



PSYCHEDELICS IN THE TREATMENT OF SUBSTANCE USE DISORDERS

Presented by Dr. Ian King, BMSc, MD, FRCPC, DRCPS
(Addiction Medicine)

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Presenter Disclosures

Presenter: Dr. Ian King

Relationships with financial interests:

- Grants/Research Support: None
- Speakers Bureau/Honoraria: None
- Consulting Fees: None
- Patents: None
- Other: None

Please note that EHN Canada does not offer any form of psychedelic programming when treating substance use disorder. This webinar is solely an educational offering to further explore the research and evidence within this industry.

Presentation at a Glance

Objectives:

1. Define **psychedelics** and provide clarity surrounding related terms
2. Provide brief historical context of psychedelic use and research
3. Discuss potential therapeutic paradigms/rationale/utility in mental health and addiction disorders

“Psyche-delic”



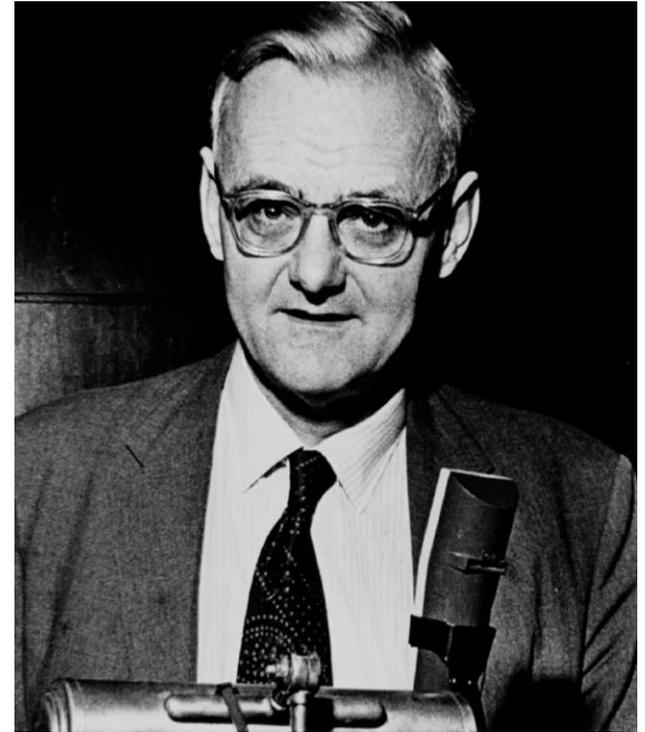
“mind/soul”



“manifesting”

“...the feature that distinguishes psychedelic agents from other classes of drugs is their capacity reliably to induce or compel states of altered perception, thought, and feeling that are not (or cannot be) experienced otherwise except in dreams or at times of religious exaltation”

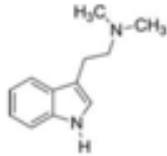
- Jaffe, 1985



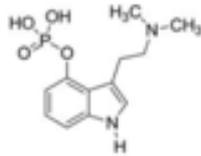
Humphry Osmond (1957)

Classic Psychedelics

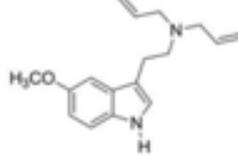
Agonism/Partial agonism at 5-HT_{2A} Receptor



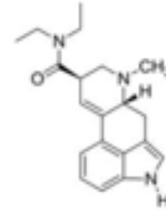
DMT



Psilocybin

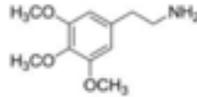


5-MeO-DALT

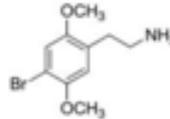


LSD

indolealkylamines



Mescaline



2C-B

phenylalkylamines



MDMA

Induction of endogenous NT release including DA and 5HT

Hallucinogens

Non-specific

- Term often includes several other substances with differing properties, mechanisms of action, risks/adverse effects
- Dissociatives/NMDA-R Antagonists: **Phencyclidine, Ketamine, Dextromethorphan**
Kappa Opioid Receptor Agonist: **Salvinorin A**
- CB1/CB2 Receptor Modulators: **Cannabinoids**

Reductive/Misnomers

- Characteristic effect of psychedelic substances is not reducible to the induction of hallucinations

Classic Psychedelics : 5-HT_{2A} Agonism

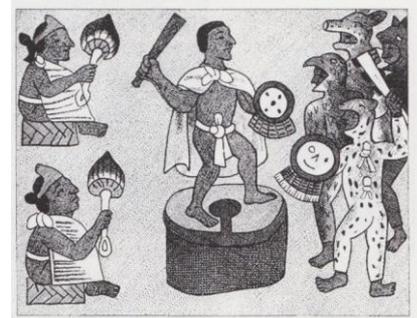
	Chemical Name	Common Name	Source	Typical Dosage	Duration of Action	Misc
	Psilocybin	Magic Mushrooms, "Shrooms"	>200 species of fungi; most commonly mushrooms from genus <i>Psilocybe</i>	10-40mg; 1-5g of dried mushroom	4-6 hours	Prodrug that is cleaved <i>in vivo</i> to produce active molecule, <u>psilocybin</u>
	N,N-Dimethyltryptamine	DMT, cohoba, yopo	<i>Psychotria viridis</i> shrub	5-75mg	6-20 minutes	Component of ayahuasca brew used in Amazonian Shamanic rituals
	Lysergic acid diethylamide	LSD, Acid	Semisynthetic; ergot derivative	50-200mcg	8-14 hours	Used on blots, gel-caps, liquid solution. First synthesized by Albert Hofmann in 1938
	3,4,5-Trimethoxyphenethylamine	Mescaline, Peyote	<i>Lophophora williamsii</i> , several species of <i>Trichocereus cacti</i>	200-500 mg sulfate salt; 10-20 g of dried peyote	8-12 hours	Evidence supports human use in Northwest Mexico/Texas as long as 8500 years ago

Adapted from: Miller, S. (2018). *The ASAM principles of addiction medicine*. Lippincott Williams & Wilkins

Historical Context

Evidence of human psychedelic use in religious/spiritual/healing/ritualistic practices for millennia

- *Soma* in Hindu Rig Veda (3500 years ago)
- *Kykeon* in Ancient Greek Eleusinian Mysteries initiation rites (5th century BC)
- Psilocybin “flesh of the gods” used in Aztec ceremonies
- DMT/Ayahuasca in healing traditions of people of Amazonian basin



Historical Context (continued)

LSD first synthesized by Albert Hofmann in 1938

- Psychoactive effects discovered when Hofmann accidentally ingested some of the substance himself

Psychedelics became an intense area of interest in 1950's and 1960's

- Initially posited that LSD could be used as a psychotomimetic to model psychotic illnesses
- Role of serotonin in the brain and biological basis of mental disorders
- Promising findings in treatment of cancer-related psychological distress and alcoholism



Historical Context (continued)

1960's: Widespread recreational use and association with anti-establishment movement

- Schedule I Substances under Controlled Substances Act (1970)
- Social/Political Factors
- Halt to psychedelic research for decades; did not re-emerge until the early-to-mid 1990's



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Challenges with Contemporary Psychopharmacological Treatments

- Multiple potential side effects
- Slow time to effect
- Most often require consistent, long-term adherence
- Loss of Efficacy
- Relapse with discontinuation/lack of lasting psychological change

Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial

Roland R Griffiths^{1,2}, Matthew W Johnson¹, Michael A Carducci³,
Annie Umbricht¹, William A Richards¹, Brian D Richards¹,
Mary P Cosimano¹ and Margaret A Klinedinst¹

- 51 cancer patients with life-threatening diagnoses and symptoms of depression and/or anxiety
- Randomized, double-blind, cross-over design; patients received sequenced low dose (placebo) and high dose (30mg/70kg) psilocybin treatments, 5 weeks apart, with follow-up assessment at 6 months.
- Treatments were administered in a soothing environment accompanied by trained staff to provide support throughout experience.
- Clinician-administered and self-administered measurements of mood, anxiety, attitudes taken throughout study and at 6 months follow-up.

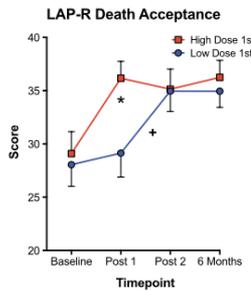
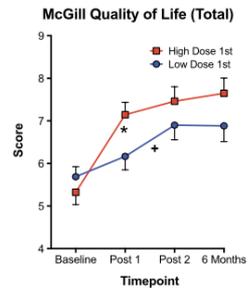
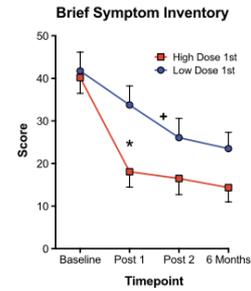
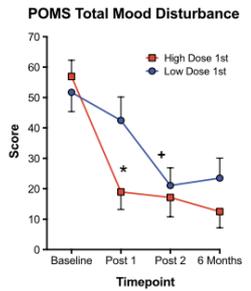
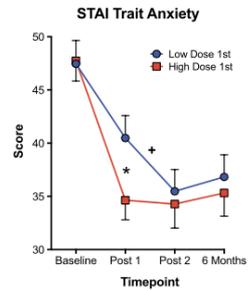
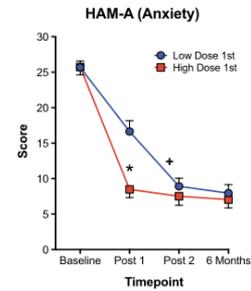
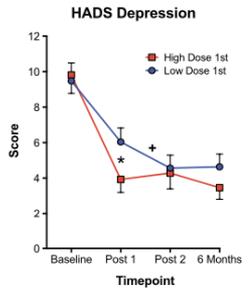
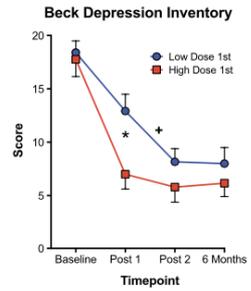
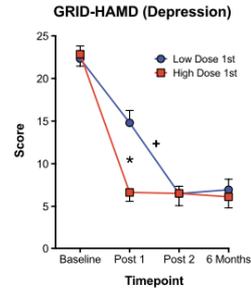


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2016, Vol. 30(12) 1181–1197
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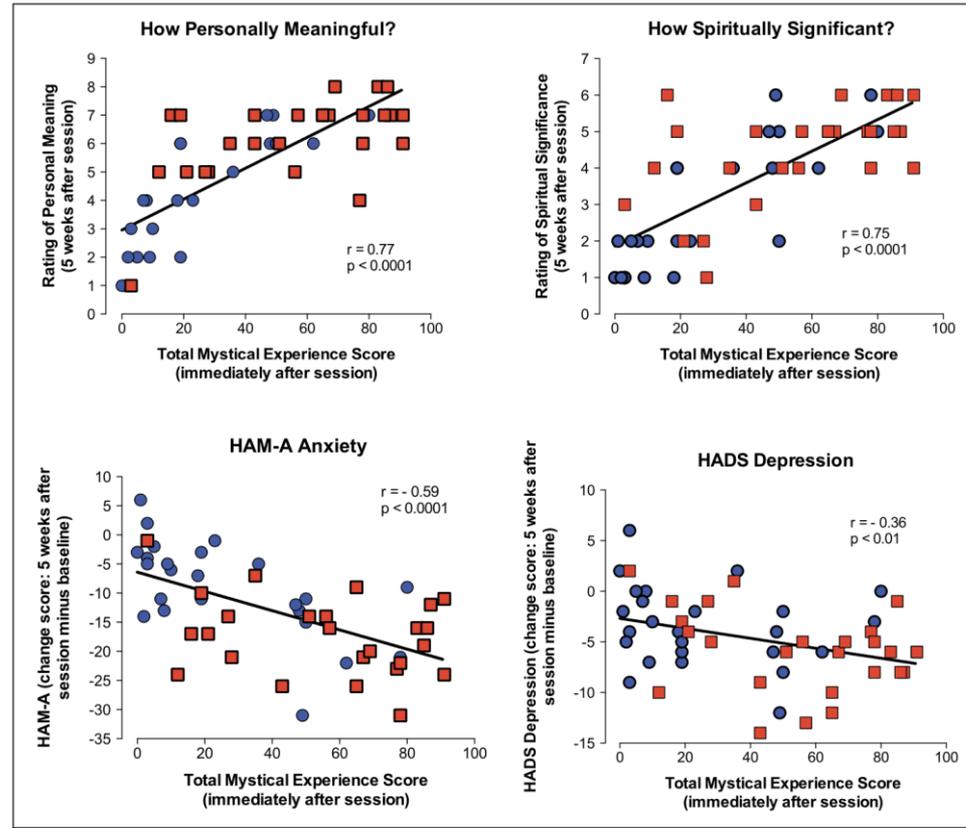


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Clinical response with regard to depression and anxiety measurements appeared to be mediated by **“mystical experience”** occasioned by psilocybin treatment



Psilocybin-assisted treatment for alcohol dependence: A proof-of-concept study

**Michael P Bogenschutz¹, Alyssa A Forcehimes¹, Jessica A Pommy¹,
Claire E Wilcox¹, PCR Barbosa² and Rick J Strassman¹**

Journal of Psychopharmacology
2015, Vol. 29(3) 289–299
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DOI: 10.1177/0269881114565144
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- Single group, open-label, proof-of-concept study
- Ten patients with alcohol dependence (DSM-IV) received orally-administered psilocybin on two occasions (at 4 weeks and 8 weeks) in addition to Motivational Enhancement Therapy
- Assessed multiple dimensions of alcohol use disorder (heavy drinking days, abstinence, craving etc.) up to 36 weeks

- Following first administration of psilocybin, significant decreases in **drinking days** and **heavy drinking days** relative to **baseline** and **MET only**
- Large correlations were observed between **intensity of acute effects of psilocybin** and changes in drinking behavior, craving and self-efficacy

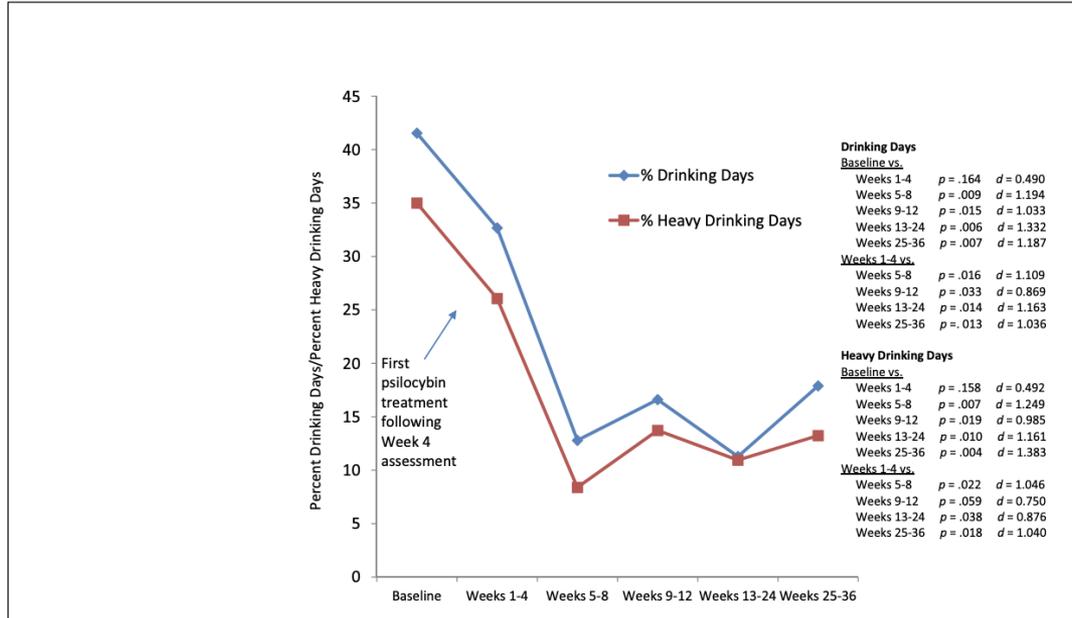
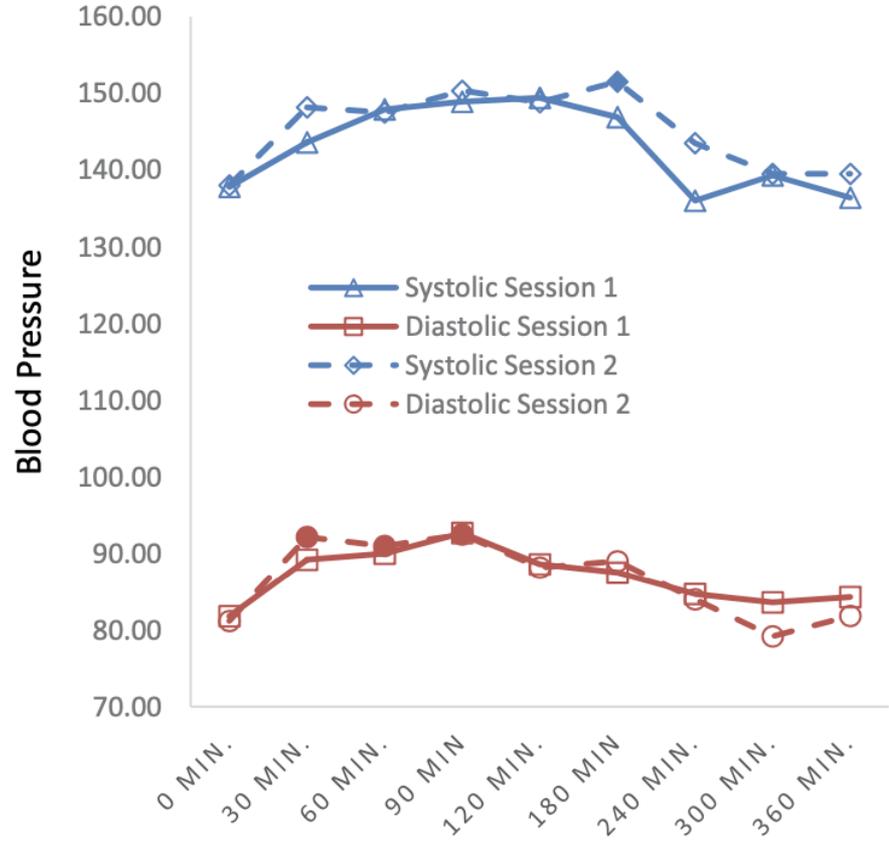


Figure 3. Drinking outcomes and effect sizes.

Means shown are for all available data ($n = 10$ at baseline, $n = 9$ at all other time points). p -values are from paired t -tests ($df = 8$). Cohen's d is shown for the contrast between baseline or weeks 1-4 and each follow-up time point.

- **Zero** participants required medication or intervention for adverse effects
- 5 participants reported mild headache which resolved within 24 hours
- Transient, mild increases in heart rate and blood pressure following psilocybin administration



Classic Psychedelic Studies in SUD Treatment.

Thomas et al., 2013	Hendricks et al., (2018b)	Savage & McCabe, 1973	Garcia-Romeu et al., 2014	Johnson et al., 2014; Johnson, Garcia-Romeu, & Griffiths, 2017	Bogenschutz et al., 2015	Krebs & Johansen, 2012	Study
Various	Cocaine	Heroin	Tobacco	Tobacco	Alcohol	Alcohol	Drug of Addiction
Ayahuasca	Psilocybin	LSD	Psilocybin	Psilocybin	Psilocybin	LSD	Classic Psychedelic
Observational study	Randomized controlled clinical trial [ongoing]	Randomized controlled clinical trial	Secondary analysis	Open-label	Open-label	Meta-analysis of randomized control trials	Method
12	10 (expected 40)	78	15	15	10	536	N=
Self-reported alcohol, tobacco, and cocaine use declined, but that of cannabis and opiates did not.	The psilocybin group reported significantly fewer days of cocaine use compared to those receiving diphenhydramine, significant through the 6 month follow up	At the 12-month follow up, 25% of LSD participants were abstinent, as compared to 5% of controls	Smoking cessation outcomes were correlated with mystical experience ratings.	12 out of 15 participants (80%) showed abstinence at 6-month follow up. Long-term follow up found 67% to be abstinent at 12 months and 60% at ≥16 months	Increased abstinence, with both drinking and heavy drinking days significantly reduced.	Significant larger decline in alcohol misuse for LSD patients (59% vs. 38%).	Outcomes

“While the mechanisms underlying the therapeutic efficacy of classic psychedelics are yet to be conclusively elucidated, several clinical studies have found a moderate to strong correlation between treatment outcomes and the level of *'mystical' experience a participant reports*”

-Yaden et al. 2021

Mystical Experience/Quantum Change

“sudden, distinctive, benevolent, and often profoundly meaningful experiences that are said to result in personal transformations that affect a broad range of personal emotions, cognitions, and behaviors “

- Baca and Miller, 2001

Four Factors in the Mystical Experience Questionnaire (MEQ30)

Factor 1: Mystical

Internal Unity

Experience of pure being and pure awareness (beyond the world of sense impressions).

External Unity

Experience of oneness or unity with objects and/or persons perceived in your surroundings.

Noetic Quality

Certainty of encounter with ultimate reality (in the sense of being able to “know” and “see” what is really real at some point during your experience.

Sacredness

Sense of being at a spiritual height.

Factor 2: Positive Mood

Experience of amazement.

Factor 3: Transcendence of Time and Space

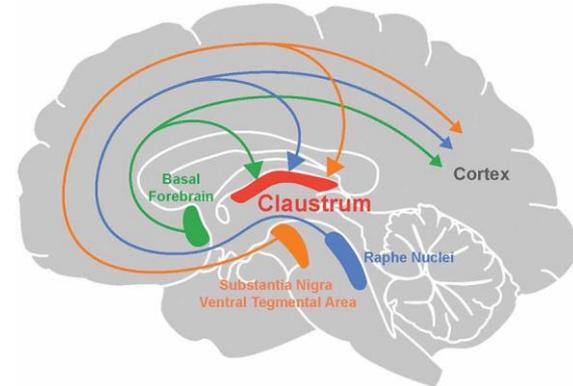
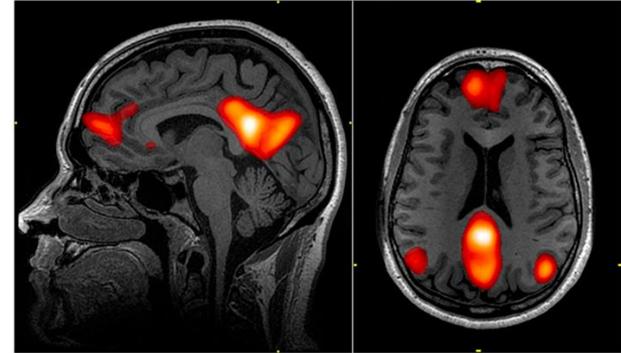
Loss of your usual sense of time or space.

Factor 4: Ineffability

Sense that the experience cannot be described adequately in words.

Mystical Experience/Quantum Change

- Claustrum = most dense expression of 5-HT_{2A} receptors in brain
- Desynchronization of Default Mode Network related areas
- Profound changes in functional connectivity correlated with “ego-dissolution” (Carhart-Harris et al. 2016)



Positive psychological effects persistent after 14 months in healthy volunteers

Griffiths, R. R., Richards, W. A., Johnson, M. W., McCann, U. D., & Jesse, R. (2008). Mystical-type experiences occasioned by psilocybin mediate the attribution of personal meaning and spiritual significance 14 months later. *Journal of psychopharmacology*, 22(6), 621-632

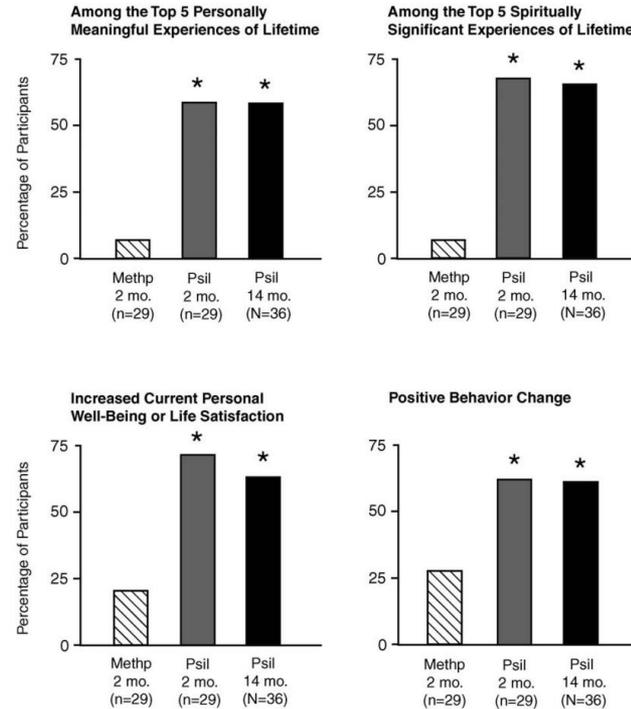


Figure 2 Percentage of volunteers endorsing specific answers on the Persisting Effects Questionnaire completed 2 months following the methylphenidate (Methp) and psilocybin (Psil) sessions ($n = 29$), and again retrospectively for psilocybin at the 14-month follow-up ($N = 36$). For ratings of personally meaningful and spiritually significant (top two panels), the data are the percentage rating 'among the top 5' or 'the single most'. For ratings of increased well-being or life satisfaction, the data were the percentage rating 'increased moderately' or 'increased very much'. For ratings of positive behavioural change, the data were the percentage rating 'moderate', 'strong' or 'extreme'. Asterisks show significant differences ($p < 0.05$, z-test of proportions, $n = 29$ at each assessment) from the methylphenidate 2-month assessment; there were no significant differences between the psilocybin 2-month condition and the psilocybin 14-month follow-up assessment. For the methylphenidate results, the data presented are from the first methylphenidate session for the five subjects who received methylphenidate on two sessions and who completed this questionnaire.

Adjunct to Twelve-Step Facilitation?

D.B. Yaden, A.P. Berghella, P.S. Regier et al.

International Journal of Drug Policy 98 (2021) 103380

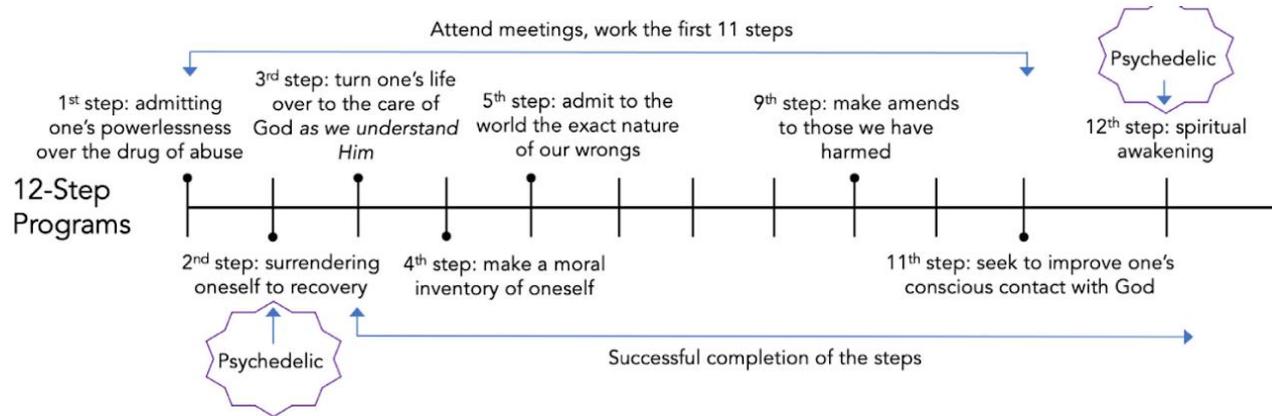
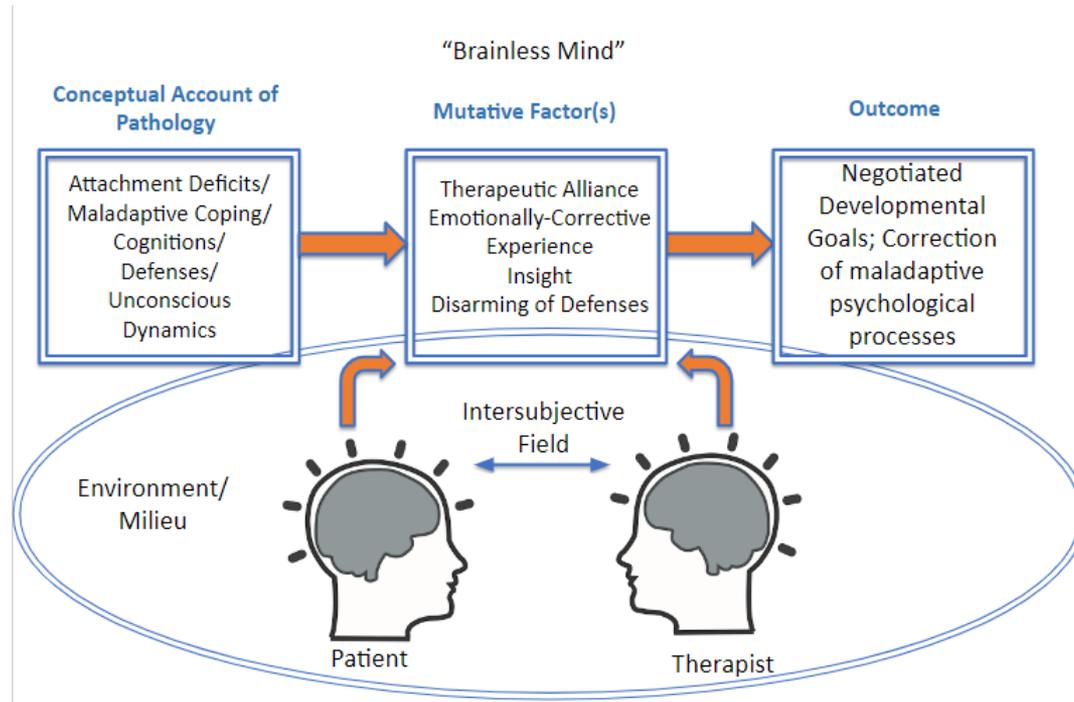


Figure 1. Incorporation of Classic Psychedelic Therapy into Twelve Step Facilitation.

Yaden, D. B., Berghella, A. P., Regier, P. S., Garcia-Romeu, A., Johnson, M. W., & Hendricks, P. S. (2021). Classic psychedelics in the treatment of substance use disorder: Potential synergies with twelve-step programs. *International Journal of Drug Policy*, 98, 103380.

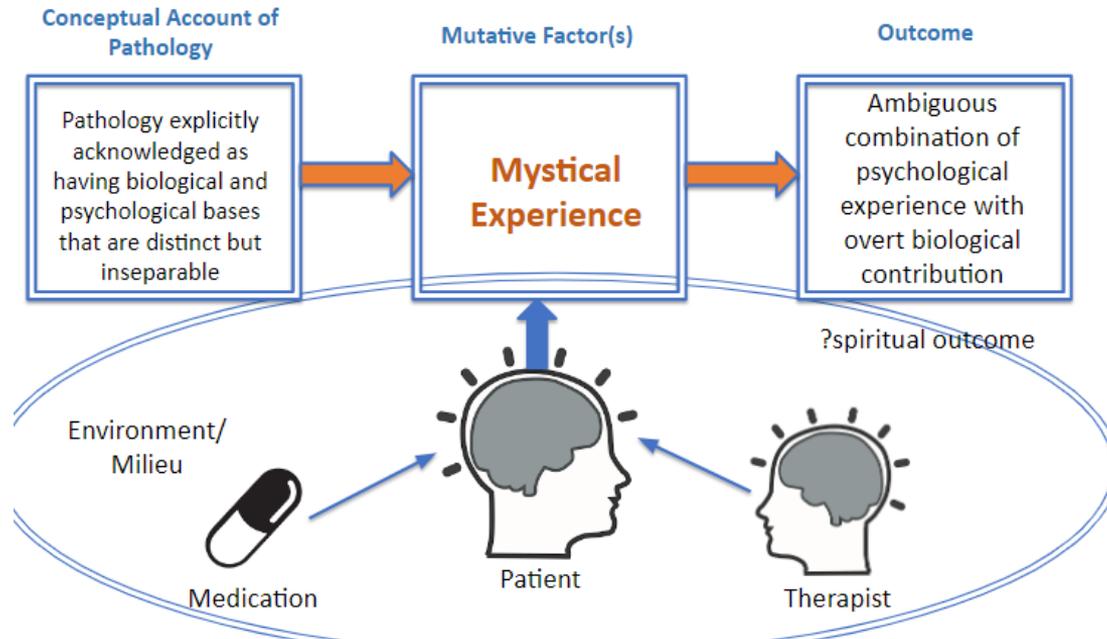
Psychedelic Therapy

An Interesting Departure from a Strictly Biomedical Model of Psychopharmacological Treatment Provision



Psychedelic Therapy

An Interesting Departure from a Strictly Biomedical Model of Psychopharmacological Treatment Provision



Low Toxicity

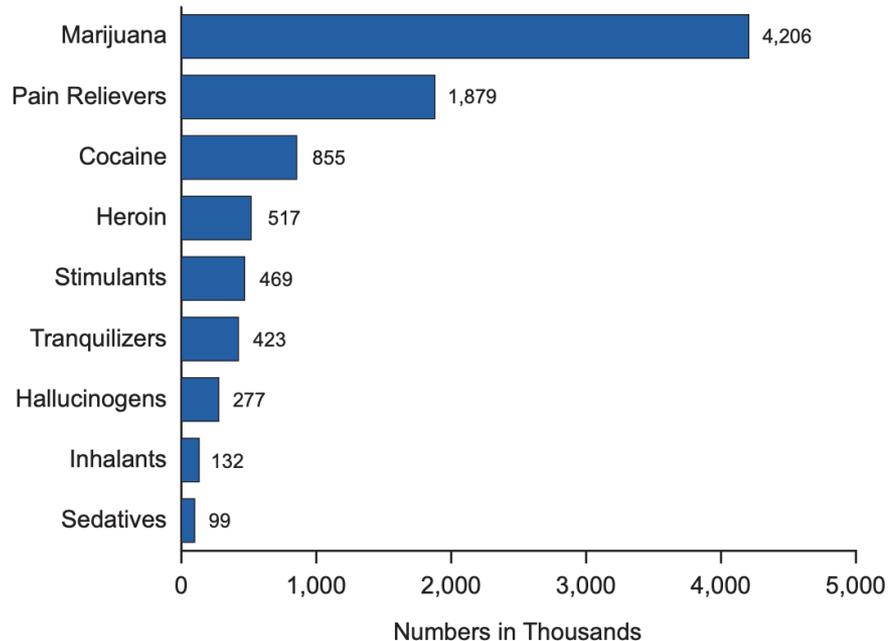
Table 1. Acute Toxicity and Dependence Potential of Psychoactive Substances^a

Substance	Effective dose ^b	Lethal dose	Safety margin	Dependence potential
Narcotics (opiates):				
Heroin (intravenous)	4 mg	30 mg	Very small	Very high
Morphine (intramuscular)	10 mg	90 mg	Very small	High
Opium (smoked)	100 mg	800 mg	Very small	High
Sedative-hypnotics (depressants):				
Barbiturates:				
Secobarbital (oral)	100 mg	2500 mg	Small	Moderate/high
Benzodiazepines:				
Diazepam (oral)	2 mg	2000+ mg	Very large	Moderate
Ethanol:				
Alcohol (oral)	27 g (2 beers) ^d	270 g	Very small	Moderate
Metnaquatone (oral)	75 mg	10,000 mg	Moderate	High
Hallucinogens:				
LSD-25 (oral)	50 mcg	14,000 mcg ^m	Large	Very low
MDMA (oral) ("Ecstasy")	125 mg	1875 mg	Small	Moderate/low
Mescaline (oral)	350 mg	6000 mg	Small	Very low
Psilocybin (oral)	4 mg (4 'shrooms) ^o	14,000 mg	Very large	Very low
Cannabis:				
Marijuana (smoked)	1.5 mg (1/2 joint) ^o	4000 mg	Very large	Low/moderate

Gable, R. S. (1993). Toward a comparative overview of dependence potential and acute toxicity of psychoactive substances used nonmedically. *The American journal of drug and alcohol abuse*, 19(3), 263-281

Low Addiction/Abuse Liability

Figure 7.2 Specific Illicit Drug Dependence or Abuse in the Past Year among Persons Aged 12 or Older: 2013



Center for Behavioral Health Statistics and Quality. (2013). National survey on drug use and health.

Relatively Low Overall Harm

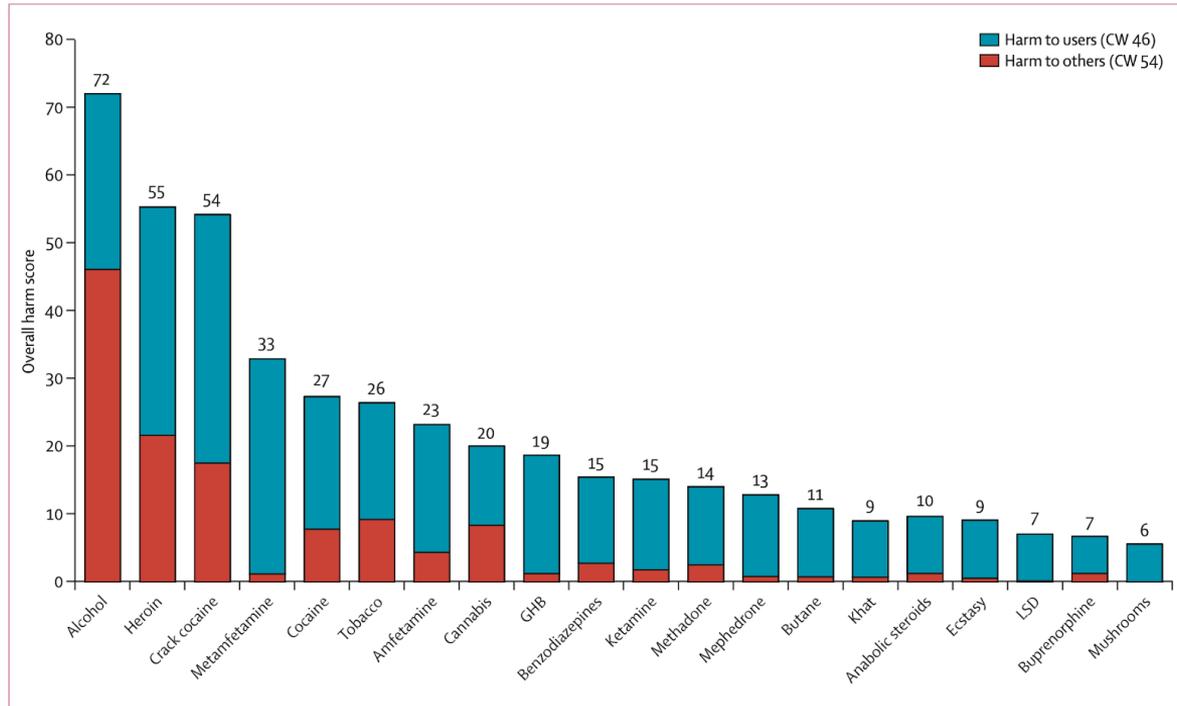


Figure 2: Drugs ordered by their overall harm scores, showing the separate contributions to the overall scores of harms to users and harm to others
The weights after normalisation (0–100) are shown in the key (cumulative in the sense of the sum of all the normalised weights for all the criteria to users, 46; and for all the criteria to others, 54). CW=cumulative weight. GHB=γ hydroxybutyric acid. LSD=lysergic acid diethylamide.

Nutt, D. J., King, L. A., & Phillips, L. D. (2010). Drug harms in the UK: a multicriteria decision analysis. *The Lancet*, 376(9752), 1558-1565.

Recent Surge for Intellectual Property & Patents in Psychedelic Therapies & Drug Development

USA - English ▼

Financialnewsmedia.com News Commentary

Recent Surge for
in Psychedelics

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Final

Growing popularity of psychedelic therapy creates demand for underground guides



Unaccredited therapists can be detrimental to effort to legalize psychedelics, says researcher

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Recent Surge for 'in Psychedelic' Growing popularity of psychedelic therapy creates demand for underground guides

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Unaccredited therapists can be detrimental to researcher

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Welcome to the trip of your life: the rise of underground LSD guides

Some Americans searching for alternative paths to healing have turned to psychedelics. But how does one forge a career as a guide when the substances are illegal?

Canada's #1 Online Magic Mushrooms Dispensary

MagicMushroomsDispensary.ca is Canada's most reputable & top rated online shrooms dispensary with over 10,000 heartfelt customer reviews from satisfied customers. We are Canada's experts in magic mushrooms and microdosing mushrooms. Whether you're experimenting with psychedelic drugs, looking for a great trip or you're ready to dive deeper in unlocking your mind, you have come to the right place.

Recent in Psychedelic Growing potential demand for unaccredited therapists can be detrimental to research

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Some Americans searching for paths to healing have turned to psychedelics, says... But how does one forge a career as a therapist when the substances are illegal?

The Life-Changing Magic of Tripping

Mark Kleiman, the drug-policy scholar who died last week, thought certain hallucinogens should be legalized.

IN PSYCHEDELIC

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Growing potential demand for unaccredited therapists can be detrimental to research



Unaccredited therapists can be detrimental to research

Psychedelic therapy creates

Mushrooms Dispensary

title

Some Americans searching for paths to healing have turned to psychedelics, says researcher. But how does one forge a career as a therapist when the substances are illegal?

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IDEAS

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THE PAST — AUGUST 5, 2021

How the CIA used LSD to fight communism

Before it fueled Woodstock and the Summer of Love, LSD was brought to America to make spying easier.

BUT NOW DOES ONE FORGE A CAREER AS A GOVERNMENT EMPLOYEE WHEN THE SUBSTANCES ARE ILLEGAL?

IDEAS

The Life-Changing Magic of Tripping

Mark Kleiman, the drug-policy scholar, argues that certain hallucinogens should be legalized.

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THE PAST — AUGUST 5, 2021

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The Life-Changing Magic of Trips

British Columbia

As psychedelic therapy goes mainstream, former patient warns of danger of sexual abuse



Meaghan Buisson has alleged she was sexually assaulted by her therapist during MDMA clinical trial



[Bethany Lindsay](#) · CBC News · Posted: Mar 18, 2021 4:00 AM PT | Last Updated: March 18, 2021

But now does one forge a career as a guide when the substances are illegal?

Cautions

- “Psychedelic Exceptionalism”
- Maintenance of an Empirical/Secular framework
 - consciousness “jingle fallacy”
- Boundary Demarcation
 - attachment trauma/pre-existing lack of healthy boundaries for patients with addictive disorders
- Harm Reduction

Summary

- Psychedelics are a distinct class of compounds with a longstanding history in sacramental/religious/spiritual practice
- Historical prohibition and suppression of research was largely due to political/social factors and ambiguity in classification. There does not appear to be robust objective evidence of harm that is comparable to other common substances
- Psychedelic therapy represents a unique opportunity to explore a paradigm-shift in psychopharmacological treatment provision that eschews the artificial mind-body split inherent in a strictly biomedical model

Summary

- Therapeutic use of psychedelics for substance use or any other indication remains in the **very preliminary phases** of development
- Psychedelics, like any substance capable of altering consciousness, introduces unique risks and vulnerabilities that may be exceptionally salient for patients with substance use disorders
- Open dialogue with inquiring patients, acknowledging **both** the potential benefits and the remaining uncertainties in a balanced and non-judgmental manner will be crucial as psychedelics continue to rise in prominence, demand and availability.

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QUESTIONS?

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