data acquisition, data analysis, interpretation of results, drafting the article, revision of the article, and final approval of the version to be submitted. IAW: data acquisition, interpretation of results, drafting the article, revision of the article, and final approval of the version to be submitted. DM: data acquisition, interpretation of results, revision of the article, and final approval of the version to be submitted. MJM: study management, data acquisition, revision of the article, and final approval of the version to be submitted. DAD: conception and design of the study, study management, data acquisition, revision of the article, and final approval of the version to be submitted. MS: conception and design of the study, interpretation of results, revision of the article, and final approval of the version to be submitted.

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: HDA, IAW, MJM, and DM declare that they have no conflict of interest. DAD and MS declare that they co-founded Reconnect Labs, an academic spin-off at the University of Zurich, focused on the development of psychedelic medicines for mental health.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: We gratefully acknowledge grant funding that supported this publication from the SNSF Swiss National Science Foundation (HD Aicher, Grant P0ZHP1_191935; M Scheidegger and D Meling, Spark CRSK-1_196833), from the Bioentrepreneur Fellowship UZH (DA Dornbierer, BIOEF-18-009), from the Forschungskredit PostDoc UZH (M Scheidegger, Grant No. FK-18-052), from the BIAL Foundation (M Scheidegger and D Meling, No. 333/20), from the Reconnect Foundation (D Meling), and from private donations (MJ Mueller). The content is solely the responsibility of the authors and does not necessarily represent the official views of the funders.

Research ethics and patient consent

The study was conducted according to the World Medical Association Declaration of Helsinki. The study was approved by the Cantonal Ethics Committee of the Canton of Zurich (Basec-Nr. 2018-01385) and the Swiss Federal Office of Public Health (BAG-Nr (AB)-8/5-BetmG-2019/009268).

Clinical trial registration

Neurodynamics of Prosocial Emotional Processing Following Serotonergic Stimulation With N,N-Dimethyltryptamine (DMT) and Harmine in Healthy Subjects. https://clinicaltrials.gov/ct2/show/NCT04716335

ORCID iDs

Helena D Aicher https://orcid.org/0000-0001-5915-7086

Ilhui A Wicki https://orcid.org/0000-0002-5511-7981

Daniel Meling https://orcid.org/0000-0001-9118-5431

Data availability statement

The datasets presented in this article are available on OSF (https://osf.io/zrqh9/).

Supplemental material

Supplemental material for this article is available online.

References

Ables JL, Israel L, Wood O, et al. (2024) A Phase 1 single ascending dose study of pure oral harmine in healthy volunteers. *J Psychopharmacol* 38: 911–923.

Aicher HD, Mueller MJ, Dornbierer DA, et al. (2024) Potential therapeutic effects of an ayahuasca-inspired N,N-DMT and harmine formulation: A controlled trial in healthy subjects. *Front Psychiatry* 14: 1302559.

Andersen KAA, Carhart-Harris R, Nutt DJ, et al. (2021) Therapeutic effects of classic serotonergic psychedelics: A systematic review of modern-era clinical studies. *Acta Psychiatr Scand* 143:101–118.

Baer RA, Smith GT, Hopkins J, et al. (2006) Using self-report assessment methods to explore facets of mindfulness. *Assessment* 13: 27–45.

Barker SA (2022) Administration of N,N-dimethyltryptamine (DMT) in psychedelic therapeutics and research and the study of endogenous DMT. *Psychopharmacology* 239: 1749–1763.

Barker SA, McIlhenny EH and Strassman R (2012) A critical review of reports of endogenous psychedelic N, N-dimethyltryptamines in humans: 1955–2010. *Drug Test Anal* 4: 617–635.

Bates D, Mächler M, Bolker BM, et al. (2015) Fitting linear mixed-effects models using lme4. *J Statist Softw* 67: 1–48.

Bouso JC, González D, Fondevila S, et al. (2012) Personality, psychopathology, life attitudes and neuropsychological performance among ritual users of ayahuasca: A longitudinal study. *PLoS One* 7: e42421.

Brown KW and Ryan RM (2003) The benefits of being present: Mindfulness and its role in psychological well-being. *J Personal Soc Psychol* 84: 822–848.

Carhart-Harris R, Giribaldi B, Watts R, et al. (2021) Trial of psilocybin versus escitalopram for depression. *N Engl J Med* 384: 1402–1411.

Carhart-Harris RL, Bolstridge M, Rucker J, et al. (2016) Psilocybin with psychological support for treatment-resistant depression: An open-label feasibility study. *Lancet Psychiatry* 3: 619–627.

Clark M (2019) Soma and Haoma: Ayahuasca analogues from the late bronze age. *J Psyched Stud* 3: 104–116.

Coffey KA, Hartman M and Fredrickson BL (2010) Deconstructing mindfulness and constructing mental health: Understanding mindfulness and its mechanisms of action. *Mindfulness* 1: 235–253.

de Osório FL, Sanches RF, Macedo LR, et al. (2015) Antidepressant effects of a single dose of ayahuasca in patients with recurrent depression: A preliminary report. *Braz J Psychiatry* 37: 13–20.

Dean JG, Liu T, Huff S, et al. (2019). Biosynthesis and extracellular concentrations of N,N-dimethyltryptamine (DMT) in mammalian brain. *Scient Rep* 9: 9333.

Domínguez-Clavé E, Soler J, Elices M, et al. (2016) Ayahuasca: Pharmacology, neuroscience and therapeutic potential. *Brain Res Bullet* 126: 89–101.

Dornbierer DA, Marten L, Mueller J, et al. (2023) Overcoming the clinical challenges of traditional ayahuasca: A first-in-human trial exploring novel routes of administration of N,N-Dimethyltryptamine and harmine. *Front Pharmacol* 14: 1246892.

Fábregas JM, González D, Fondevila S, et al. (2010) Assessment of addiction severity among ritual users of ayahuasca. *Drug Alcohol Depend* 111: 257–261.

Flattery DS and Schwartz M (1989) *Haoma and Harmaline: The Botanical Identity of the Indo-Iranian Sacred Hallucinogen "Soma" and Its Legacy in Religion, Language, and Middle Eastern Folklore*. Oakland, CA: University of California Press.

Franzen F and Gross H (1965). Tryptamine, N,N-Dimethyltryptamine, N,N-Dimethyl-5-hydroxytryptamine and 5-methoxytryptamine in human blood and urine. *Nature* 206: 1052.

Frecska E, Bokor P and Winkelman M (2016) The therapeutic potentials of ayahuasca: Possible effects against various diseases of civilization. *Front Pharmacol* 7: 35.

Fresco DM, Moore MT, van Dulmen MHM, et al. (2007) Initial psychometric properties of the experiences questionnaire: Validation of a self-report measure of decentering. *Behav Ther* 38: 234–246.

Garcia-Campayo J, Hijar-Aguinaga R, Barceló-Soler A, et al. (2022) Examining the relation between practicing meditation and having peak experiences and lucid dreams. A cross-sectional study. *Front Psychol* 13: 858745.

Gasser P, Kirchner K and Passie T (2015) LSD-assisted psychotherapy for anxiety associated with a life-threatening disease: A qualitative study of acute and sustained subjective effects. *J Psychopharmacol* 29: 57–68.

Gilbert P (2014) The origins and nature of compassion focused therapy. *Br J Clin Psychol* 53: 6–41.

Glennon RA (1981) Serotonin receptor interactions of harmaline and several related beta-carbolines. *Life Sci* 29: 861–865.

Goldberg SB, Riordan KM, Sun S, et al. (2022) The empirical status of mindfulness-based interventions: A systematic review of 44 meta-analyses of randomized controlled trials. *Perspect Psychol Sci* 17: 108–130.

Goyal M, Singh S, Sibinga E, et al. (2014) Meditation programs for psychological stress and well-being: A systematic review and meta-analysis. *Deutsche Zeitschrift Für Akupunktur* 57: 26–27.

Grossman P (2008) On measuring mindfulness in psychosomatic and psychological research. *J Psychosom Res* 64: 405–408.

Grossman P (2011) Defining mindfulness by how poorly I think I pay attention during everyday awareness and other intractable problems for psychology's (re)invention of mindfulness: Comment on Brown et al. (2011). *Psychol Assess* 23: 1034–1040.

Gu J, Baer R, Cavanagh K, et al. (2020) Development and psychometric properties of the Sussex-Oxford Compassion Scales (SOCS). *Assessment* 27: 3–20.

Gukasyan N, Davis AK, Barrett FS, et al. (2022) Efficacy and safety of psilocybin-assisted treatment for major depressive disorder: Prospective 12-month follow-up. *J Psychopharmacol* 36: 151.

Herraiz T, González D, Ancín-Azpilicueta C, et al. (2010) β-Carboline alkaloids in Peganum harmala and inhibition of human monoamine oxidase (MAO). *Food Chem Toxicol* 48: 839–845.

Jungaberle H, Thal S, Zeuch A, et al. (2018) Positive psychology in the investigation of psychedelics and entactogens: A critical review. *Neuropharmacology* 142: 179–199.

Kamboj SK, Walldén YSE, Falconer CJ, et al. (2018) Additive effects of 3,4-Methylenedioxymethamphetamine (MDMA) and compassionate imagery on self-compassion in recreational users of ecstasy. *Mindfulness* 9: 1134–1145.

Kärkkäinen J, Forsström T, Tornaeus J, et al. (2005) Potentially hallucinogenic 5-hydroxytryptamine receptor ligands bufotenine and dimethyltryptamine in blood and tissues. *Scand J Clin Lab Investig* 65: 189–199.

Khoury B, Lecomte T, Fortin G, et al. (2013) Mindfulness-based therapy: A comprehensive meta-analysis. *Clin Psychol Rev* 33: 763–771.

Kirby JN, Tellegen CL and Steindl SR (2017) A meta-analysis of compassion-based interventions: Current state of knowledge and future directions. *Behav Ther* 48: 778–792.

Ko K, Kopra EI, Cleare AJ, et al. (2023) Psychedelic therapy for depressive symptoms: A systematic review and meta-analysis. *J Affect Disord* 322: 194–204.

Kuyken W, Watkins E, Holden E, et al. (2010) How does mindfulness-based cognitive therapy work? *Behav Res Ther* 48: 1105–1112.

Lenth RV, Buerkner P, Herve M, et al. (2021) *emmeans: Estimated Marginal Means, aka Least-Squares Means* [Computer software]. Available at: https://rvlenth.github.io/emmeans/

López-Muñoz F, Álamo C, Juckel G, et al. (2007) Half a century of antidepressant drugs: On the clinical introduction of monoamine oxidase inhibitors, tricyclics, and tetracyclics. Part I: Monoamine oxidase inhibitors. *J Clin Psychopharmacol* 27: 555–559.

Luoma JB, Chwyl C, Bathje GJ, et al. (2020) A meta-analysis of placebo-controlled trials of psychedelic-assisted therapy. *J Psychoact Drugs* 52: 289–299.

Meling D, Egger K, Aicher HD, et al. (2024) Meditating on psychedelics. A randomized placebo-controlled study of DMT and harmine in a mindfulness retreat. *J Psychopharmacol* 38: 897–910.

Millard LA, Wan MW, Smith DM, et al. (2023) The effectiveness of compassion focused therapy with clinical populations: A systematic review and meta-analysis. *J Affect Disord* 326: 168–192.

Mithoefer MCMCM, Wagner MTMT, Mithoefer ATAT, et al. (2021) Psychedelic-assisted psychotherapy: A paradigm shift in psychiatric research and development. *Psychopharmacology* 9: 1–13.

Mueller MJ, Aicher HD, Dornbierer DA, et al. (2025) Pharmacokinetics and pharmacodynamics of an innovative DMT/harmine formulation in healthy participants: A randomized controlled trial. *Int J Neuropsychopharmacol* 28: pyaf001.

Muthukumaraswamy S, Forsyth A and Lumley T (2021) Blinding and expectancy confounds in psychedelic randomized controlled trials [Preprint]. *PsyArXiv*. https://doi.org/10.31234/osf.io/q2hzm

Neff K (2003) Self-compassion: An alternative conceptualization of a healthy attitude toward oneself. *Self Ident* 2: 85–101.

Palhano-Fontes F, Barreto D, Onias H, et al. (2019) Rapid antidepressant effects of the psychedelic ayahuasca in treatment-resistant depression: A randomized placebo-controlled trial. *Psychol Med* 49: 655–663.

Pots W and Chakhssi F (2022) Psilocybin-assisted compassion focused therapy for depression. *Front Psychol* 13: 812930.

Reangsing C, Rittiwong T and Schneider JK (2021) Effects of mindfulness meditation interventions on depression in older adults: A meta-analysis. *Aging Mental Health* 25: 1181–1190.

Reiff CM, Richman EE, Nemeroff CB, et al. (2020) Psychedelics and psychedelic-assisted psychotherapy. *Am J Psychiatry* 177: 391–410.

Riba J, Rodriguez-Fornells A, Urbano G, et al. (2001) Subjective effects and tolerability of the South American psychoactive beverage Ayahuasca in healthy volunteers. *Psychopharmacology* 154: 85–95.

Romeo B, Hermand M, Pétillion A, et al. (2021) Clinical and biological predictors of psychedelic response in the treatment of psychiatric and addictive disorders: A systematic review. *J Psychiatr Res* 137: 273–282.

RStudio Team (2019) *RStudio: Integrated Development for R*. Boston, MA: RStudio, Inc. http://www.rstudio.com/

Sampedro F, Revenga MDLF, Valle M, et al. (2017) Assessing the psychedelic "after-glow" in ayahuasca users: Post-acute neurometabolic and functional connectivity changes are associated with enhanced mindfulness capacities. *Int J Neuropsychopharmacol* 20: 698–711.

Sanches RF, de Lima Osório F, dos Santos RG, et al. (2016) Antidepressant effects of a single dose of ayahuasca in patients with recurrent depression: A SPECT study. *J Clin Psychopharmacol* 36: 77–81.

Sarris J, Perkins D, Cribb L, et al. (2021) Ayahuasca use and reported effects on depression and anxiety symptoms: An international cross-sectional study of 11,912 consumers. *J Affect Disord Rep* 4: 100098.

Scheidegger M (2021a) Comparative phenomenology and neurobiology of meditative and psychedelic states of consciousness: Implications for psychedelic-assisted therapy. In: Grob C and Grigsby J (eds.) *Handbook of Medical Hallucinogens*. New York, NY: Guilford Press, pp. 395–413.

Scheidegger M (2021b) Psychedelic medicines: A paradigm shift from pharmacological substitution towards transformation-based psychiatry. In Labate B and Cavnar C (eds.) *Ayahuasca Healing and Science*. Cham: Springer.

Schenberg EE (2018) Psychedelic-assisted psychotherapy: A paradigm shift in psychiatric research and development. *Front Pharmacol* 9: 1–11.

Soler J, Cebolla A, Feliu-Soler A, et al. (2014) Relationship between meditative practice and self-reported mindfulness: The MINDSENS composite index. *PLoS ONE* 9: e86622.

Soler J, Elices M, Franquesa A, et al. (2016) Exploring the therapeutic potential of Ayahuasca: Acute intake increases mindfulness-related capacities. *Psychopharmacology* 233: 823–829.

Studerus E, Gamma A, Kometer M, et al. (2012) Prediction of psilocybin response in healthy volunteers. *PLoS One* 7: e30800.

Teasdale JD, Moore RG, Hayhurst H, et al. (2002) Metacognitive awareness and prevention of relapse in depression: Empirical evidence. *J Consult Clin Psychol* 70: 275–287.

Thomas G, Lucas P, Capler N, et al. (2013) Ayahuasca-assisted therapy for addiction: Results from a preliminary observational study in Canada. *Curr Drug Abuse Rev* 6: 30–42.

Tullis P (2021) How ecstasy and psilocybin are shaking up psychiatry. *Nature* 589: 506–509.

Uthaug MV, Mason NL, Toennes SW, et al. (2021) A placebo-controlled study of the effects of ayahuasca, set and setting on mental health of participants in ayahuasca group retreats. *Psychopharmacology* 238: 1899–1910.

Van Dam NT, van Vugt MK, Vago DR, et al. (2018) Mind the hype: A critical evaluation and prescriptive agenda for research on mindfulness and meditation. *Perspect Psychol Sci* 13: 36–61.

van Oorsouw K, Toennes SW and Ramaekers JG (2022) Therapeutic effect of an ayahuasca analogue in clinically depressed patients: A longitudinal observational study. *Psychopharmacology* 239: 1839–1852.

von Rotz R, Schindowski EM, Jungwirth J, et al. (2023) Single-dose psilocybin-assisted therapy in major depressive disorder: A placebo-controlled, double-blind, randomized clinical trial. *eClinicalMedicine* 56: 101809.

Wakelin KE, Perman G and Simonds LM (2022) Effectiveness of self-compassion-related interventions for reducing self-criticism: A systematic review and meta-analysis. *Clin Psychol Psychother* 29: 1–25.

Wheeler SW and Dyer NL (2020) A systematic review of psychedelic-assisted psychotherapy for mental health: An evaluation of the current wave of research and suggestions for the future. *Psychol Conscious Theory Res Pract* 7: 279–315.

Wilson AC, Mackintosh K, Power K, et al. (2019) Effectiveness of self-compassion related therapies: A systematic review and meta-analysis. *Mindfulness* 10: 979–995.

Youdim MBH, Edmondson D and Tipton KF (2006) The therapeutic potential of monoamine oxidase inhibitors. *Nat Rev Neurosci* 7: 295–309.

Zeifman RJ, Palhano-Fontes F, Hallak J, et al. (2019) The impact of ayahuasca on suicidality: Results from a randomized controlled trial. *Front Pharmacol* 10: 1325.