

Psilocybin-Induced Mystical Experience is Associated with Less Heavy Drinking in Patients with Alcohol Use Disorder

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METHODOLOGICAL ISSUE BEING ADDRESSED

Can the subjective psychedelic experience serve as a marker of treatment efficacy in psilocybin therapy for alcohol use disorder?

INTRODUCTION

Psilocybin shows promise for treating substance use disorders, but its mechanisms remain unclear. Previous pilot studies of psilocybin for alcohol¹ and tobacco dependence² have identified significant correlations between psilocybin-induced mystical experiences and reductions in substance use. However, these findings have not yet been evaluated in a controlled trial. Here, we present the results of a randomized clinical trial³ comparing psilocybin to an active control and explore whether the subjective psychedelic experience is associated with improvements in drinking behavior.

CONTROLLED TRIAL OVERVIEW

- **Trial Registration:** NCT02061293
- **Design:** Double-blind, randomized, parallel-group study
- **Participants:** 93 patients with alcohol use disorder
 - **Demographics:** Average age 46, 44% female, 79% white
 - **Baseline Drinking:** Average 53% heavy drinking days per month (≥ 5 drinks/day for men and 4 drinks/day for women)
 - **Psilocybin group:** Medium dose 25 mg per 70 kg of body weight (session 1); High dose 30 or 40 mg / 70 kg (session 2, based on session 1 response) (n = 48)
 - **Control group:** Diphenhydramine 50 mg (session 1); 50 or 100 mg (session 2, based on session 1 response) (n = 45)
- **Dosing:** Two sessions per participant, spaced 1 month apart
- **Therapy:** 12 sessions led by a two-person team; 4 sessions before each dose and 4 sessions after the second dose
- **Measures:** Subjective experience was assessed post-dosing using four scales: MEQ (analyzed as MEQ-43 and MEQ-30), M-Scale, ASC (analyzed as 5D-ASC and 11D-ASC), and HRS.
- **Outcome:** Alcohol use tracked for 8 months via timeline follow-back.

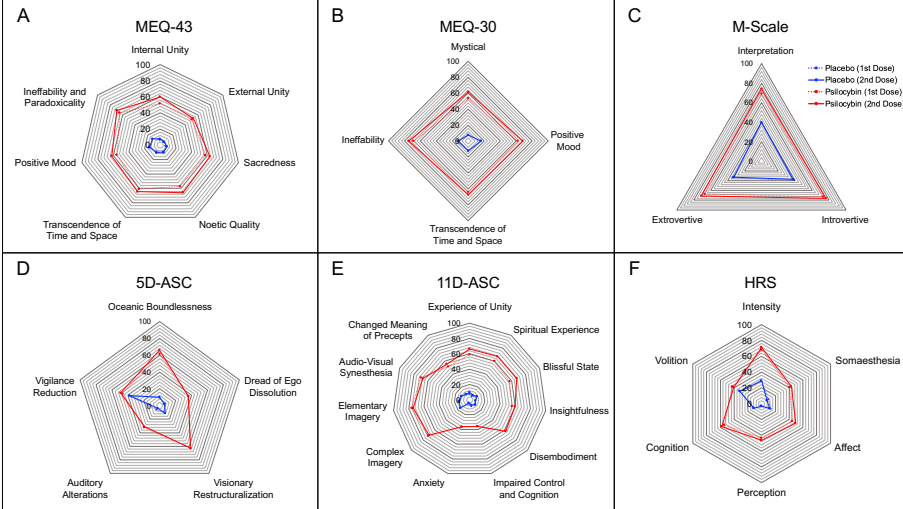
METHODS

- ❖ **Principal Components Analysis:** MEQ-30, M-Scale, 11D-ASC, and HRS were reduced to core components. MEQ-43 and 5D-ASC were excluded to minimize redundancy, as they share items with the MEQ-30 and 11D-ASC in their factor structure.
- ❖ **Key Analysis:** Simultaneous multiple linear regression examined associations between PCA components and post-treatment heavy drinking, controlling for baseline heavy drinking levels.

RESULTS 1

- All measures of subjective experience were significantly higher in the psilocybin group relative to active control (Figure 1).
- Percentage of heavy drinking days during follow-up was 9.7% for the psilocybin group and 23.6% for the control group, a mean difference of 13.9% (95% CI 3.0-24.7; $F_{1,86} = 6.43$; $P = .01$).

FIGURE 1: ACUTE SUBJECTIVE EFFECTS



RESULTS 2

- ❖ PCA identified 4 core psychedelic components (Table 1).

1. **Mystical Experience 1:** Unity, bliss, spirituality, changed precepts, altered perception of time/space, insightfulness
2. **Sensory Physical Change:** Complex imagery, synesthesia, somaesthesia, disembodiment
3. **Mystical Experience 2:** Ineffability, M-scale
4. **Challenging Experience:** Anxiety, impaired control and cognition

- ❖ In the psilocybin group, only **Mystical Experience 1** was significantly associated with less heavy drinking (Table 2).

- ❖ The subjective psychedelic experience and baseline heavy drinking together account for 26% of the variance in post-treatment heavy drinking.

CONCLUSIONS

- Therapeutic benefit is associated with a specific drug effect - mystical experience, and not the intensity or general drug effects.
- Mystical experience (characterized by unity, bliss, altered perception of time/space, changed precepts, and insight) may therefore serve as an efficacy signal in psychedelic drug development, especially if replicated in an independent sample.
- The 30-item MEQ may be the most time-efficient rating scale for capturing this efficacy signal, with minimal participant burden.

REFERENCES

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3. M. P. Bogenschutz et al., Percentage of Heavy Drinking Days Following Psilocybin-Assisted Psychotherapy vs Placebo in the Treatment of Adult Patients With Alcohol Use Disorder: A Randomized Clinical Trial. *JAMA Psychiatry* 79, 953-962 (2022).

TABLE 1: PRINCIPAL COMPONENTS

COMPONENT	1	2	3	4
EIGENVALUE	11.98	3.61	1.77	1.35
% VARIANCE EXPLAINED	49.92%	15.02%	7.36%	5.63%
LOADING INTERPRETATION	Mystical Experience 1	Sensory-Physical Change	Mystical Experience 2	Challenging Experience
MEQ-30				
Mystical	0.828	0.204	0.378	0.001
Positive Mood	0.825	0.292	0.235	-0.142
Time & Space	0.526	0.408	0.309	0.504
Ineffability	0.341	0.036	0.567	0.403
M-Scale				
Introvertive Mysticism	0.324	0.141	0.876	0.067
Extrovertive Mysticism	0.375	0.180	0.758	-0.134
Religious Interpretation	0.529	0.159	0.769	-0.155
11D-ASC				
Experience of Unity	0.811	0.326	0.315	0.071
Spiritual Experience	0.824	0.192	0.258	0.210
Blissful State	0.826	0.286	0.187	-0.171
Insightfulness	0.803	0.225	0.339	0.047
Disembodiment	0.443	0.709	-0.128	0.220
Impaired Control & Cognition	0.033	0.250	-0.088	0.876
Anxiety	0.036	0.226	-0.117	0.863
Complex Imagery	0.410	0.646	0.233	-0.018
Elementary Imagery	0.083	0.729	0.398	0.180
Audio-Visual Synesthesia	0.223	0.784	0.111	0.148
Changed Meaning of Precepts	0.517	0.279	0.131	0.490
HRS				
Intensity	0.137	0.538	0.528	0.245
Somaesthesia	0.276	0.709	-0.062	0.249
Affect	0.738	0.470	0.163	0.246
Perception	0.217	0.727	0.260	0.278
Cognition	0.448	0.659	0.156	0.421
Volition	-0.341	0.186	0.291	0.706

TABLE 2: MODEL SUMMARY

Model Summary	R ²	Adjusted R ²	SEE	F _(m)	p			
	0.26	0.18	20.66	3.00 (3,42)	0.02			
Predictor	B	SE	β	t	95% CI for B	F zero-order	r partial	r part
Mystical Experience 1	-7.11	3.10	-0.31	-2.29	0.03 [-13.37, -0.85]	-0.37	-0.33	-0.30
Sensory Physical Experience	2.10	3.03	0.09	0.69	0.49 [-4.00, 8.21]	0.11	0.11	0.09
Mystical Experience 2	-4.27	3.03	-0.19	-1.41	0.17 [-10.38, 1.84]	-0.21	-0.21	-0.19
Challenging Experience	-3.57	3.03	-0.16	-1.18	0.25 [-9.69, 2.54]	-0.13	-0.18	-0.16
Baseline Heavy Drinking	0.21	0.12	0.24	1.73	0.09 [-0.04, 0.45]	0.32	0.26	0.23

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