ACCEPT

Addiction & Co-morbid Conditions: Enhancing Prevention & Therapeutics

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Session Date: Friday, June 21, 2024

Didactic Topic and Presenter:
Research into Psychedelic Compounds as Treatment for SUDs

Randall Brown MD, PhD, DFASAM

Content Experts: Sheila Weix and Joe Galey

- 12:15 PM: Attendance text-in – Introductions
- 12:25 PM: Case Presentation
    - Presenter: David Leinweber, MD – *UW Madison, SMPH, DFMCH*
- 1 PM: Didactic Presentation and Discussion
    - Presenter: Randall Brown MD, PhD, DFASAM
- 1:15 PM End of Session

Funding for this service was made possible by 435200-G-18-11448-285932-880 from Wisconsin Department of Health Services. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government or the State of Wisconsin.

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Interprofessional Continuing Education Partnership
UNIVERSITY OF WISCONSIN-MADISON
School of Medicine and Public Health
School of Nursing
School of Pharmacy

Project ECHO®
University of Wisconsin

ECHO ACCEPT
Addiction & Co-morbid Conditions: Enhancing Prevention & Therapeutics
2022-2024
Research into Psychedelic Compounds as Treatment for SUDs
6/21/2024
Didactic Presenter: Randy Brown, MD
Case Presenter: David Leinweber, MD

Provided by the University of Wisconsin–Madison Interprofessional Continuing Education Partnership (ICEP)

Intended Audience:

Nurses, Nurse Practitioners, Pharmacists, Physicians, Physician Assistants, Pharmacy Technicians, Psychologists, Social Workers, Patient/Caregivers, Students

Objectives:

As a result of this educational regularly scheduled series, learners as members of the healthcare team will be able to:

- Discuss theoretical foundations of the therapeutic potential of psychedelics in the setting of use disorders
- Describe typical aspects of psychedelic clinical trials come, including interventional compound and behavioral therapy
- Describe basic evidence surrounding the microdosing of psychedelics

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Name	Role	Financial Relationship Disclosures	Discussion of Unlabeled/Unapproved uses of drugs/devices in presentation?	COI completion date
Randall Brown	RSS Chair	Usona Institute (Grant / Contract), multi-disciplinary association for psychedelic studies (Grant / Contract)	Yes	1/29/2024
Nada Rashid	RSS Coordinator	No relevant financial relationships to disclose	No	2/5/2024
Kathleen Maher	RSS Coordinator	No relevant financial relationships to disclose	No	2/6/2024
Ritu Bhatnagar	Planner	No relevant financial relationships to disclose	Yes	2/8/2024
Paul Hutson	Planner	No relevant financial relationships to disclose	Yes	1/29/2024
Susan Mindock	Planner	No relevant financial relationships to disclose	No	1/29/2024
Sheila Weix	Planner	No relevant financial relationships to disclose	No	2/9/2024
Kellene Eagen	Planner	No relevant financial relationships to disclose	No	1/29/2024
Joseph Galey	Planner	No relevant financial relationships to disclose	No	2/13/2024
David Leinweber	Planner	No relevant financial relationships to disclose	Yes	1/20/2024
Randy Brown	Presenter	No relevant financial relationships to disclose	Yes	6/10/2024

David Leinweber	Presenter	No relevant financial relationships to disclose	Yes	6/14/2024

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Case Presentation

Presenter Name: David Leinweber

Presenter Organization: UW Health

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Pharmacists and Pharmacy Technicians must enter their NABP number in their profile in order to receive credit.

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For this educational activity there are no reported conflicts of interest

Case Introduction

- One-liner (including age/sex): 53 y/o Male who presents as potential study subject for a Phase I Safety Trail of Psilocybin in patients with Opioid Use Disorder

- Primary question for discussion: What interest did this subject see in participating in the clinical trail?

Medical & Behavioral Health Diagnosis:	Current Medications:
• Chronic Bilateral Knee Pain • Opioid Use Disorder Severe	• Ibuprofen and Aspirin PRN for chronic knee pain • Multivitamin Daily

Substance Use

- History:
  - First use at age 19 y/o (Heroin)
  - Intermittently uses cocaine as well, daily marijuana use, daily tobacco use
  - Current use is intranasal but has used by injection in the past
- Consequences of Substance Use:
  - Social/occupational/educational:
    - Current use is causing conflict with his wife
    - Incarceration
  - Physical (including evidence of tolerance/withdrawal):
    - When he stops his current use does experience withdrawal (sweats, nausea). Withdrawal leads to return to use.
- Past treatments:
  - Methadone in the past (longest duration 1 year)
  - Has been prescribed buprenorphine but never used
  - Has heard of naltrexone IM but has never used
  - Attended residential treatment at Tellurian (~2015)

Social History:	Family History:
• Social Factors/History: • Has stable housing with partner in apartment • Income source: started new job as a car mechanic • In the past has worked at multiple settings (construction, odd jobs, cashier, etc.)	• Brother alcohol use disorder • Denies any family history of cardiac, renal, or liver disease

Patient strengths & protective factors:	Risk factors:
• Stable housing • New Job	• Is afraid of buprenorphine causing withdrawal (has not successfully used buprenorphine in the past)

Labs

- Unremarkable CBC, CMP and urinalysis

Patient Goals & Motivations for Treatment

- Heard of study through a friend who saw it on TV
  - Wants to abstain from heroin/opioids.
    - Notes he cannot achieve the same “high” as he had in the past
    - Save money
    - Improve relationship with his partner
    - Be there for his grandchildren
    - Difficulty with doing it on his own due to withdrawal
    - Is concerned regarding use of buprenorphine as just another opioid

Proposed Diagnoses

- Opioid Use Disorder – severe
- Cocaine use
- Alcohol Use
- Tobacco Use

Proposed Treatment Plan

- Participant was deemed eligible for the study
- Due to fear of withdrawal proposed a low dose initiation
  - This was successful after a 2-week period of low dose initiation and frequent phone calls (lower health literacy and required guidance on low dose initiation)

Discussion:

- Past experience with MOUD
  - Has had poor experience with Methadone in the past (felt like he was “high” while using it)
  - Buprenorphine – is concerned regarding precipitated withdrawal (felt that his friends have had withdrawal from it in the past). Has not used
- During study buprenorphine was decreased from 8-2 mg TID to 8 mg daily due to erectile dysfunction
  - During study recommended follow up with PCP who initiated sildenafil which helped with symptoms
- During study experienced significant stressors (relationship, financial) which led to stopping buprenorphine and returning to use.
- Also heard from his dentist that he is losing his teeth due to buprenorphine

Discussion:

- Initial dosing session led to more openness regarding trauma that they have experienced
- End of Study – encouraged to resume buprenorphine with consideration of transition to extended-release buprenorphine
  - Will not experience withdrawal when discontinuing medication (experience of withdrawal increases desire to use)
  - Notes though that he feels not “clean” while using buprenorphine
  - Connected with PCP for resuming buprenorphine with consideration of extended release
  - Connected with counseling as participant found counseling during study beneficial

DSM-5 Substance Use Disorder ("Addiction")

- Tolerance
- Withdrawal

} **Physical Dependence ≠ Use Disorder**

- Larger amts/longer periods than intended
- Persistent desire/failed attempts to quit/control use
- Much time obtaining/using/recovering
- Important activities sacrificed
- Continued use despite known adverse effects
- Failure to fulfill major obligations
- Recurrent hazardous use
- Craving
- Ongoing use despite interpersonal problems

2-3 = mild
4-5 = moderate
≥ 6 = severe

By initialing here DQL you have acknowledged that Project ECHO case consultations do not create or otherwise establish a provider-patient relationship between any ECHO clinician and any patient whose case is being presented in a teleECHO clinic.

Research into Psychedelic Compounds as Treatment for SUDs

Randall Brown MD, PhD, DFASAM

UW Project ECHO ACCEPT

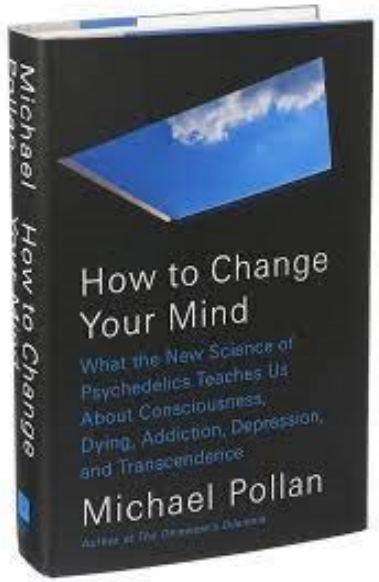
June 21, 2024

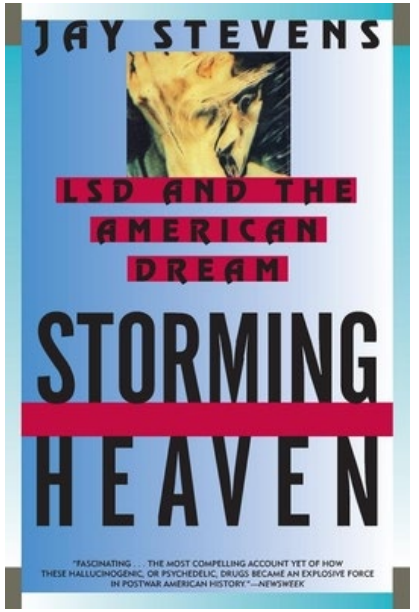
PROTEA

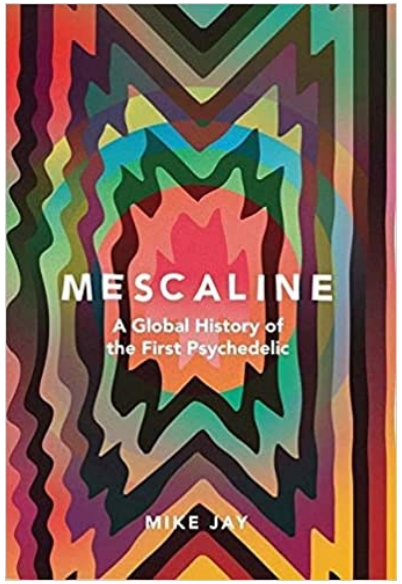
Program for Research, Outreach, Therapeutics, & Education in the Addictions

Definitions

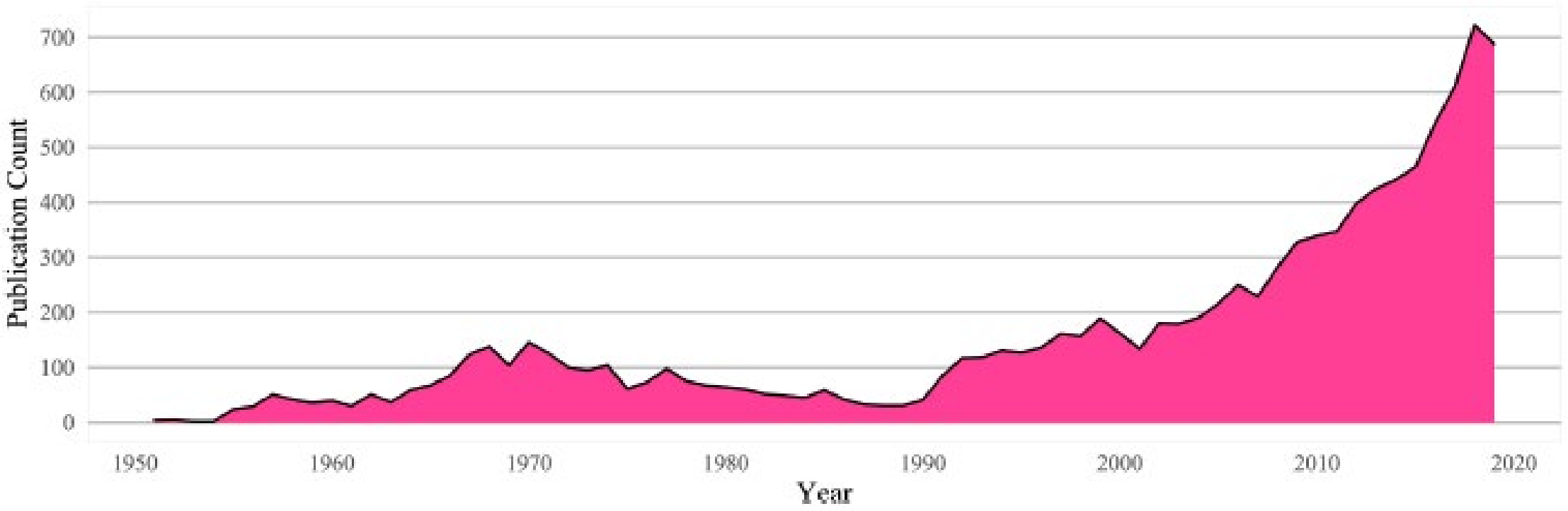
- Psychedelic:
- “mind-manifesting capability, revealing” or having “useful or beneficial properties of the mind” (Osmond, 1957)
  - **“Classic psychedelics”**: psilocybin, mescaline, DMT, LSD (5-HT2a agonists)
  - Hallucinogen: causes changes in perception or hallucinations
  - Entheogen: substance that “generates God or the divine within” (Ruck, 1979)
  - Entactogen/Empathogen (MDMA): “touching within” but by the definition above could be considered a “psychedelic”



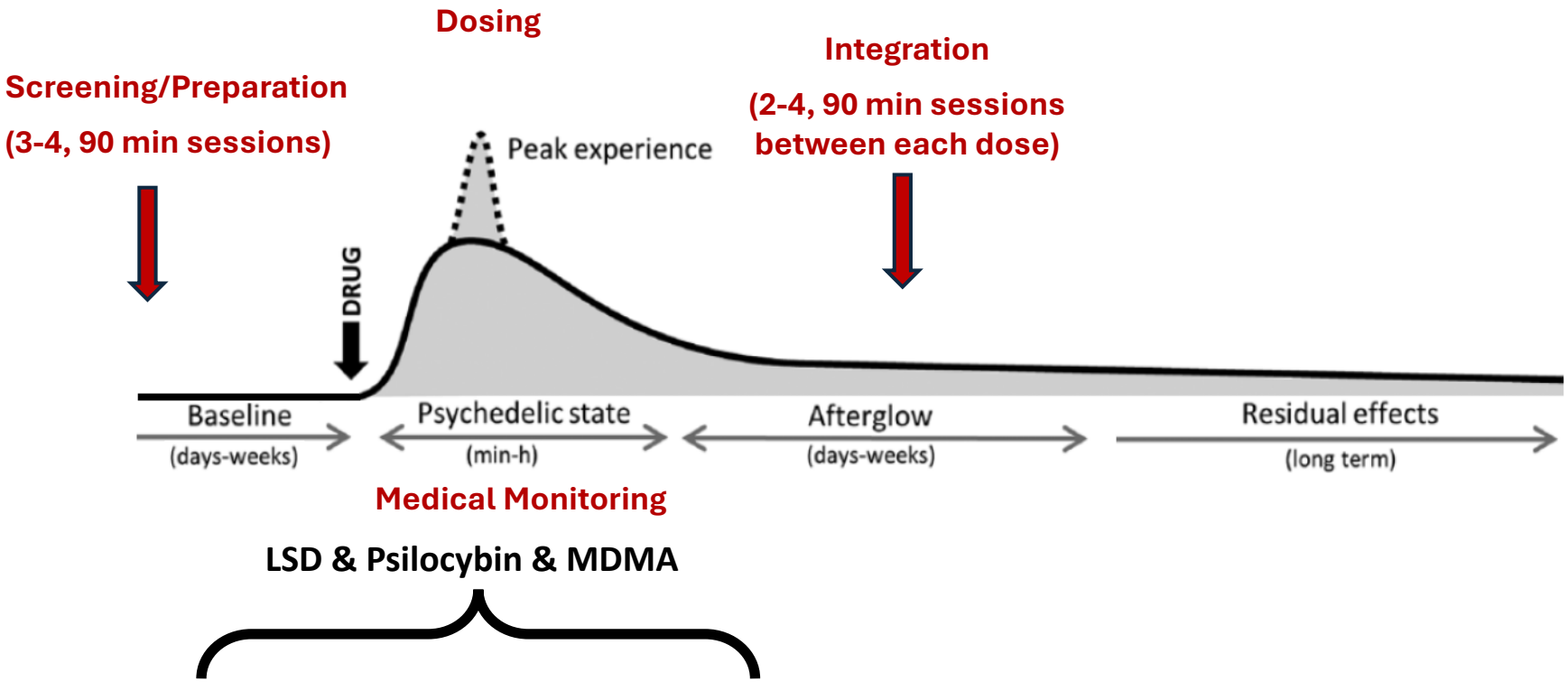




Web of Science Psychedelic Publication Count by Year



Possible Therapeutic Time Course for LSD, Psilocybin & MDMA



- **Single oral dose onset**: ~30-60 min
- **Peak effects**: ~2 hours (in MDMA may extend peak with supplemental half-dose)
- **Total duration**: 6-12 hours

Majic et al.(2015). J of Psychopharmacology

Set and Setting

Set: the participant's psychological state

- Pre-dose preparation
- Careful screening & assessment
- Expectations/concerns
- Integration

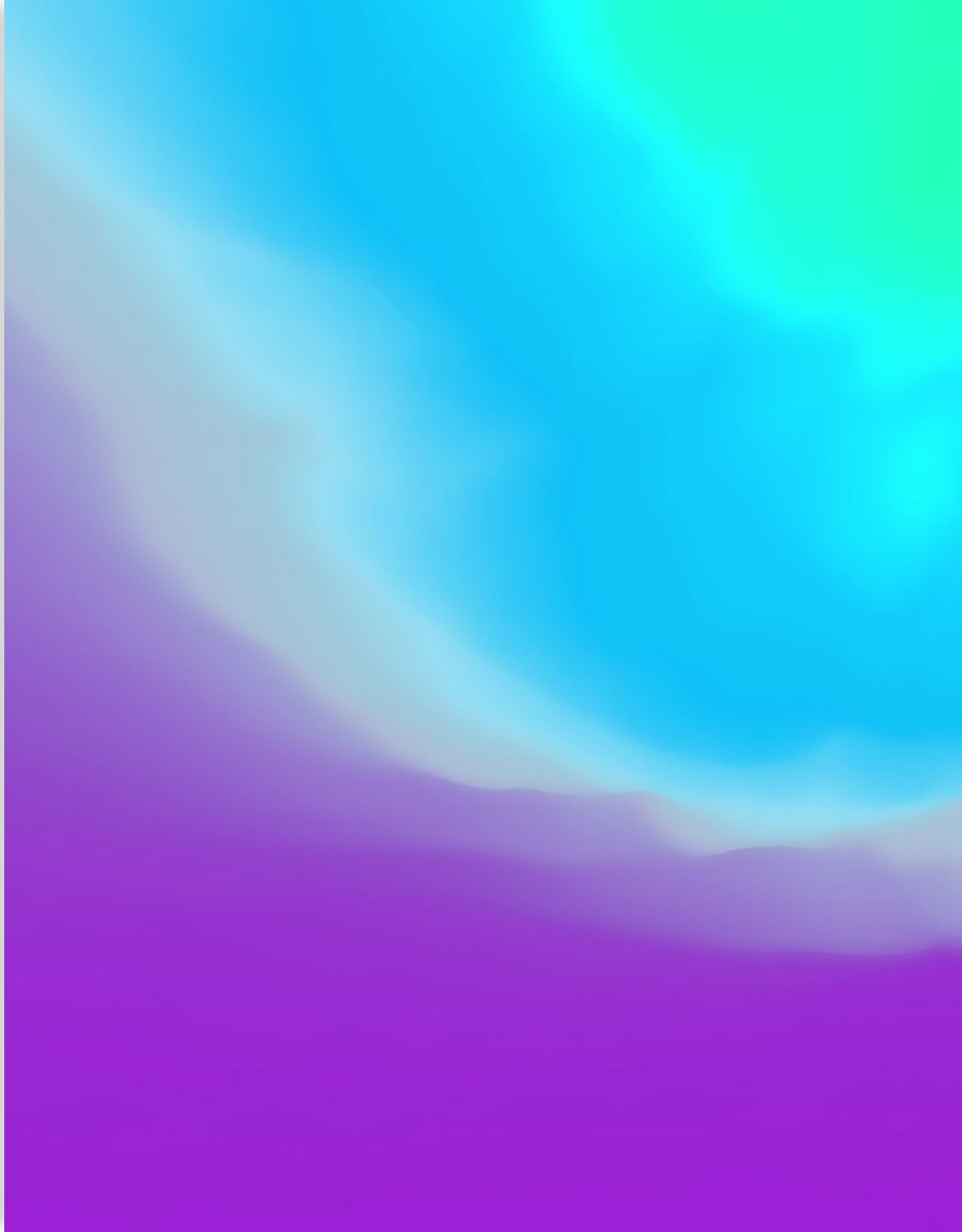
UW School of Pharmacy Dosing room

Setting: environment & context

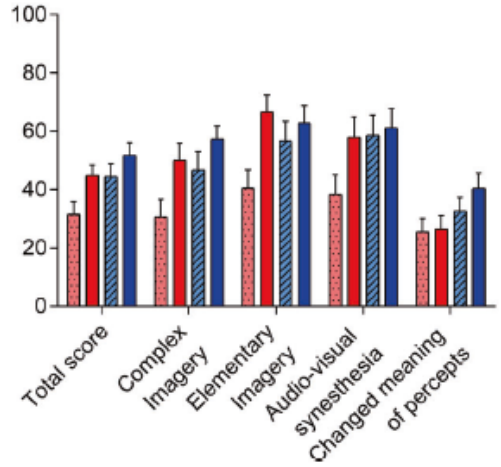
- Interpersonal support
- Safe & secure room
- Room with comfortable & positive décor
- Personal objects if possible
- Predictable and familiar

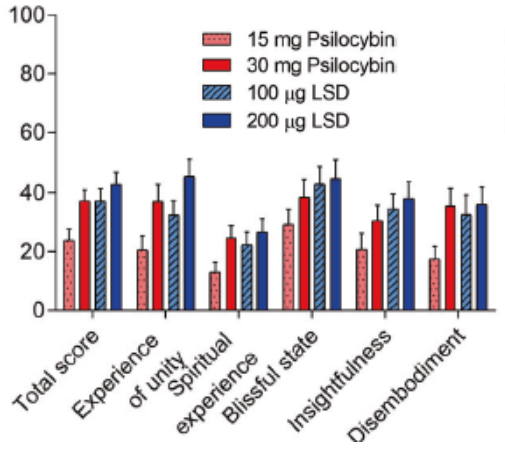
General dosing procedures for Psilocybin & MDMA

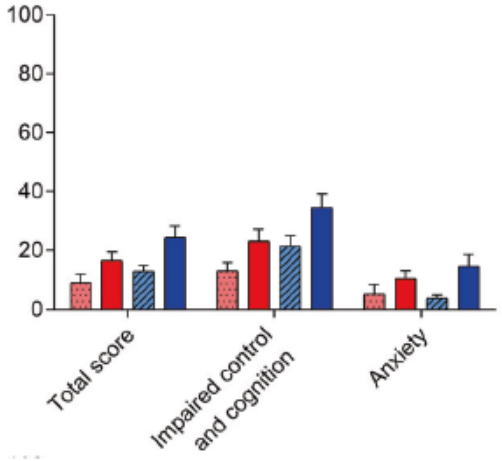
- In a safe, secure, and supportive setting
- Two facilitators/guides/monitors/therapists
- Study physician & research coordinator(s)
- Eye-shades, headphones for pre-set instrumental music playlist
- May stay overnight in Clinical Research Unit or discharge under care of their support person
- Integration session the next morning
- Phone check-ins and additional integration sessions prior to next dose



Experience of LSD and Psilocybin







- Emotional range
- Divergent thinking
- Dereal-/personalization
- Sensory hallucinations

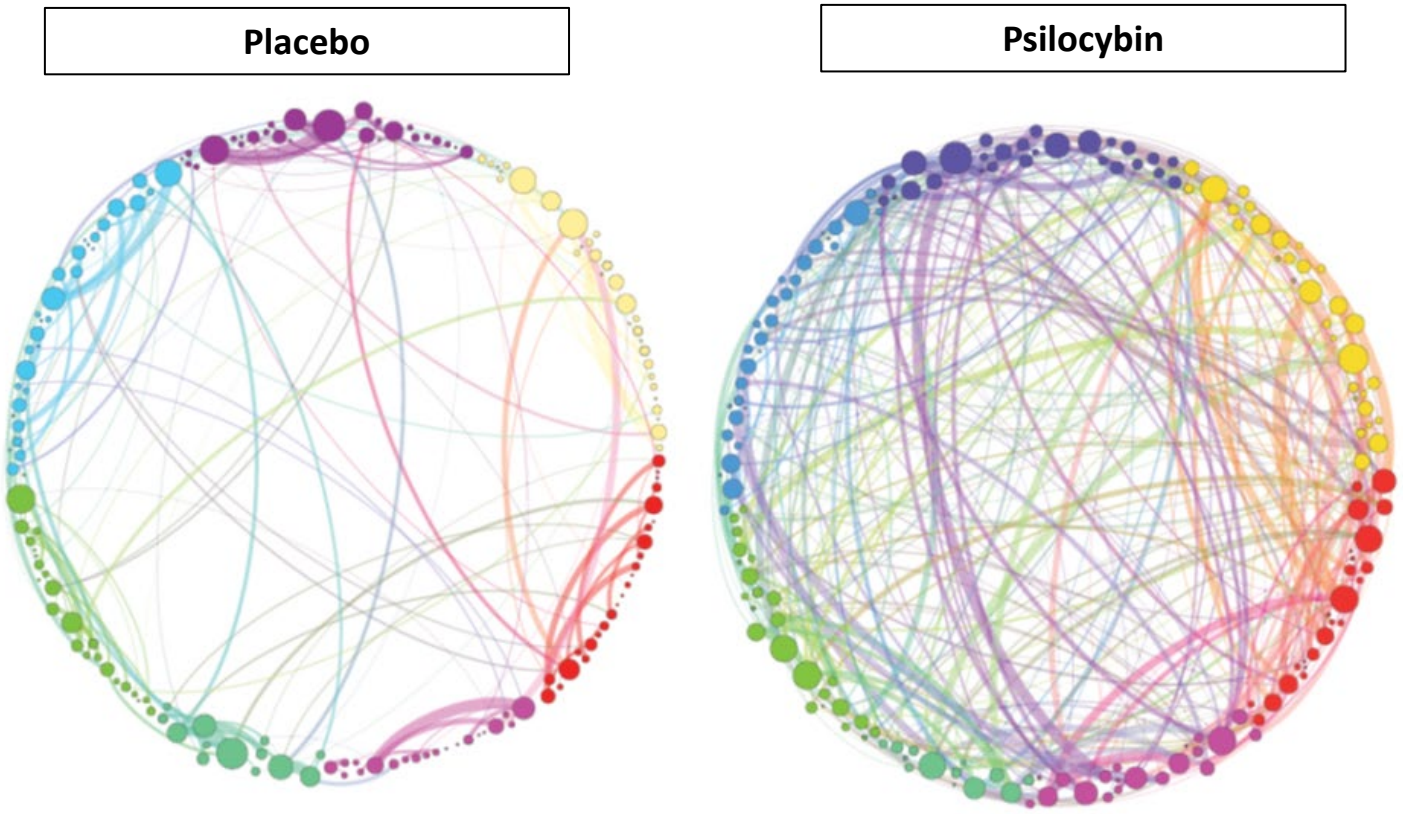
- Loss of body control
- Synesthesia
- Paradoxicality
- Aberrant salience

Holze, 2022, Neuropsychopharmacology

Safety

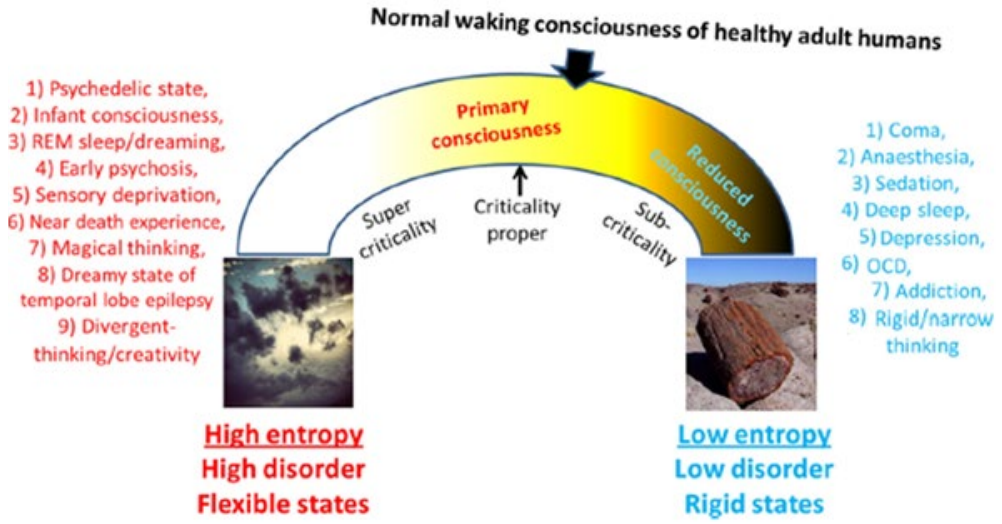
- 25-50 mg dosing
- No evidence of such potential neurotoxic effects
- Temporarily elevated pulse and both systolic and diastolic blood pressure
- Possible headache within 24 hours after dosing
- Impairs judgement thus context, support, and preparation are important
- Anti-addictive properties, no withdrawal
- Low risk of hallucinogen persisting perceptual disorder (HPPD)
- Negative interaction with serious psychiatric diagnoses (e.g. psychosis, bipolar)
- Increases suggestibility and aberrant salience

Increased Brain Inter-connectivity



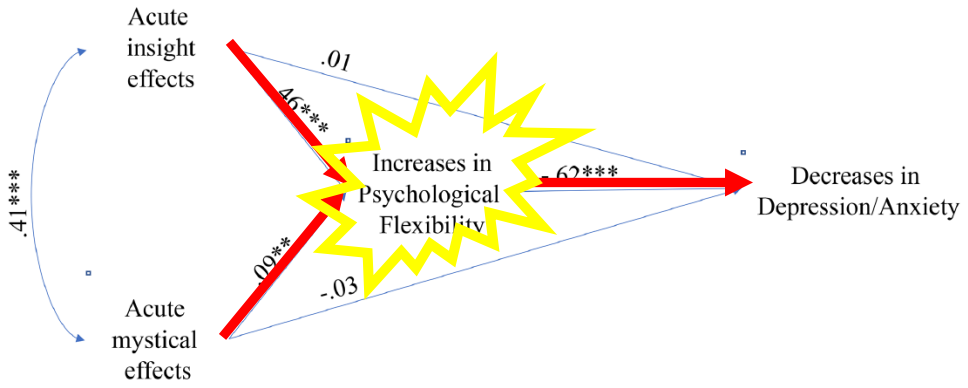
Petri (2014). Journal of the Royal Society

Relaxed Beliefs and Psychological Flexibility



Psychological flexibility mediates subjective effects and change in depression/anxiety

- Stimulate 5-HT2ARs on deep pyramidal cells encode, expectations, “priors”, and/or beliefs.
- The resulting disinhibition lightens the felt precision of higher-level expectations/beliefs
- More open to new internal and external information



Davis et al. (2020). J Contextual Behavioral Science
Carhart-Harris et al. (2019). Psychopharmacological Reviews

Personally Meaningful and Existential Experiences

Themes

- Relational/Connection/Love
- Self-compassion
- Forgiveness
- Emotional breakthrough
  Reprioritizing values
- Existential
- Rebirth
- Meaning
- Nihilism
- Challenge

Psychospiritual

- **Mystical Experience***

  ~Ineffability~

  ~Positive Affect~

  ~Timelessness~

  ~Sense of Unity/Noetic Consciousness~

  Ex. Mystical Experience Questionnaire
- **Ego-Dissolution**

  Recession of self

  Ex. Ego Dissolution Scale
- **Awe**

  Ex. Awe Experience Scale

****Ko et al., 2022 Frontiers in Psychiatry***

Challenging Experiences

- Fear
- Grief
- Dyscontrol
- Isolation
- Experience of dying
- Insanity
- Physiological distress
- Paranoia
- Regret
- Ex. Challenging Experiences Questionnaire*

Barrett et al., 2016 Journal of Psychopharmacology

Bill W. & LSD

"I am certain that the LSD experience has helped me very much. I find myself with a heightened color perception and an appreciation of beauty almost destroyed by my years of depression…The sensation that the partition between "here" and "there" has become very thin is constantly with me."

Letter from Wilson to Heard on Jan. 18, 1957

"Some of my AA friends and I have taken the material (LSD) frequently and with much benefit….a great broadening and deepening and heightening of consciousness"

Letter from Wilson to Jung on March 9, 1961

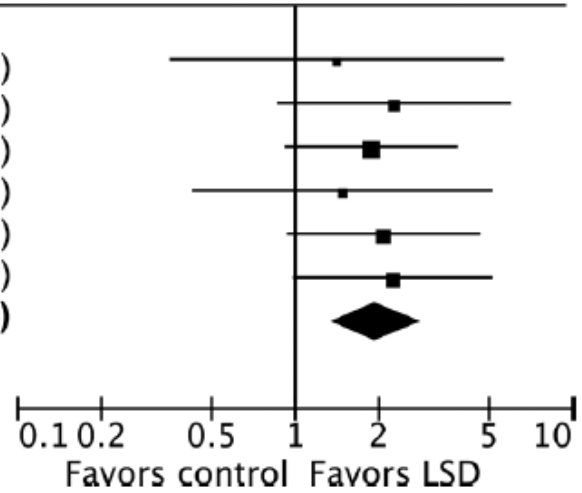
Bill Wilson, LSD and Role that Psychedelics Played in the History of Alcoholics Anonymous – Don Lattin -http://www.donlattin.com/

Meta-analysis of LSD for Alcoholism

	Follow-up (months)	LSD (n/N)	Control (n/N)	Weight	Odds Ratio (95% CI)
First follow-up					
Smart *et al.*, 1966	6	[a]/10	[a]/20	7.2%	1.41 (0.36-5.60)
Hollister *et al.*, 1969	2	18/36	11/36	14.7%	2.27 (0.87-5.94)
Ludwig *et al.*, 1969	1	94/132	25/44	27.3%	1.88 (0.93-3.81)
Bowen *et al.*, 1970	12	9/22	7/22	8.9%	1.48 (0.43-5.10)
Pahnke *et al.*, 1970	6	34/73	13/44	21.6%	2.08 (0.94-4.60)
Tomsovic & Edwards, 1970	3	30/52	17/45	20.4%	2.25 (0.99-5.10)
Total		**325**	**211**	**100%**	**1.96 (1.36-2.84)**

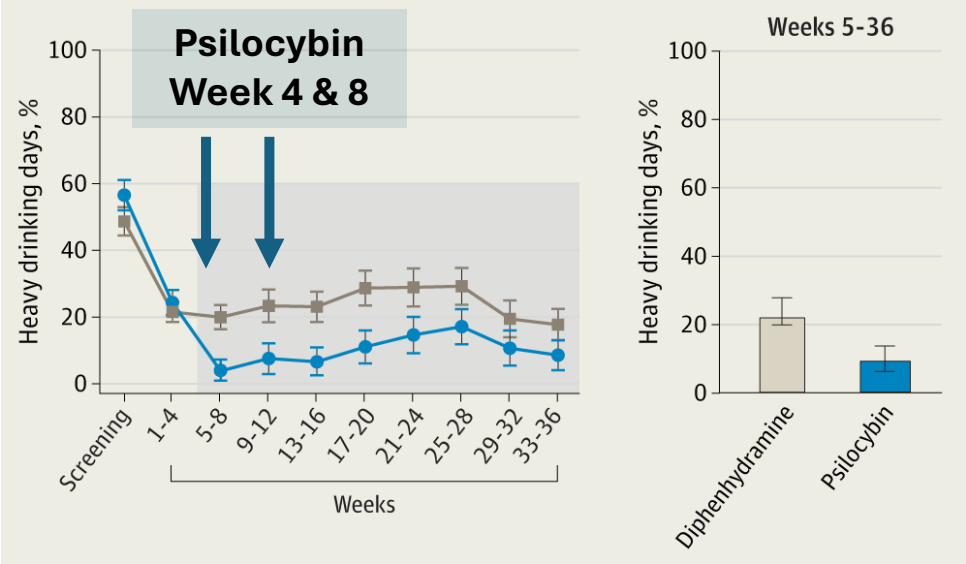
Test for heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 0.65$, df = 5 ($P = 0.99$); $I^2 = 0\%$

Test for overall effect: $Z = 3.59$ ($P = 0.0003$)



Krebs et al. (2012). Journal of Psychopharmacology

Psilocybin for Alcohol Use Disorder



Percent heavy drinking days

Psilocybin=9.7%

Diphenhyramine=23.6%

Mean difference, 13.9 (95% CI, 3.0-24.7; *P* = .01)

		No. (%)[a]	
	Follow-up period	Diphenhydramine (n = 45)	Psilocybin (n = 48)
Abstinence	Weeks 5-36	4 (8.9)	11 (22.9)
	Weeks 33-36	11 (24.4)	23 (47.9)
No heavy drinking	Weeks 5-36	5 (11.1)	16 (33.3)
	Weeks 33-36	18 (40.0)	30 (62.5)

- N= 95, (42% Female, Age 46 yo, 80% Non-Hispanic White)
- Two doses of psilocybin (25 mg/70 kg dose 1; 30-40mg/70) versus diphenhydramine (50mg, 100mg)
- 12 sessions of combination of motivational enhancement therapy and CBT

Bogenschutz et al. (2022). JAMA Psychiatry

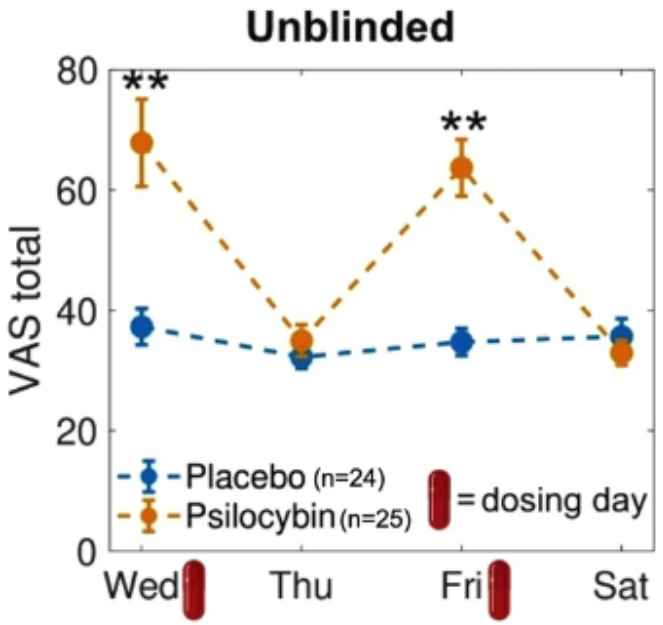
Microdosing Psychedelics

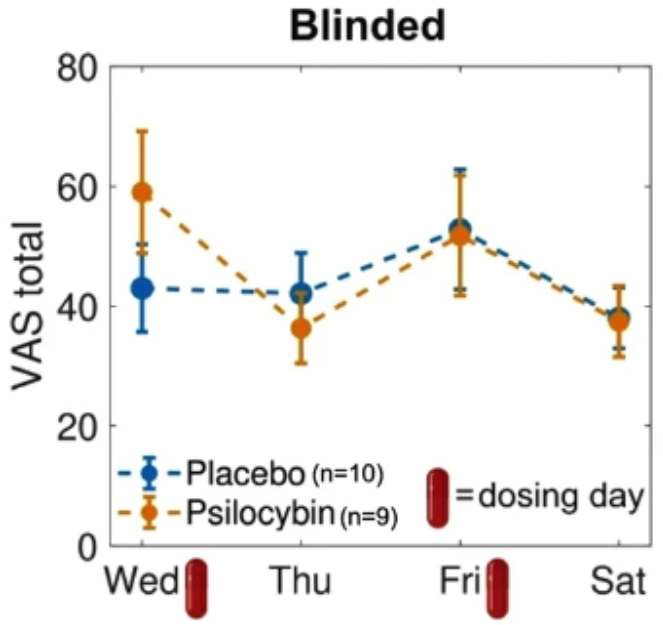
- "Micro-dosing" roughly defined as one tenth to one twentieth of a recreational psychedelic dose.
- Self-selected, micro-dosing individuals report mood improvements vs non-micro-dosing (Rootman et al 2022. Sci Reports.)

RCT LSD (13mcg) similarly found no impact on cog fxn or creativity vs placebo (Beshad et al 2019. Biol Psych)

Cavanna et al 2022. *Translational psychiatry*.

- 34 healthy adults
- Randomized, placebo-controlled trial (5mg psilocybin vs placebo)
- 2 wk psil, 2 wk placebo w/ 1 wk "washout" intervening
- Some subjective and EEG fx, but no fx on creativity, cognition, MH/well-being
  - Observed fx on VAS due to expectancies
- Impairment on some cognitive tasks





Psilocybin for Opioid Use Disorder Safety-Feasibility Study

PI: Randall Brown MD, PhD

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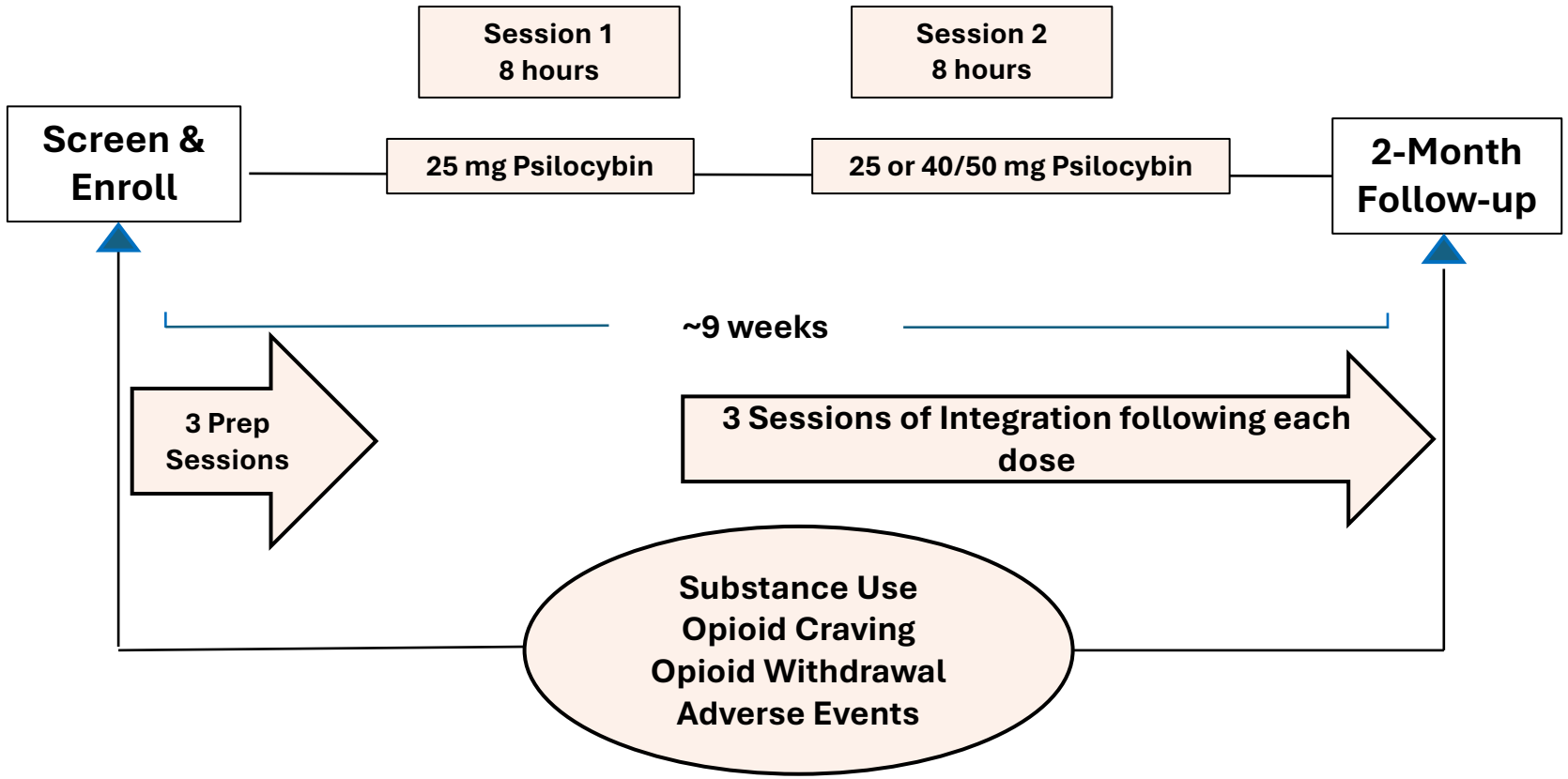

- N=10, adults with active Opioid Use Disorder who transition to MOUD (buprenorphine) prior to dosing
- Supportive therapy with 2 facilitators
- ECG/Vitals monitored throughout each dosing session

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Radar Chart - Altered States of Consciousness

Psilocybin for Methamphetamine Use Disorder Safety-Feasibility Study

PI: Christopher Nicholas, PhD

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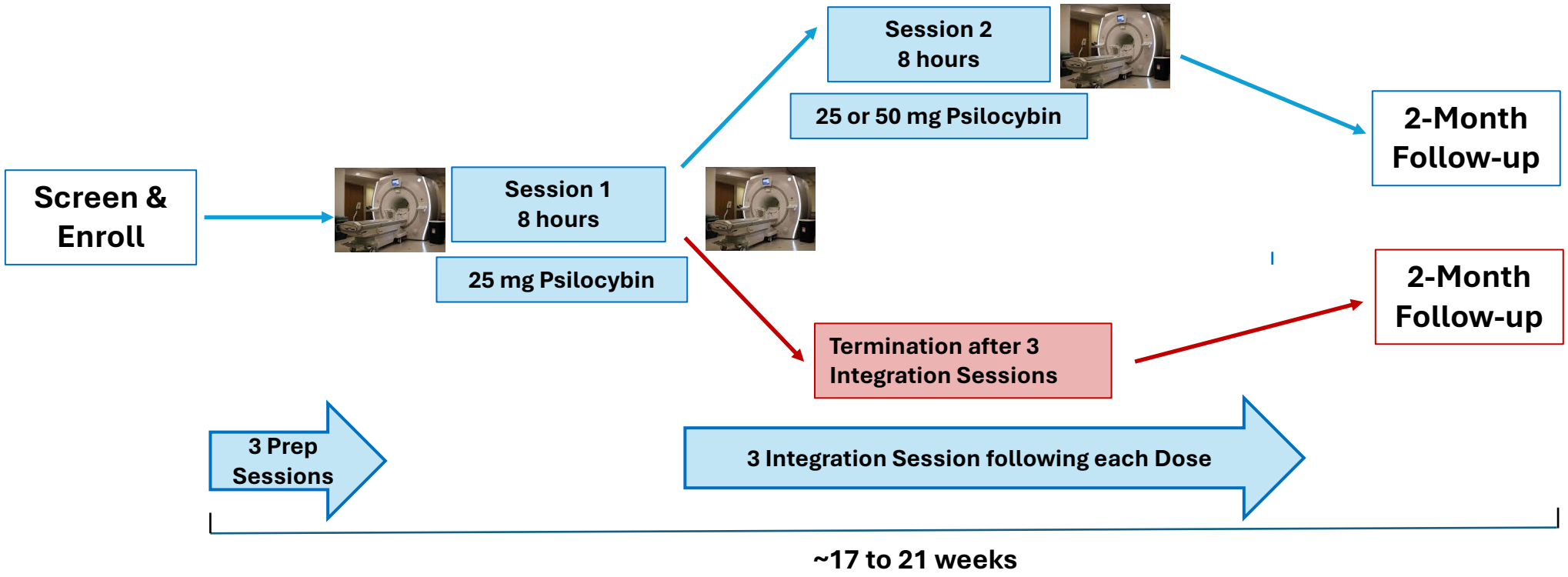
Open-label Safety Feasibility Study of Psilocybin for Methamphetamine Use Disorder



- PI: Christopher Nicholas, PhD
- N=12, adults with mild to moderate Meth Use Disorder
- Placebo + psychotherapy (Harm Reduction, MI, Mindfulness, CBT, Emotion/Somatic-Focused)
- Strategies to optimize retention

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Thank you!

Questions?

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Site w/ info on research and contacts for potentially interested participants

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