

**Psilocybin-assisted Psychotherapy to Treat Psychiatric &  
Existential Distress in Life-Threatening Medical Illnesses &  
Palliative Care**

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# Disclosures

- Active Research Funding Sources
  - National Institute on Drug Abuse (NIDA)
  - Usona Institute
  - Reser Pharmaceuticals



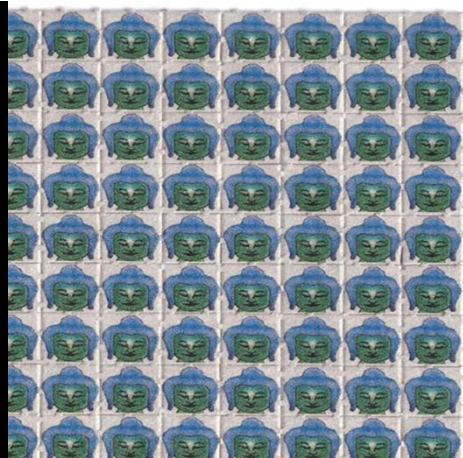
*Psilocybe mexicana* (Jalisco Strain)  
Photo by Workman of SporeWorks.com. © 2003 SporeWorks.com



*Psilocybe cubensis*  
Photo by Raoul, © 2000 Erowid.org



**LSD Bottle**  
Photographer Unknown



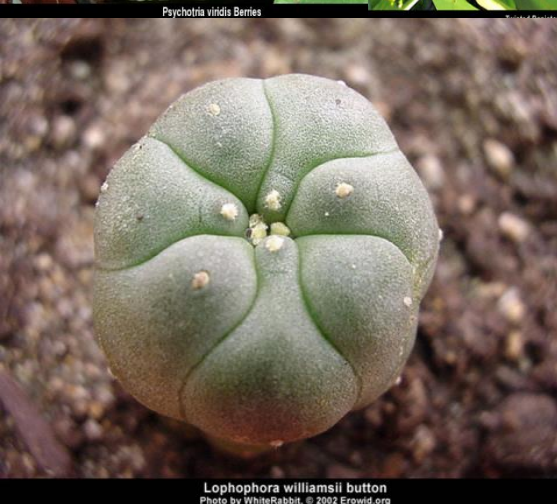
**LSD Blotter (Buddha)**  
Photo by Monkey, © 2003 Erowid.org



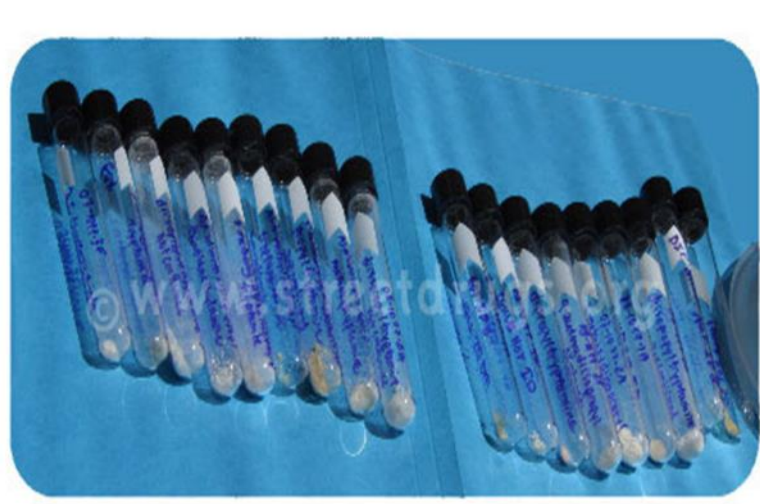
*Psychotria viridis* Berries



**Tabernaemontana iboga**  
Photo by Knehnav



*Lophophora williamsii* button  
Photo by WhiteRabbit, © 2002 Erowid.org



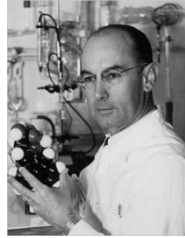
**99 Ecstasy Tablets (2007)**  
Image by Erowid, © 2007 Erowid.org

# History of Research on Psychedelics



Used by indigenous peoples >1000 years

First LSD studies on humans 1947



First uses of LSD clinically to treat psychiatric illnesses 1953



Street use Associated with counterculture movement, Vietnam war protests 1960's



Hoffman synthesizes psilocybin 1958

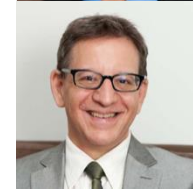
1950-1970 -> 1000 studies on Addiction, end of life anxiety, cognition, behavior -40,000 participants

22 year research halt

1970 Controlled Substances act: LSD, Psilocybin, Mescaline Schedule I

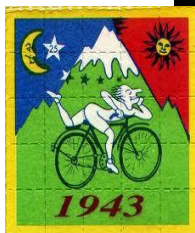


Rick Strassman (UNM) DMT studies 1992



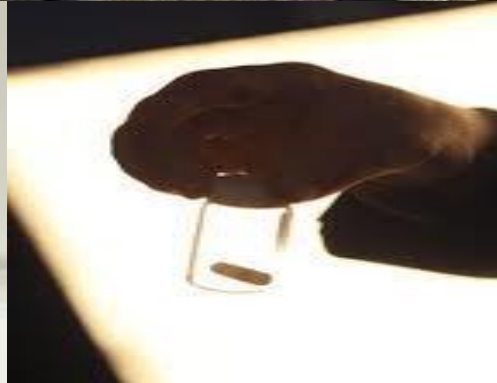
NYU Psychedelic Research Group 2006

1994-present Johns Hopkins, UCLA, Arizona, NYU, UNM, Alabama, UCSF, Yale research psilocybin, LSD, and MDMA for anxiety, depression, addiction



LSD Bottle Photographer Unknown





# Terminology

- Phantastica
- Psychotomimetic
- Psychedelic
- Hallucinogen
- Entheogen
- Mystico-mimetic

# Phenomenology in psychiatry: Intoxication=psychosis

- **Thought Content/Perceptual**
  - Perceptual Disturbances
    - Illusions
    - Hallucinations
- **Thought processes**
  - Thought disorder
    - Tangentiality
    - Loosening of associations
- **Cognitive changes**
  - Tendency towards introversion and introspection
- **Affective tone:** large spectrum of effects from euphoric states →  
anxiogenic, panic/terror

# Mystical States & Peak Experience

- ❖ **Unity** or oneness
- ❖ **Transcendence** of **time** and **space**
- ❖ **Deeply felt positive mood** (joy, peace and love)
- ❖ **Sacredness** and reverence: inspiring reality
- ❖ Psychological and/or philosophical insight ('**noetics**): ultimate reality
- ❖ **Ineffability**
- ❖ **Paradoxicality**
- ❖ **Transiency**

(Stace 1961)

(Pahnke, Richards 1966)





# Molecular Neuropharmacology

## • Serotonin:

- **5HT2a agonism** as primary mechanism of action of subjective effects
  - Also 5HT2b and 5HT2c agonism; 5HT1a agonism

## • Glutamate and Neurotrophic effects

- ↑ glutamate via 5HT2a agonism (Nichols 2004)
  - 5HT2a densely expressed on apical dendrites layer 5 pyramidal neurons in PFC → increased glutamate activity → AMPA and NMDA activation → **BDNF expression**

## • Dopamine

- Direct (ie LSD- D1/2 agonism) and indirect agonism
- **But, no appreciable activation of VTA-->nucleus accumbens** (Gresch 2002)

## • Adrenergic

- Activation of sympathetic nervous system

## Psychedelics Promote Structural and Functional Neural Plasticity

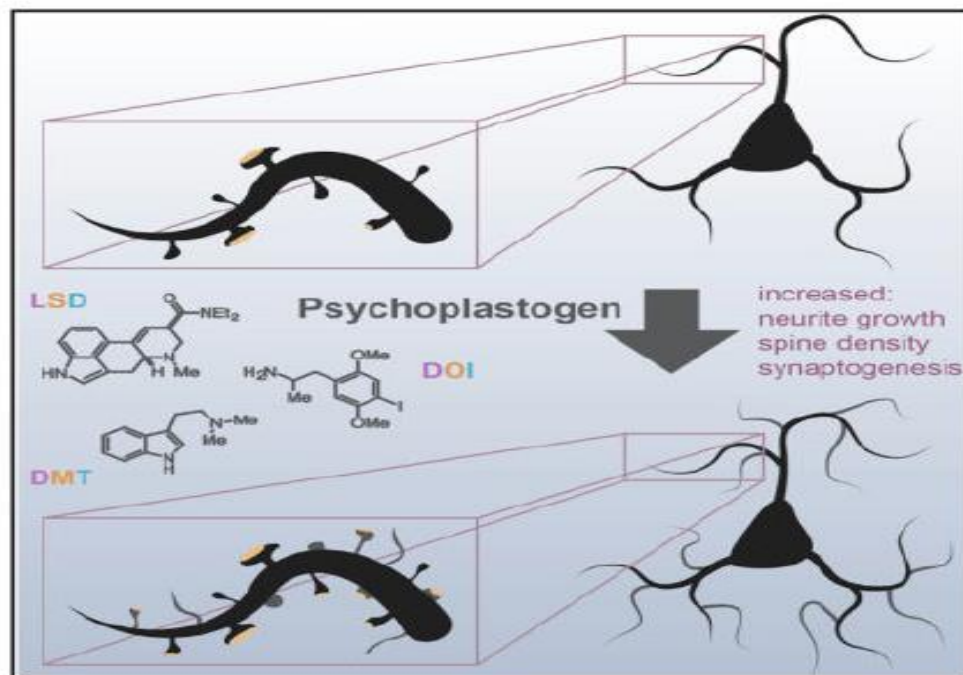
Calvin Ly<sup>1</sup>, Alexandra C. Greb<sup>1</sup>, Lindsay P. Cameron<sup>2</sup>, Jonathan M. Wong<sup>2</sup>, Eden V. Barragan<sup>2</sup>, Paige C. Wilson<sup>3</sup>, Kyle F. Burbach<sup>4</sup>, Sina Soltanzadeh Zarandi<sup>1</sup>, Alexander Sood<sup>5</sup>, Michael R. Paddy<sup>3</sup>, Whitney C. Duim<sup>1</sup>, Megan Y. Dennis<sup>4,6,7</sup>, A. Kimberley McAllister<sup>5,8,9</sup>, Kassandra M. Ori-McKenney<sup>3</sup>, John A. Gray<sup>5,8</sup>, and David E. Olson<sup>1,5,6,10,\*</sup>

<sup>1</sup>Department of Chemistry, University of California, Davis, Davis, CA 95616, USA

<sup>2</sup>Neuroscience Graduate Program, University of California, Davis, Davis, CA 95618, USA

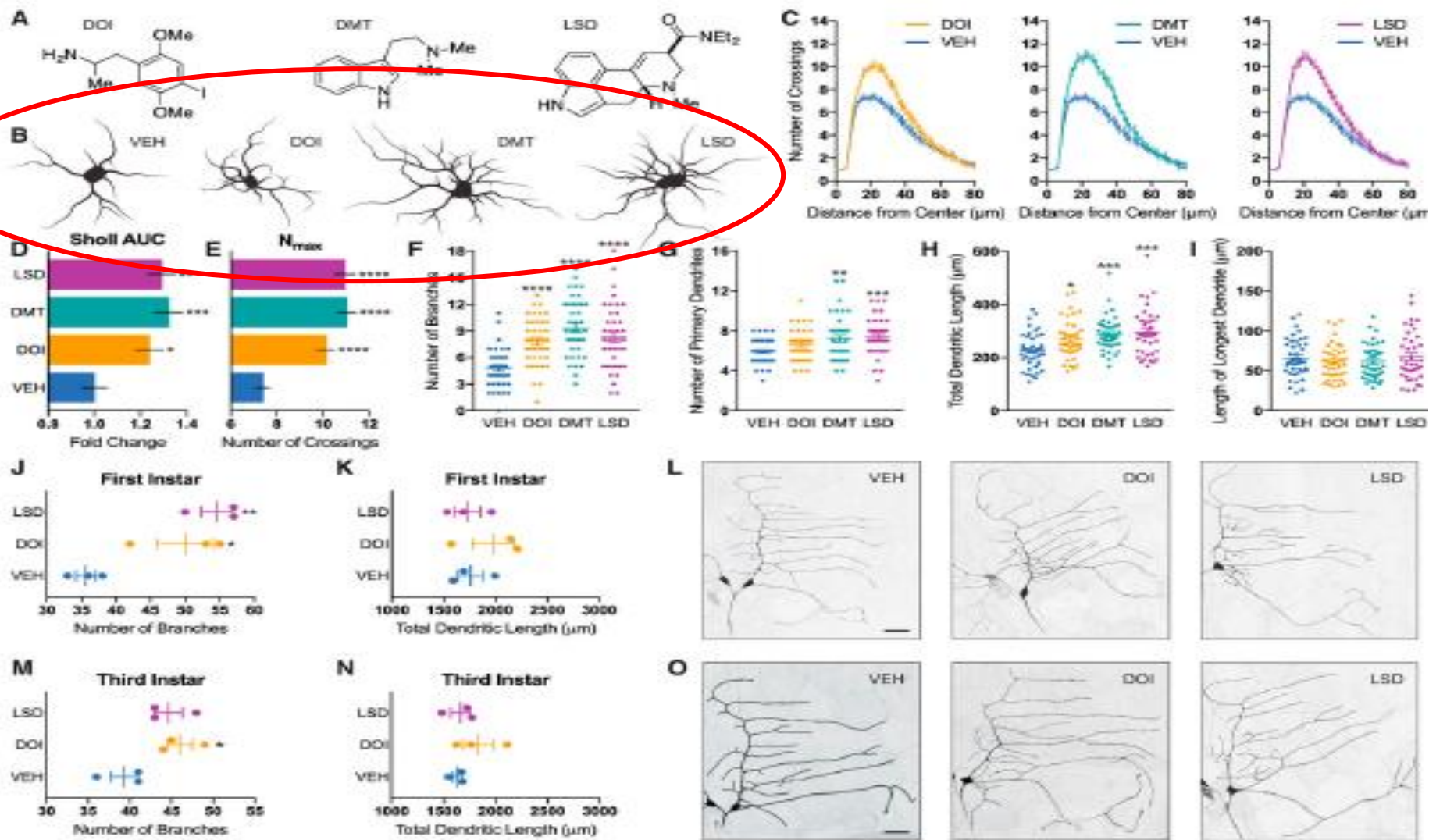
<sup>3</sup>Department of Molecular and Cellular Biology, University of California, Davis, Davis, CA 95616, USA

Ly et al. demonstrate that psychedelic compounds such as LSD, DMT, and DOI increase dendritic arbor complexity, promote dendritic spine growth, and stimulate synapse formation. These cellular effects are similar to those produced by the fast-acting antidepressant ketamine and highlight the potential of psychedelics for treating depression and related disorders.



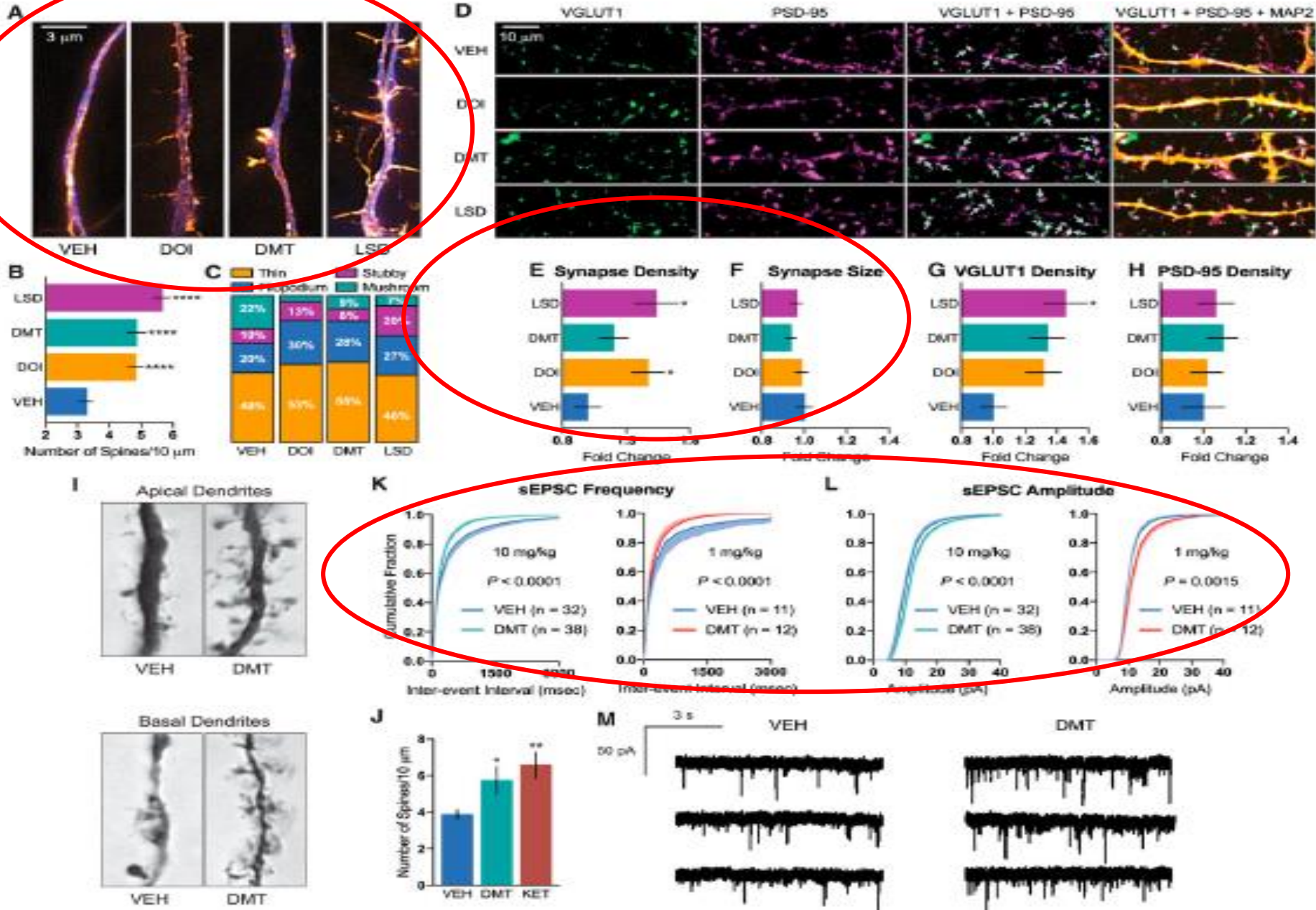
**In vitro**  
Experiments:  
cortical cell  
cultures from  
embryonic day  
18 (E18)  
Sprague-  
Dawley rats

# Psychedelics promote neuritogenesis (dendritic arborization) in cortical neurons

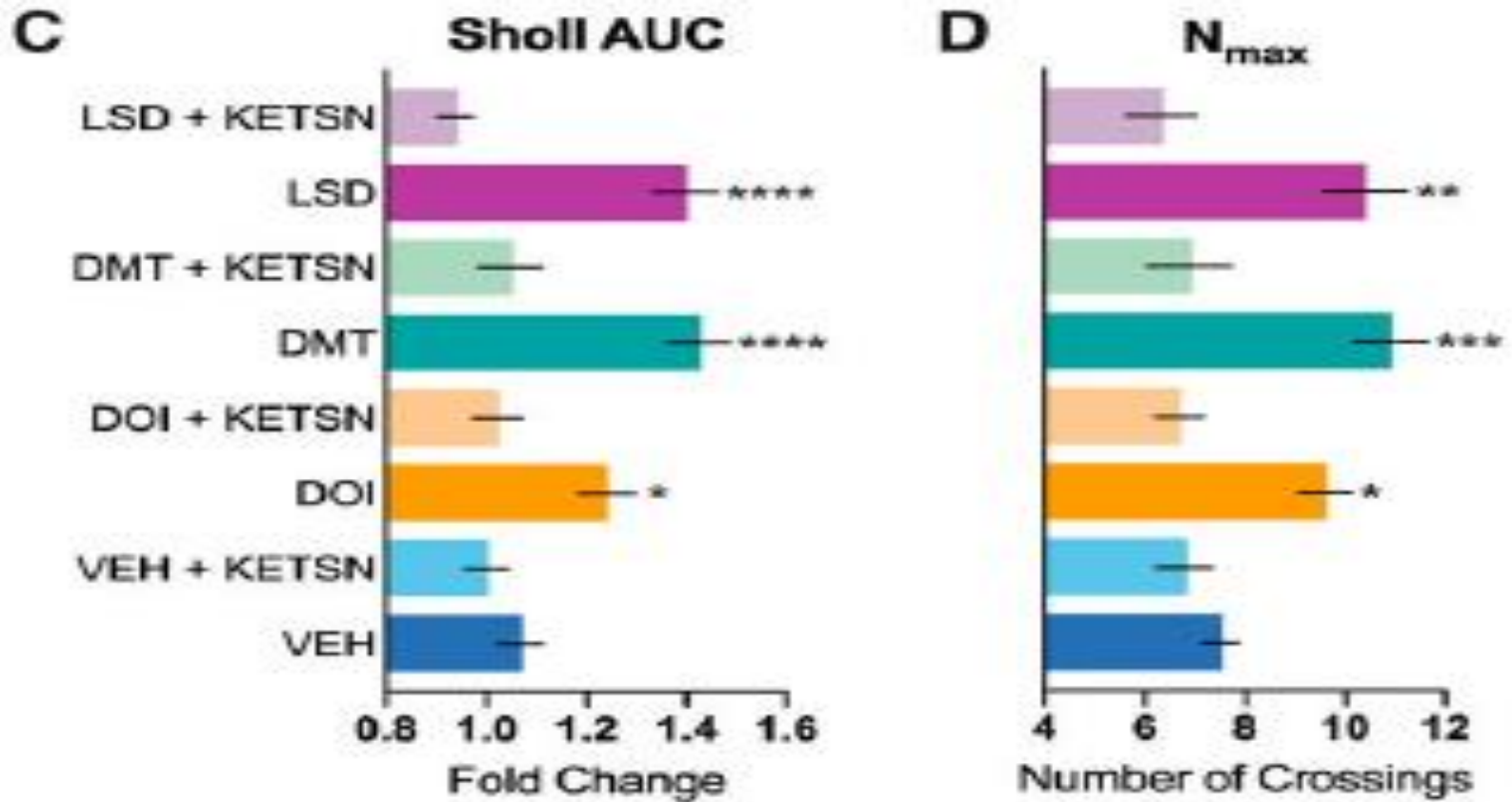


**Figure 1. Psychedelics Promote Neuritogenesis both *In Vitro* and *In Vivo***

# Psychedelics promote spinogenesis, synaptogenesis & functional plasticity in cortical neurons



# 5HT2a receptor mediates effects of psychedelics on structural plasticity



**Dendritic Arbor complexity**

**Ketanserin: 5HT2A inhibitor**

# Mechanisms promoting plasticity

- Down stream effects of psychedelics on **gene expression**
- LSD upregulates several transcripts (i.e. nor1, ania3, egr-2, mkp1, arrdc2) in PFC via 5HT2a activation in animal models (Nichols 2016)
  - Many involved in synaptic plasticity
- **Effects on BDNF**
- Highly expressed in hippocampus & cortex
- Involved in maintenance & survival of neurons
  - Regulation of **synaptic plasticity** (i.e. LTP)
- Formation of new neurons (**neurogenesis**) in hippocampus
- ↑ BDNF → mediated through activation of tropomyosin-related kinase B (**TrkB**) & mammalian target of rapamycin (**mTOR**)
- DOI in rats ↑ BDNF mRNA in frontal, temporal, parietal cortices
- Ayahuasca ↑ serum BDNF in RCT of depressed humans

# Neuroimaging: Psychedelics

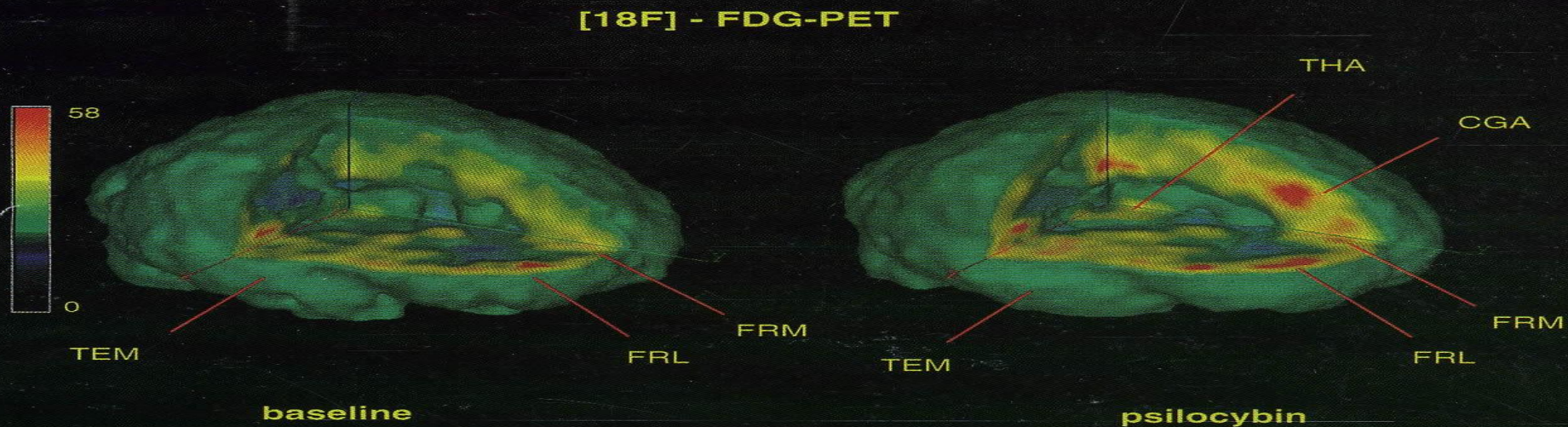
- Acute effects of psychedelics (mescaline, psilocybin, LSD, DMT) have been assessed with respect to
  - Glucose metabolism
  - Blood oxygenation level dependent (BOLD) signal
  - Cerebral blood flow (CBF) using techniques of
    - SPECT
    - PET
    - fMRI
- Different models proposed
  - Hyperfrontality and decreased thalamic gating (Geyer, Vollenweider 2008)
  - Alterations in brain hub functioning (i.e. DMN de-activation) (Carhart-Harris 2012)
- Caveats
  - Few studies
  - Small sample sizes
  - Often different methodological approaches (i.e. PET vs fMRI; oral vs IV administration) making comparison difficult
  - Replication studies scarce and mixed

# Psilocybin: PET Neuroimaging

Positron Emission Tomography and Fluorodeoxyglucose Studies of Metabolic Hyperfrontality and Psychopathology in the Psilocybin Model of Psychosis



*F. X. Vollenweider, M.D., K. L. Leenders, M.D., C. Scharfetter, M.D., P. Maguire, Ph.D., O. Stadelmann, Ph.D., and J. Angst, M.D.*



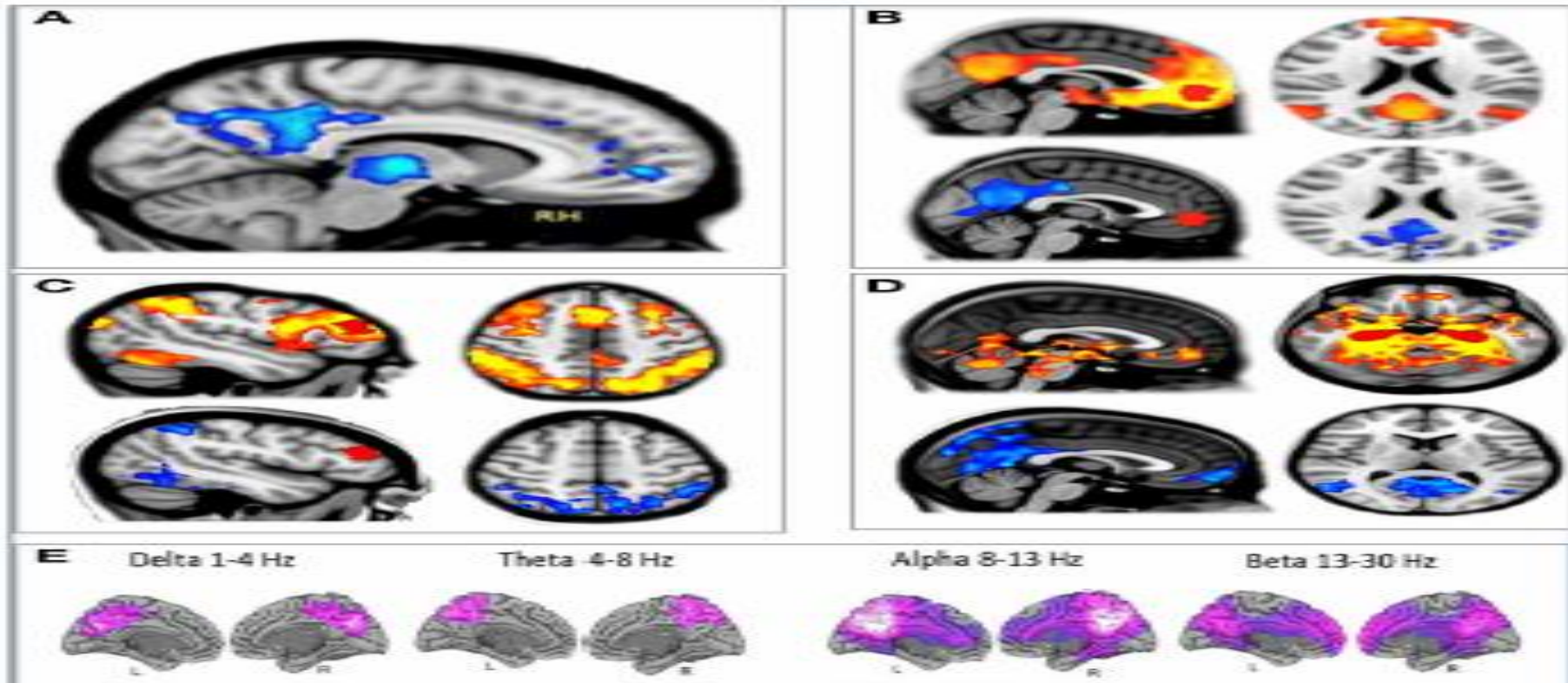


# Psilocybin: PET Neuroimaging

- PFC and temporomedial cortex activation
- Activation of insula
- Decreased thalamic activation
- Sum: **Hyperfrontality & temporal** activation with divergent prefrontal-subcortical activation
  - Increases cognitive & affective processing in context of
  - Reduced gating and
  - Reduced focus on external stimulus processing



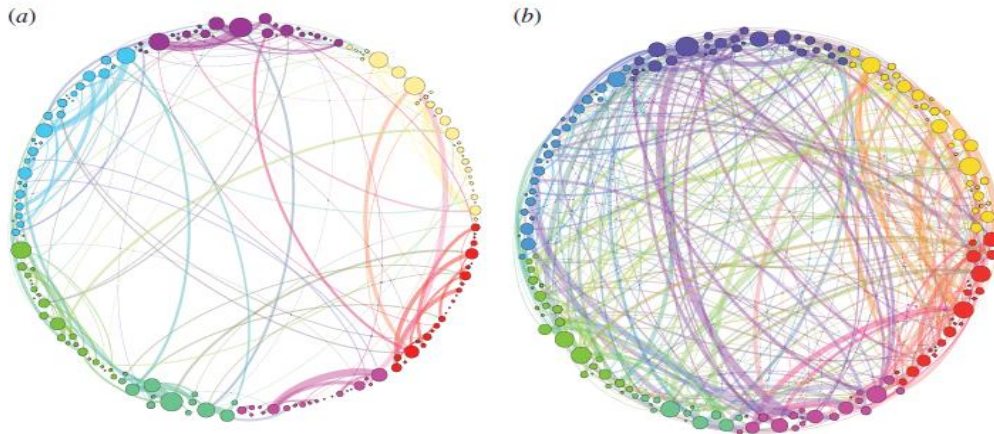
# Imperial College London



**FIGURE 2 | The effect of psilocybin on fMRI and MEG measures of brain activity. (A)** Decreased CBF post-psilocybin. **(B)** Ventromedial PFC (red) resting state functional connectivity (RSFC) at baseline (top, orange) and decreases post-psilocybin (bottom, blue). **(C)** Dorsolateral PFC (red) RSFC at baseline (top, orange) and decreases post-psilocybin (bottom, blue). **(D)** Hippocampal (red) RSFC at baseline (top, orange) and decreases post-psilocybin (bottom, blue). **(E)** Decreases in oscillatory power (purple) post-psilocybin measured with MEG. All spatial maps were whole-brain cluster corrected  $Z > 2.3$ ,  $p < 0.05$ .

# Results from MEG and fMRI studies

- Overall **reduction** in brain activity
  - **Within** (modularity) brain networks, including PFC
  - **Between** (integration) brain networks
  - From fMRI, EEG, MEG data
  - In particular, the **DMN** (i.e. precuneus, mPFC, PCC) is **de-activated**
    - DMN involved in self-referential activities
  - Conflicts with PET/SPECT data on hyperfrontality
- After ‘disintegration’ of brain networks → Re-organization into new local range networks (Petri 2014)
  - Increase repertoire of connectivity motifs within a limbic-paralimbic network

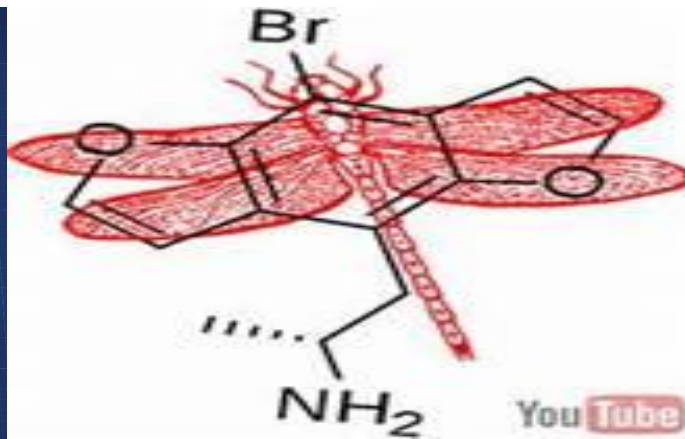
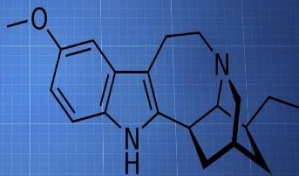


- **Increased plasticity**: Number of transient, distinct brain patterns compared to waking consciousness (Tagliazucchi 2014; Shartner 2017)

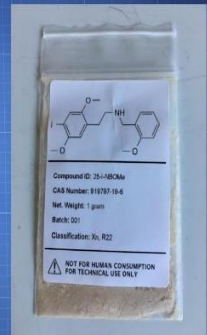
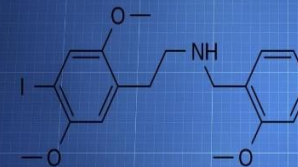
# Physiologic Safety Profile

- **In general**, psychedelics are **safe** drugs from a **physiologic/medical** perspective in humans and not associated with
  - Organ damage
    - Cardiac
    - Neurologic
    - Hepatic
    - Renal
  - Carcinogenicity
  - Teratogenicity
  - Overdose deaths
  - Enduring neuropsychological deficits
- **Exceptions**

## Ibogaine



## 25I-NBOMe



# Psychological Safety Profile: Adverse Events

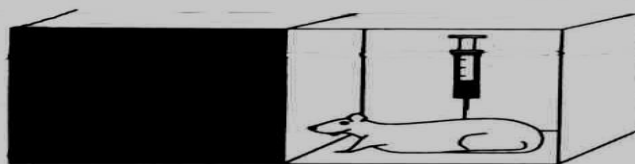
- Acute psychological distress: **‘bad trip’**
- Psychosis
- Hallucinogen Persisting Perceptual Disorder (HPPD)
- Hallucinogen misuse/abuse-- ?Addiction

# Physiological & Psychological Safety Profile: Adverse Events (Summary)

- Modern data: mostly with psilocybin
- Data derived from clinical trials at academic medical centers
  - Open label
  - Dose escalating
  - RCTs
  - Normal volunteers and various sub-populations (i.e. cancer, addiction)
- N=275 participants (Usona IB 2018)
  - **N=579** doses of psilocybin from very low dose (45µg/kg) to very high dose (0.6mg/kg)
- Results → No treatment-related SAEs including **no** reports of
  - Serious **medical toxicity**
  - **Prolonged psychosis**
  - **HPPD** cases
  - Evidence of **Addiction** to hallucinogens or other drugs

# Schedule I

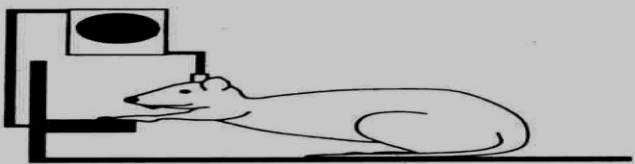
- No currently accepted medical use in the US
- Lack of safety for use under medical supervision
- High potential for Addiction



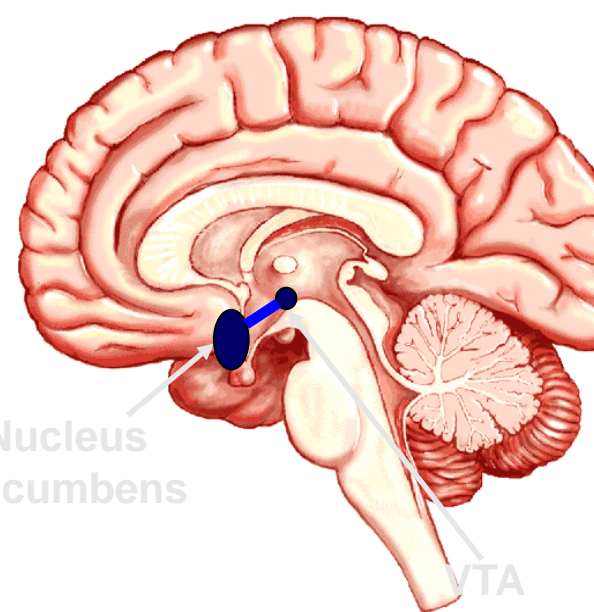
CONDITIONED PLACE PREFERENCE



SELF-ADMINISTRATION



INTRACRANIAL SELF-STIMULATION

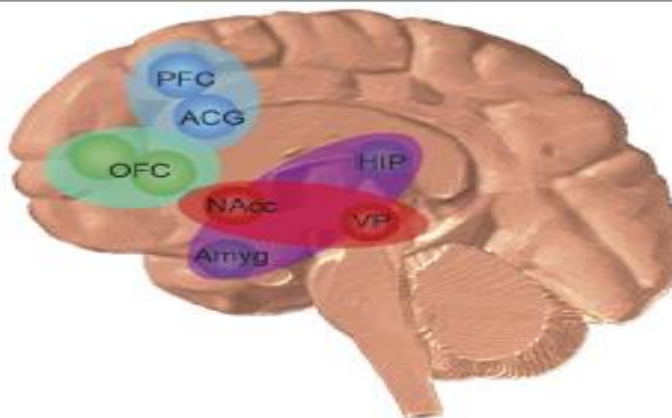


Nucleus accumbens

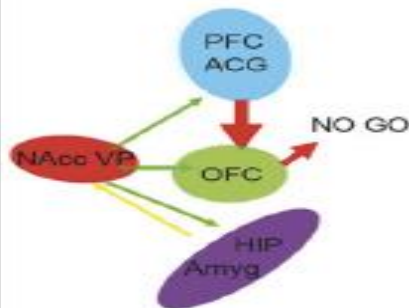
VTA



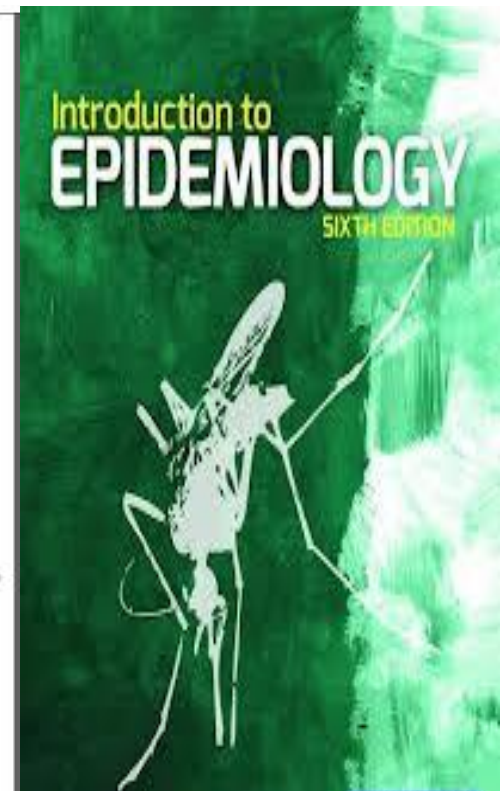
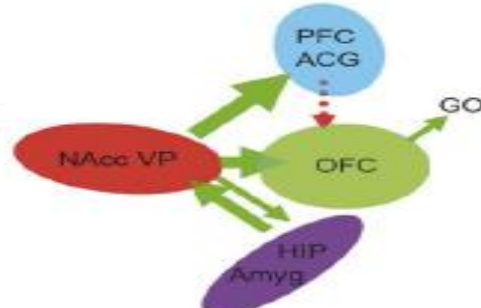
(a)



(b) NON-ADDICTED BRAIN



ADDICTED BRAIN



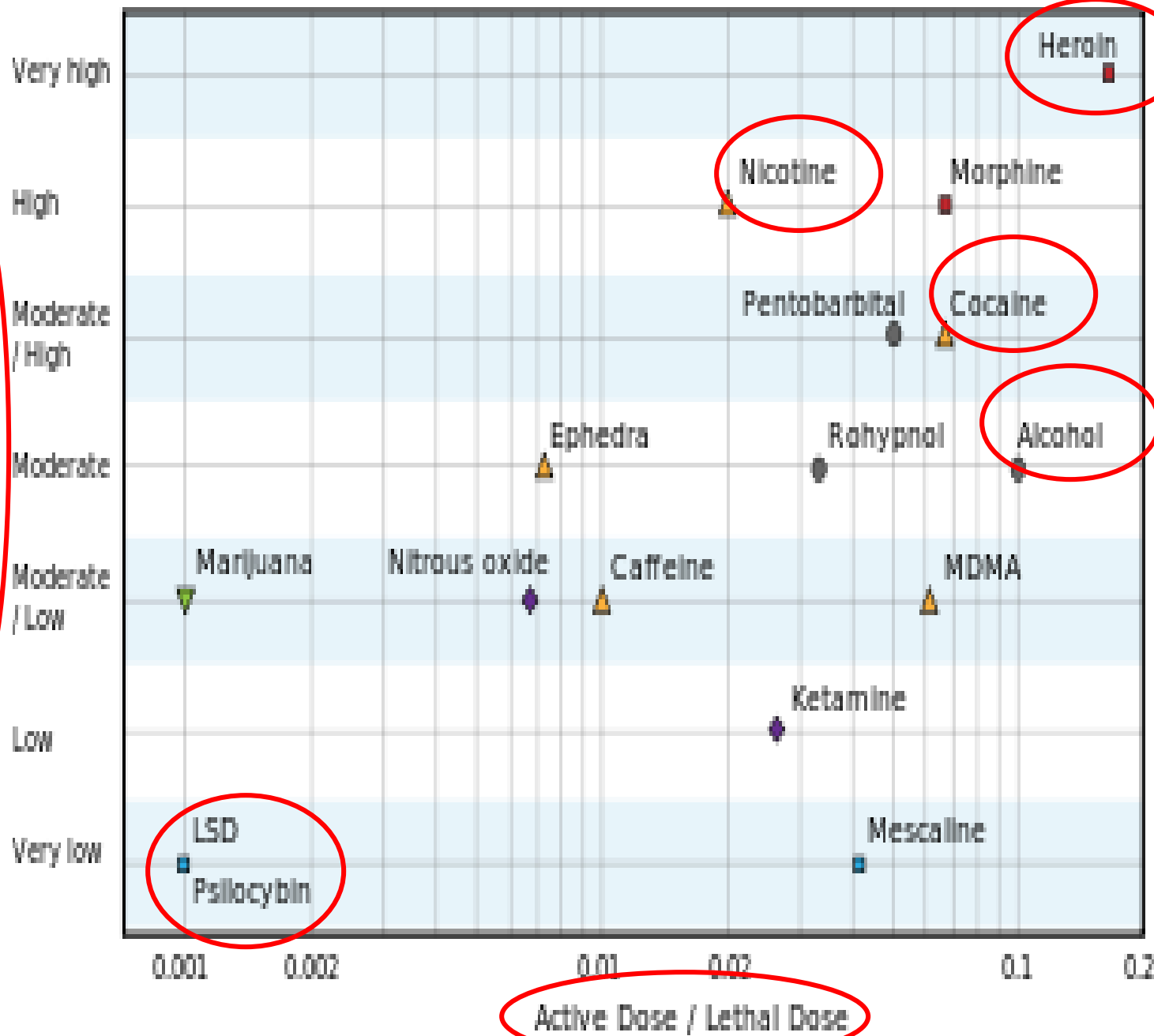


# Preventable Causes of Death

(McGinnis, JAMA, Nov. 10, 1993)

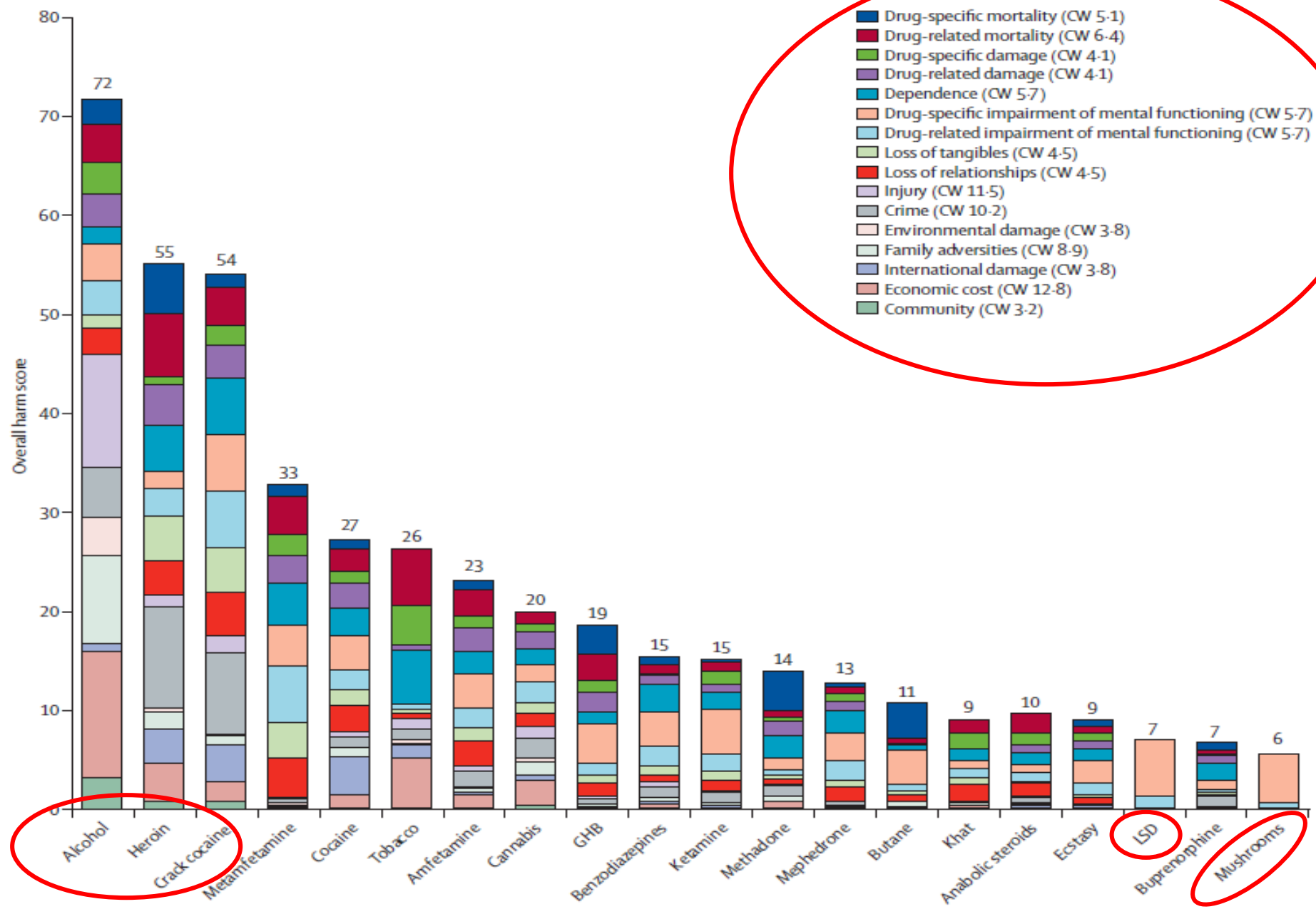
Cause	Estimated No.	% of total Deaths
<b><u>Tobacco</u></b>	<b><u>400,000</u></b>	19
Diet/Activity	300,000	14
<b><u>Alcohol</u></b>	<b><u>100,000</u></b>	5
Microbial Agents	90,000	4
Toxic Agents	60,000	3
Firearms	35,000	2
Sexual Behavior	30,000	1
Motor Vehicles	25,000	1
Illicit Drug Use	25,000	<1
<b>TOTAL</b>	<b>1,060,000</b>	<b>50</b>

Dependence Potential



Legend

- Narcotics
- Depressants
- Stimulants
- Anesthetics
- Hallucinogens
- Cannabis



**Figure 4: Overall weighted scores for each of the drugs**  
 The coloured bars indicate the part scores for each of the criteria. The key shows the normalised weight for each criterion. A higher weight indicates a larger difference between the most harmful drug on the criterion and no harm. CW=cumulative weight. GHB=γ hydroxybutyric acid. LSD=lysergic acid diethylamide.

# Psychiatric Disorders in Cancer

- Major Depression
- Anxiety Spectrum Disorders
- Adjustment Disorders
- Prevalence as high as 30%-40%

# Psychiatric Distress associated with

- ↓ Quality of Life
- ↓ Social Function
- ↑ Disability
- ↓ Medication Compliance
- ↑ ER & hospital visits
- ↑ Desire for Hastened Death
- ↑ Suicide
- ↑ Adverse Medical Outcomes
- ↓ Survival from Cancer

# Evidence-based treatments

- Pharmacologic & Psychosocial treatments commonly used
- No established best practice algorithms of care
- Effectiveness is limited & mixed
- Several meta-analyses of RCTs of anti-depressants (ADs) for cancer-related Depression
  - Failed to demonstrate clear effect AD > Placebo

# Existential Distress

- **Existential ‘Plight’**: Confrontation with existence & non-existence in face of life threatening cancer
- Spectrum of responsivity to diagnosis of advanced/terminal cancer
  - Denial
  - Search for Meaning
    - Victor Frankl
  - **Existential Distress**
    - **Up to 50% of patients with advanced cancer**

# Existential Distress: Facing Death

- Demoralization Syndrome
- Death Anxiety
  
- Absence of purpose or meaning
- Loss of Dignity
- Futility
- Isolation
- Loss of
  - Love
  - Hope
  - Connection
  - Organization
  - Spirituality



# Criteria for Demoralization Syndrome

Kissane, Clarke, & Street, J Palliative Care, 2001; Kissane 2014

**Persisting mental state over two or more weeks as a result of a stressor event, with features of:**

- A. Lowered morale & resultant distress**
- B. Difficulty in coping & meeting expectations of self or others**
- C. 3 (or more) of following symptoms:**
  - 1. Meaninglessness, pointlessness**
  - 2. Hopelessness or helplessness**
  - 3. Loss of purpose, goals**
  - 4. Entrapment, sense of stuckness**
  - 5. Sense of failure & reduced self-worth**
  - 6. Social isolation, aloneness, alienation**
  - 7. Desire to die, Suicidal thoughts &/or plans**
- D. Level of low morale & poor coping cause significant distress or impairment in social, occupational or other functioning**



# Adverse effects of Existential Distress: Cancer

- ↑ Anxiety
- ↑ Depression
- ↑ Desire for Hastened Death (DHD)
- ↑ Suicidal ideation and behavior
- ↑ Pain perception
- ↑ Healthcare visits
- ↓ Quality of Life

# Where do you want to die?

- Hospital
- Nursing home
- Hospice
- Home



# In Search of a Good Death

- Life Review
- Pain and Symptom Management
- Importance of Spirituality and Meaning
- Resolution of Conflicts
- Completion
- Time with family and friends
- Clear Decision Making
- Time for final dialogues
- Preparation for Death

REVIEW ARTICLE

# Therapeutic use of classic psychedelics to treat cancer-related psychiatric distress

Stephen Ross

Department of Psychiatry, New York University Langone Medical Center, Bellevue Hospital Center, New York, NY, USA

## ABSTRACT

Cancer is highly prevalent and one of the leading causes of global morbidity and mortality. Psychological and existential suffering is common in cancer patients, associated with poor psychiatric and medical outcomes. Promising early-phase clinical research (1960s to early 1970s) suggested a therapeutic signal for serotonergic psychedelics (e.g. psilocybin, LSD) in treating cancer-related psychiatric distress. After several decades of quiescence, research on psychedelic-assisted therapy to treat psychiatric disorders in cancer patients has resumed within the last 2 decades in the US and Europe. This review article is based on a systematic search of clinical trials from 1960–2018 researching the therapeutic use of psychedelic treatment in patients with serious or terminal illnesses and related psychiatric illness. The search found 10 eligible clinical trials, with a total of 445 participants, with the vast majority of the patients having advanced or terminal cancer diagnoses. Six open label trials, published between 1964 and 1980 ( $n = 341$ ), suggested that psychedelic therapy (mostly with LSD) may improve cancer-related depression, anxiety, and fear of death. Four RCTs trials were published between 2011 and 2016 ( $n = 104$ ), mostly with psilocybin treatment ( $n = 92$ ), and demonstrated that psychedelic-assisted treatment can produce rapid, robust, and sustained improvements in cancer-related psychological and existential distress.

## ARTICLE

Received  
Accepted

## KEYWORD

Hallucinogen  
anxiety; d  
psilocybin

# Historical Data

- 1960s to early 1970s
- Eric Kast
  - End-of-Life Cancer & Refractory Pain Syndromes
    - Inpatient setting
- Spring Grove
  - Outpatient
  - End-of-Life Cancer



**Dr. Kast**



THE UNIVERSITY OF  
**CHICAGO**  
PRITZKER SCHOOL OF MEDICINE



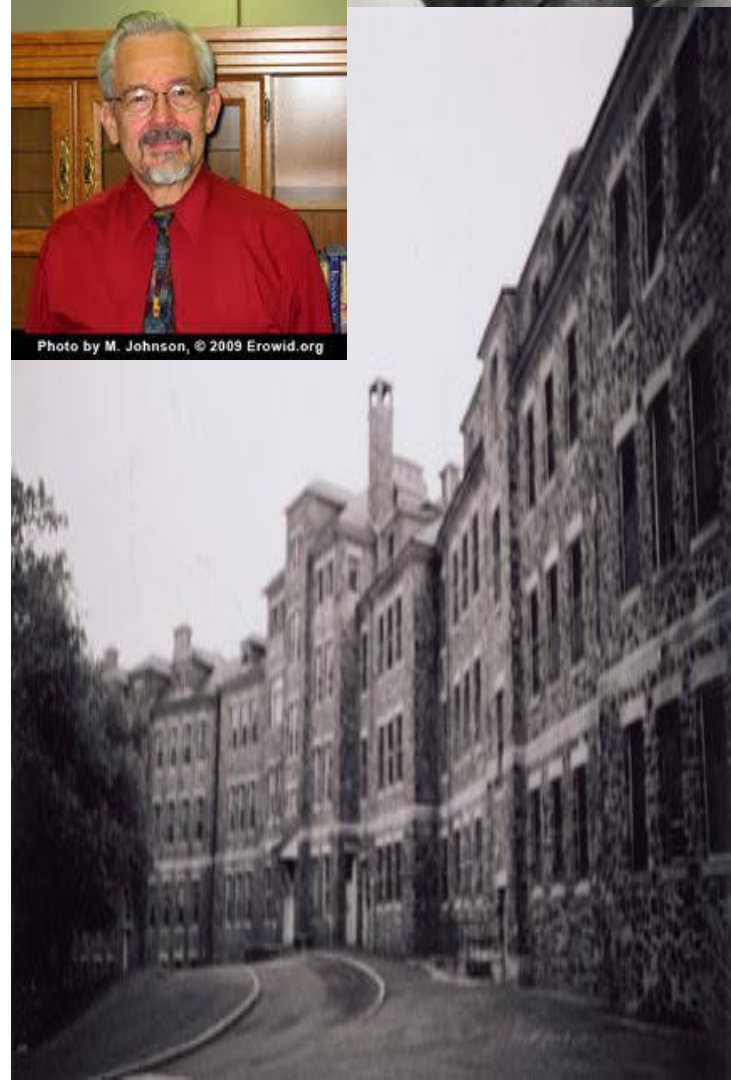


Timeline for Psychedelic Studies at Spring Grove and Maryland Psychiatric Research Center

- 1953-55 Early LSD Study of Schizophrenic Patients at Spring Grove
- 1959 Kurland & Unger Discuss Beginning LSD Psychedelic Research
- 1960 Early Pilot Work Alcoholics & Neurotics
  
- 1963 Preliminary Positive Results Published
  
- 1965 CBS Documentary "The Spring Grove Experiment" Broadcast
- 1966 Pilot Cancer Work Begins  
Report on Six Cancer Patients
- 1967
- 1969 LSD Training Program — Mental Health Professionals Begins  
LSD Inpatient Neurotic — Controlled 350µg vs Hospital Rx  
Maryland Psychiatric Research Center Opens
- 1970 Early LSD Cancer Pilot Study Published
- 1971 LSD & Alcoholics — Controlled 450µg 50µg
- 1972 LSD and Neurosis Controlled Study
- 1973 LSD & Heroin Addicts — Controlled  
Pilot Referred Outpatient Program
- 1975 Pilot DPT with Neurotic Outpatients  
Pilot Neurotic Controlled DPT, Ritalin & Sterile Water
- 1976 Pilot MDA with Staff  
Pilot MDA Neurotic Published  
DPT & Alcoholism Controlled Study Published  
Maryland Psychiatric Research Psychedelic Research Stops
  
- 1980
- 1986
- 1990
- 1991 LSD & Substance Abuse Protocol Approved by FDA
  
- 1997 Cancer work protocol submitted to FDA  
Permission (IND #3250) placed on Clinical Hold by FDA

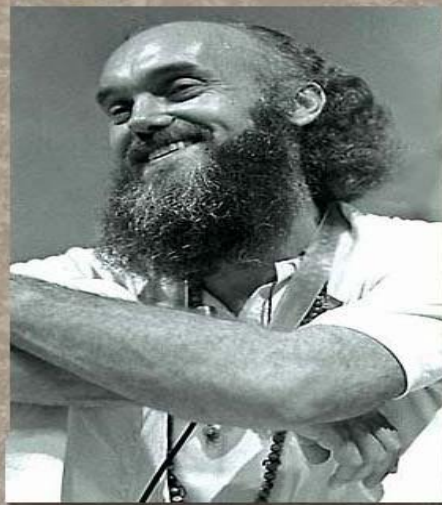


Photo by M. Johnson, © 2009 Erowid.org



# Findings

- N=233 open-label treatment mostly with single-dose LSD
- ↓ Pain
  - Acutely
  - Short-term (i.e. several weeks) sustained
- ↓ Depression
- ↓ Anxiety
- ↓ Fear of Death
- ↑ Philosophical insights
- Induction of mystical states and correlation with improved psychiatric clinical outcomes



# Resumption of Psychedelic Research in Advanced Cancer

- Early 2000 to present
- Phase I-II
- Europe
  - LSD
  - Switzerland
- US
  - Psilocybin
  - Sites
    - UCLA
    - NYULH
    - Johns Hopkins



ONLINE FIRST

# Pilot Study of Psilocybin Treatment for Anxiety in Patients With Advanced-Stage Cancer

Charles S. Grob, MD; Alicia L. Danforth, MA; Gurpreet S. Chopra, MD; Marycie Hagerty, RN, BSN, MA; Charles R. McKay, MD; Adam L. Halberstadt, PhD; George R. Greer, MD

**Context:** Researchers conducted extensive investigations of hallucinogens in the 1950s and 1960s. By the early 1970s, however, political and cultural pressures forced the cessation of all projects. This investigation reexamines a potentially promising clinical application of hallucinogens in the treatment of anxiety reactive to advanced-stage cancer.

**Objective:** To explore the safety and efficacy of psilocybin in patients with advanced-stage cancer and reactive anxiety.

**Design:** A double-blind, placebo-controlled study of patients with advanced-stage cancer and anxiety, with subjects acting as their own control, using a moderate dose (0.2 mg/kg) of psilocybin.

**Setting:** A clinical research unit within a large public sector academic medical center.

**Participants:** Twelve adults with advanced-stage cancer and anxiety.

**Main Outcome Measures:** In addition to monitoring safety and subjective experience before and during experimental treatment sessions, follow-up data including results from the Beck Depression Inventory, Profile

of Mood States, and State-Trait Anxiety Inventory were collected unblinded for 6 months after treatment.

**Results:** Safe physiological and psychological responses were documented during treatment sessions. There were no clinically significant adverse events with psilocybin. The State-Trait Anxiety Inventory trait anxiety subscale demonstrated a significant reduction in anxiety at 1 and 3 months after treatment. The Beck Depression Inventory revealed an improvement of mood that reached significance at 6 months; the Profile of Mood States identified mood improvement after treatment with psilocybin that approached but did not reach significance.

**Conclusions:** This study established the feasibility and safety of administering moderate doses of psilocybin to patients with advanced-stage cancer and anxiety. Some of the data revealed a positive trend toward improved mood and anxiety. These results support the need for more research in this long-neglected field.

**Trial Registration:** [clinicaltrials.gov](http://clinicaltrials.gov) Identifier: NCT00302744

*Arch Gen Psychiatry.* Published online September 6, 2010.  
doi:10.1001/archgenpsychiatry.2010.116

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

Roland R Griffiths<sup>1,2</sup>, Matthew W Johnson<sup>1</sup>, Michael A Carducci<sup>3</sup>, Annie Umbricht<sup>1</sup>, William A Richards<sup>1</sup>, Brian D Richards<sup>1</sup>, Mary P Cosimano<sup>1</sup> and Margaret A Klinedinst<sup>1</sup>

*Journal of Psychopharmacology*  
2016, Vol. 30(12) 1181–1197  
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DOI: 10.1177/0269881116675513  
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## Abstract

Cancer patients often develop chronic, clinically significant symptoms of depression and anxiety. Previous studies suggest that psilocybin may decrease depression and anxiety in cancer patients. The effects of psilocybin were studied in 51 cancer patients with life-threatening diagnoses and symptoms of depression and/or anxiety. This randomized, double-blind, cross-over trial investigated the effects of a very low (placebo-like) dose (1 or 3 mg/70 kg) vs. a high dose (22 or 30 mg/70 kg) of psilocybin administered in counterbalanced sequence with 5 weeks between sessions and a 6-month follow-up. Instructions to participants and staff minimized expectancy effects. Participants, staff, and community observers rated participant moods, attitudes, and behaviors throughout the study. High-dose psilocybin produced large decreases in clinician- and self-rated measures of depressed mood and anxiety, along with increases in quality of life, life meaning, and optimism, and decreases in death anxiety. At 6-month follow-up, these changes were sustained, with about 80% of participants continuing to show clinically significant decreases in depressed mood and anxiety. Participants attributed improvements in attitudes about life/self, mood, relationships, and spirituality to the high-dose experience, with >80% endorsing moderately or greater increased well-being/life satisfaction. Community observer ratings showed corresponding changes. Mystical-type psilocybin experience on session day mediated the effect of psilocybin dose on therapeutic outcomes.

# Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial

Stephen Ross<sup>1,2,3,4,5,6</sup>, Anthony Bossis<sup>1,2,4</sup>, Jeffrey Guss<sup>1,2,4</sup>, Gabrielle Agin-Liebes<sup>10</sup>, Tara Malone<sup>1</sup>, Barry Cohen<sup>7</sup>, Sarah E Mennenga<sup>1</sup>, Alexander Belser<sup>8</sup>, Krystallia Kalliontzi<sup>2</sup>, James Babb<sup>9</sup>, Zhe Su<sup>3</sup>, Patricia Corby<sup>2</sup> and Brian L Schmidt<sup>2</sup>

## Abstract

**Background:** Clinically significant anxiety and depression are common in patients with cancer, and are associated with poor psychiatric and medical outcomes. Historical and recent research suggests a role for psilocybin to treat cancer-related anxiety and depression.

**Methods:** In this double-blind, placebo-controlled, crossover trial, 29 patients with cancer-related anxiety and depression were randomly assigned and received treatment with single-dose psilocybin (0.3 mg/kg) or niacin, both in conjunction with psychotherapy. The primary outcomes were anxiety and depression assessed between groups prior to the crossover at 7 weeks.

**Results:** Prior to the crossover, psilocybin produced immediate, substantial, and sustained improvements in anxiety and depression and led to decreases in cancer-related demoralization and hopelessness, improved spiritual wellbeing, and increased quality of life. At the 6.5-month follow-up, psilocybin was associated with enduring anxiolytic and anti-depressant effects (approximately 60–80% of participants continued with clinically significant reductions in depression or anxiety), sustained benefits in existential distress and quality of life, as well as improved attitudes towards death. The psilocybin-induced mystical experience mediated the therapeutic effect of psilocybin on anxiety and depression.

**Conclusions:** In conjunction with psychotherapy, single moderate-dose psilocybin produced rapid, robust and enduring anxiolytic and anti-depressant effects in patients with cancer-related psychological distress.

Trial Registration: ClinicalTrials.gov Identifier: NCT00957359



*Journal of Psychopharmacology*

2016, Vol. 30(12) 1165–1180

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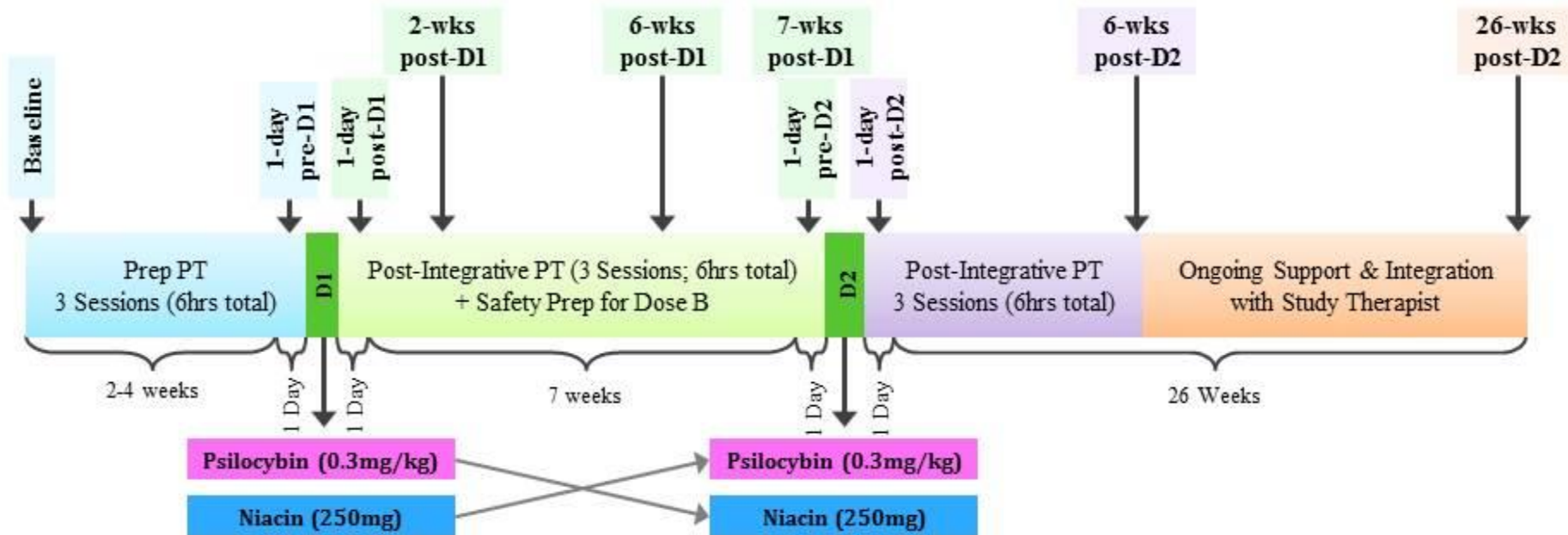
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DOI: 10.1177/0269881116675512

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Assessment Schedule		Baseline	1-day pre-Dose 1	Dose 1	1-day post-Dose 1	2-wks post-Dose 1	6-wks post-Dose 1	7-wks post-Dose 1 1-day pre-Dose 2	Dose 2	1-day post-Dose 2	6-wks post-Dose 2	26-wks post-Dose 2
Safety Assessments	Adverse Events	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	BP/HR	✓		✓					✓			
Primary Outcomes	Depression/Anxiety	✓	✓		✓	✓	✓	✓		✓	✓	✓
Secondary Outcomes	Existential Distress	✓				✓						✓
	Quality of Life	✓				✓						✓
	Spirituality	✓				✓						✓
	Persisting Effects of Psilocybin					✓						✓
	Mystical Experience			✓					✓			✓

Characteristics	Categories	Psilocybin <sup>a</sup> 1 <sup>st</sup>		Niacin <sup>b</sup> 1 <sup>st</sup>		Total	
		n=14		n = 15		n = 29	
Sex	<b>female</b>	7	50%	11	73%	18	<b>62%</b>
	male	7	50%	4	27%	11	38%
Age; mean (SD)	Range 22-75	52 (15.03)		60.27 (9.45)		<b>56.28</b> (12.93)	
Race	<b>White/ Caucasian</b>	13	93%	13	87%	26	<b>90%</b>
	Black/ African American	0	0%	0	0%	0	0%
	Hispanic/ Latino	0	0%	0	0%	0	0%
	Asian	0	0%	0	0%	0	0%
	American Indian/ Native American	0	0%	0	0%	0	0%
	Other	1	7%	2	13%	3	10%
Religious/ Spiritual Beliefs	<b>Atheist/ Agnostic</b>	4	29%	10	67%	14	<b>48%</b>
	Jewish	4	29%	1	7%	5	17%
	Catholic	2	14%	0	0%	2	7%
	Other Christian	3	21%	1	7%	4	14%
	Other Faith/ Tradition	1	7%	3	20%	4	14%
Site of Cancer	<b>Breast</b>	4	29%	5	33%	9	<b>31%</b>
	<b>Reproductive</b>	3	21%	5	33%	8	<b>28%</b>
	Digestive Cancers	3	21%	2	13%	5	17%
	Lymphoma/ Leukemia	2	14%	2	13%	4	14%
	Other Types	2	14%	1	7%	3	10%

Characteristic	Categories	Psilocybin <sup>a</sup> 1 <sup>st</sup>		Niacin <sup>b</sup> 1 <sup>st</sup>		Total	
		n=14		n = 15		n = 29	
Stage of Cancer	<b><u>Stage IV</u></b>	3	21%	7	47%	10	<b><u>34%</u></b>
	<b><u>Stage III</u></b>	4	29%	4	27%	8	<b><u>28%</u></b>
	Stage II	1	7%	4	27%	5	17%
	Stage I	5	36%	0	0%	5	17%
	Other	1	7%	0	0%	1	3%
SCID (DSM-IV) Diagnosis	Adjustment Disorder w/ anxiety & depressed mood, chronic	2	14%	6	40%	8	28%
	Adjustment Disorder w/anxiety, chronic	10	71%	8	53%	18	62%
	Generalized Anxiety Disorder	2	14%	1	7%	3	10%
Hallucinogen Use	<b><u>No</u></b>	7	50%	6	40%	13	<b><u>45%</u></b>
	Yes	7	50%	9	60%	16	55%

# Adverse Events (AEs)

- **Medical**

- Mild elevations in blood pressure 76%
- Headache/migraine: 28%
- Nausea: 14%

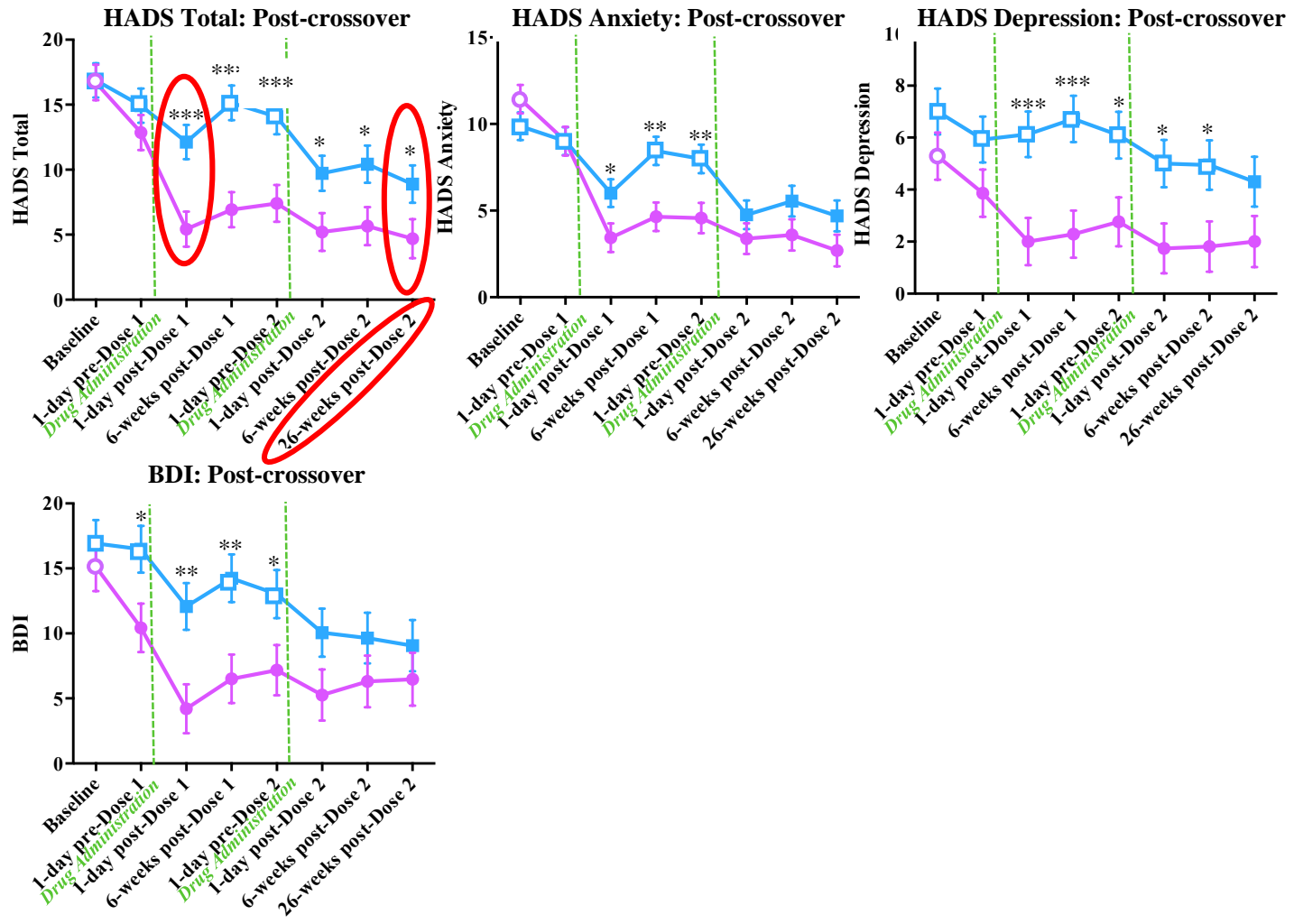
- **Psychiatric**

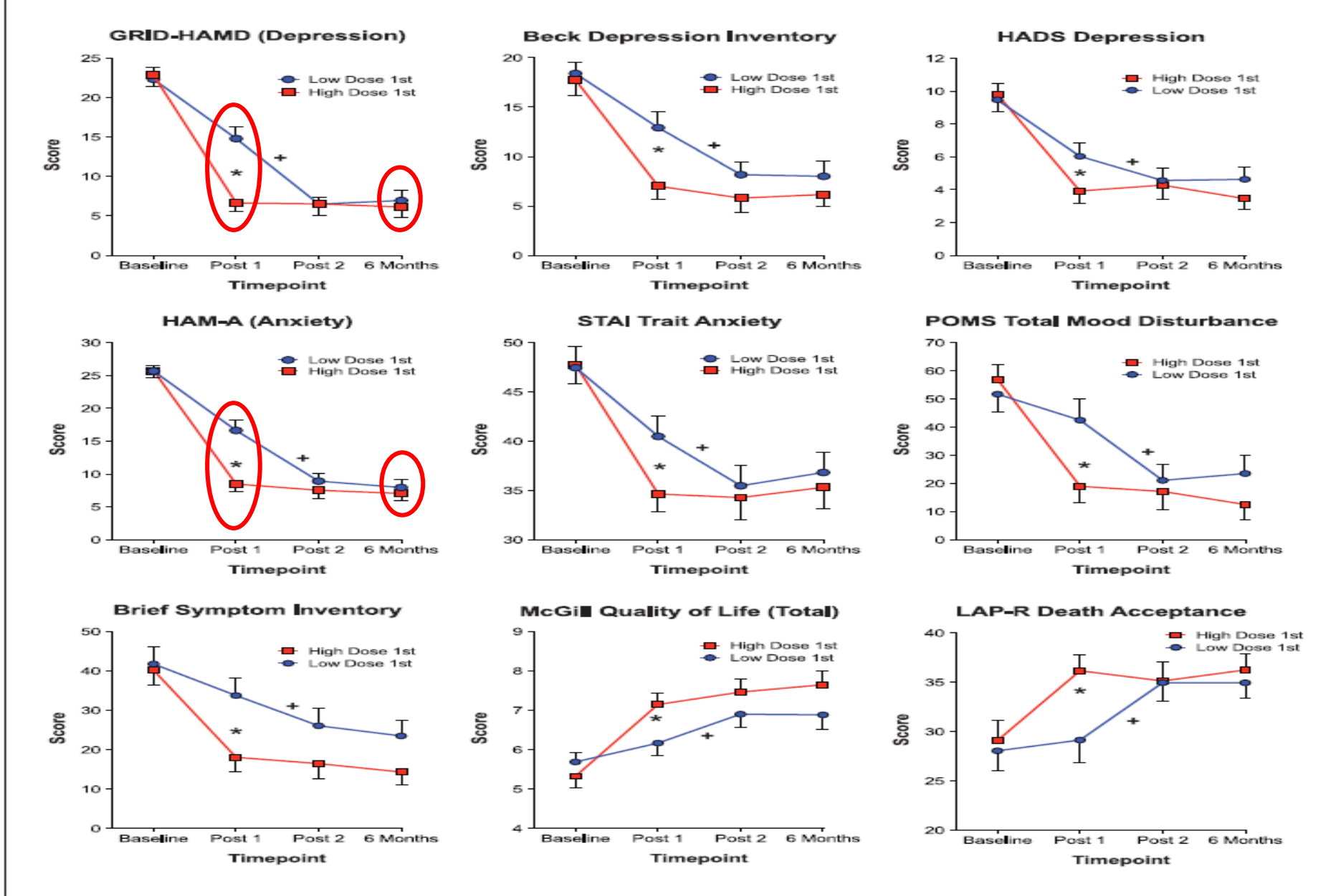
- Transient anxiety: 17%
- Transient psychotic-like symptoms: 7%

- **Serious Adverse Events (SAEs)**

- Medical: *None*
- Psychiatric *None*
  - No need for pharmacologic interventions
  - No Psychosis
  - No psychiatric hospitalizations
  - No HPPD

# Rapid & Sustained Anti-depressant & Anxiolytic Effects

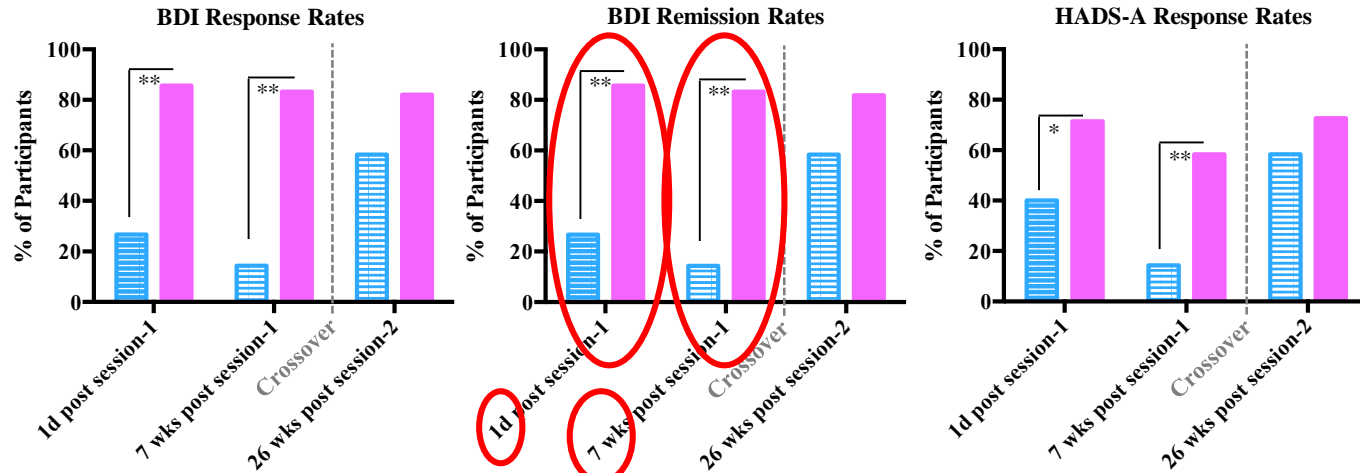


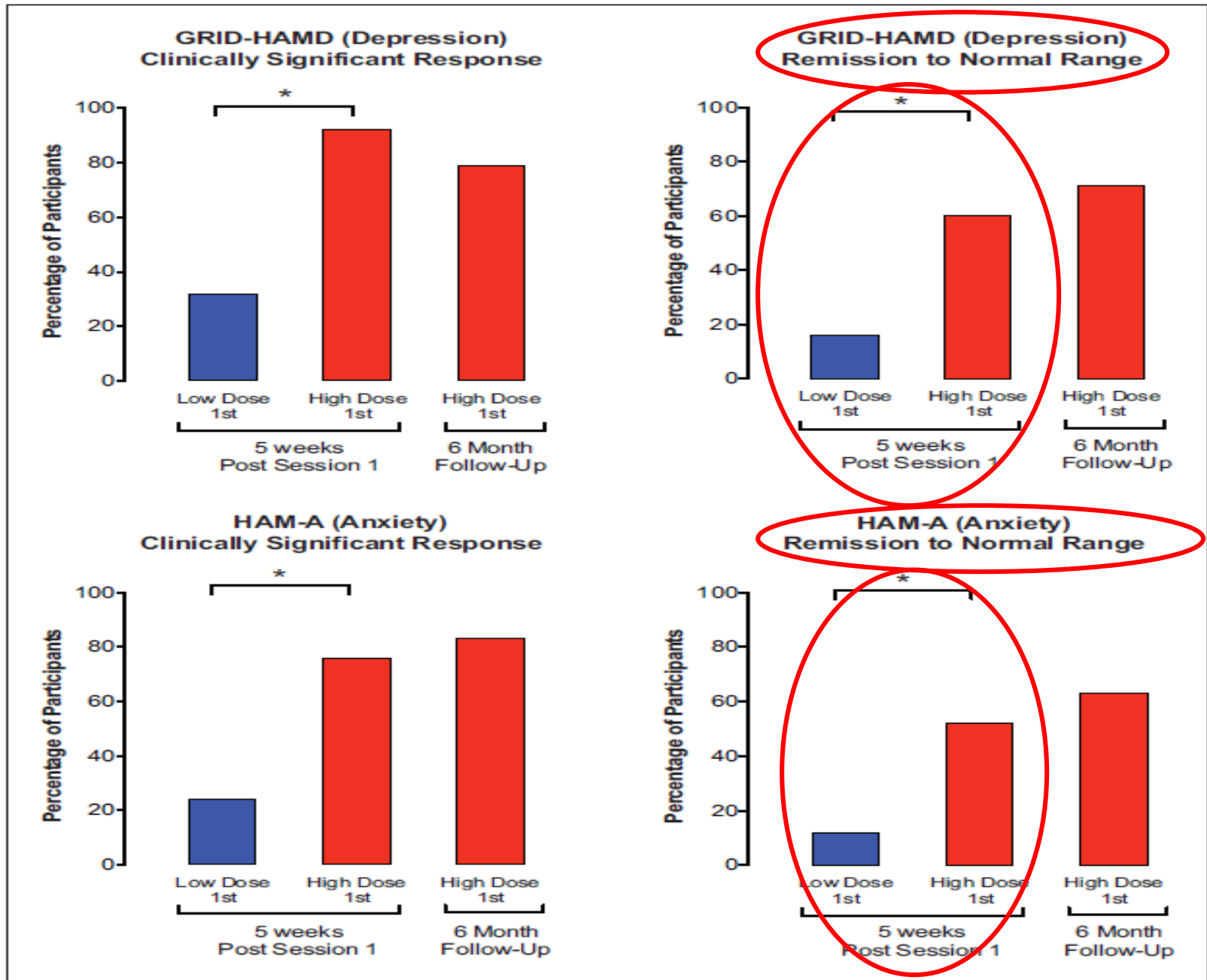


**Figure 3.** Effects of psilocybin on selected outcome measures that were assessed at Baseline, Post-session 1 (5 weeks after Session 1), Post-session 2 (5 weeks after Session 2), and 6-month follow-up. Data points show means; brackets indicate 1 SEM; circles represent the group that received a low dose on the 1st session and a high dose on the 2nd session ( $n = 25, 25, 24,$  and  $22$  at Baseline, Post-session 1, Post-session 2, and 6 months, respectively); squares represent the group that received a high dose on 1st session and a low dose on the 2nd session ( $n = 26, 26, 25,$  and  $24$  at Baseline, Post-session 1, Post-session 2, and 6 months, respectively). Star symbol indicates a significant difference between the two groups at the Post-session 1 time-point ( $p < 0.05$ , planned comparison). Cross symbol indicates a significant difference between the Post-session 1 and Post-session 2 time-points in the Low-Dose-1st (High-Dose-2nd) Group ( $p < 0.05$ , planned comparison).

# Clinically Significant Anti-depressant and Anxiolytic response and remission rates

Response/Remission Rates by Treatment Group



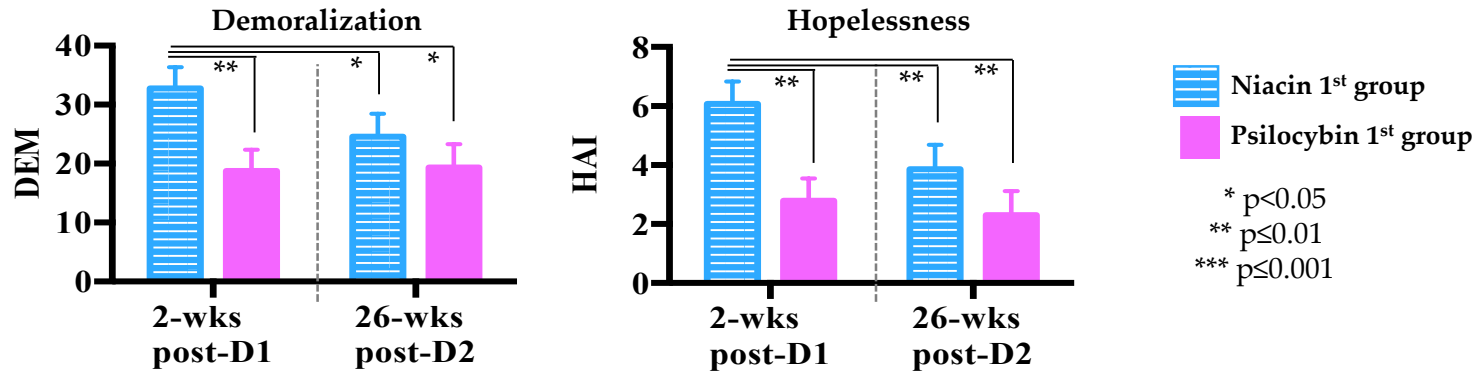


**Figure 4.** Effects of psilocybin on clinically significant response rate and symptom remission rate as assessed with clinician-rated measures of depression and anxiety. Data are percentage of participants fulfilling criteria at Post-session 1 (5 weeks after Session 1) and at 6 months. Asterisks indicates that the low and high-dose groups were significantly different at 5 weeks ( $p > 0.001$ ); data at 6 months show these effects were sustained at follow-up. See Table 6 for other details.

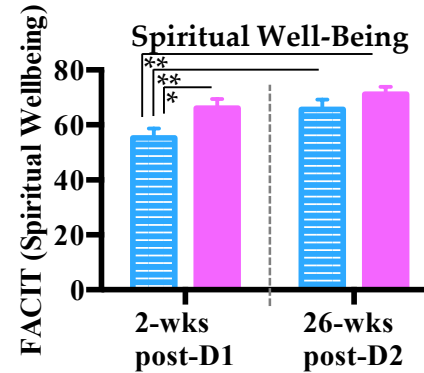


# Psilocybin led to acute and sustained

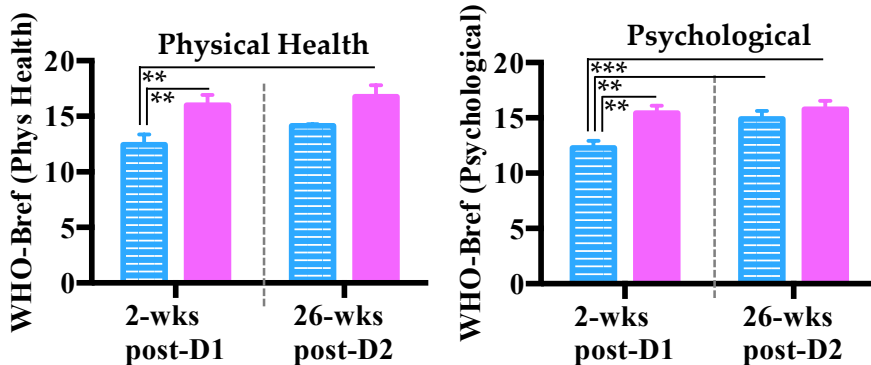
↓ cancer-related demoralization and hopelessness:



↑ spiritual well-being



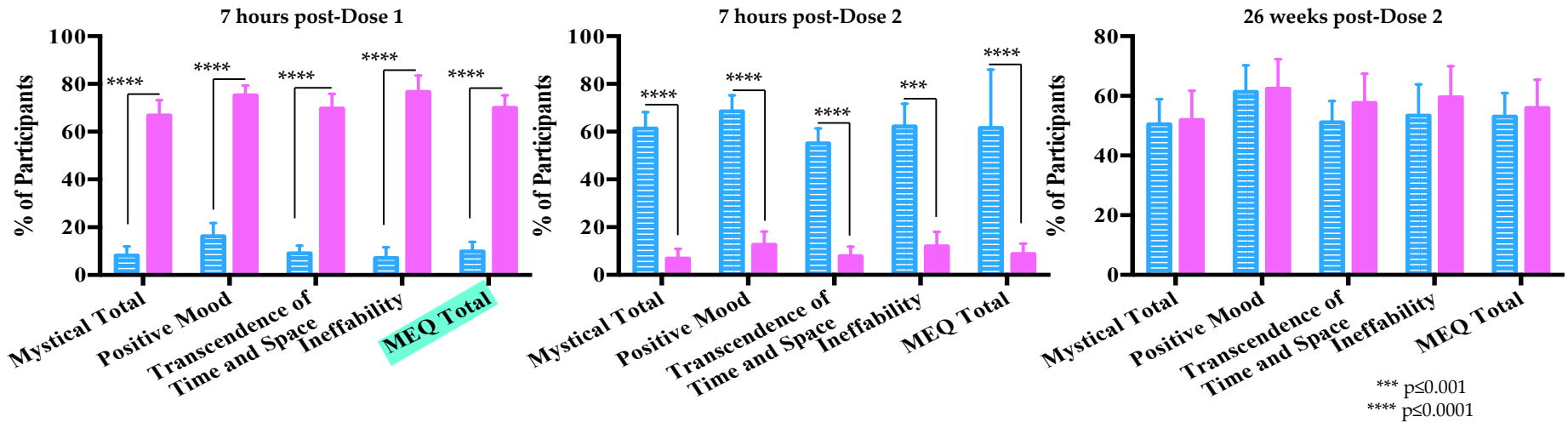
↑ quality of life:



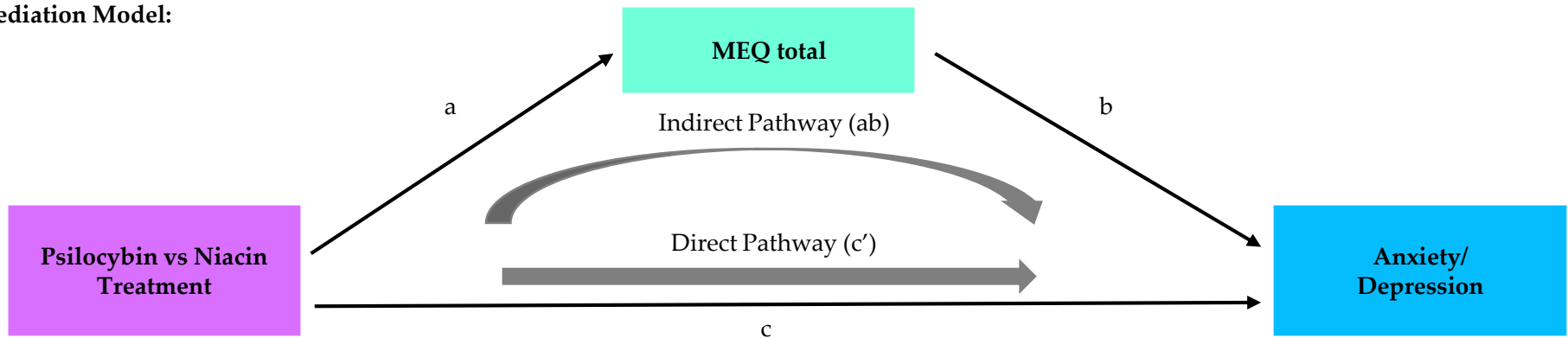
...compared to placebo medication

# Scores on the Mystical Experience Questionnaire mediated the impact of psilocybin treatment on anxiety/depression measures: potential psychological mechanism of action

MEQ Factor Scores by Treatment Group



## Mediation Model:



ab = Indirect effect of psilocybin on anxiety/depression mediated by mystical experience  
c' = Direct effect of psilocybin on anxiety/depression not mediated by mystical experience

# Long-term follow-up of psilocybin-assisted psychotherapy for psychiatric and existential distress in patients with life-threatening cancer

Gabrielle I Agin-Liebes<sup>1,2</sup> , Tara Malone<sup>2,3</sup>, Matthew M Yalch<sup>1</sup>, Sarah E Mennenga<sup>2</sup>, K Linnae Ponté<sup>4</sup>, Jeffrey Guss<sup>2,3,5</sup>, Anthony P Bossis<sup>2,3,5</sup>, Jim Grigsby<sup>6,7</sup>, Stacy Fischer<sup>6,7</sup> and Stephen Ross<sup>2,3,5</sup>

Psychopharm

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2020, Vol. 34(2) 155–166

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DOI: 10.1177/0269888119897615

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## Abstract

**Background:** A recently published randomized controlled trial compared single-dose psilocybin with single-dose niacin in conjunction with psychotherapy in participants with cancer-related psychiatric distress. Results suggested that psilocybin-assisted psychotherapy facilitated improvements in psychiatric and existential distress, quality of life, and spiritual well-being up to seven weeks prior to the crossover. At the 6.5-month follow-up, after the crossover, 60–80% of participants continued to meet criteria for clinically significant antidepressant or anxiolytic responses.

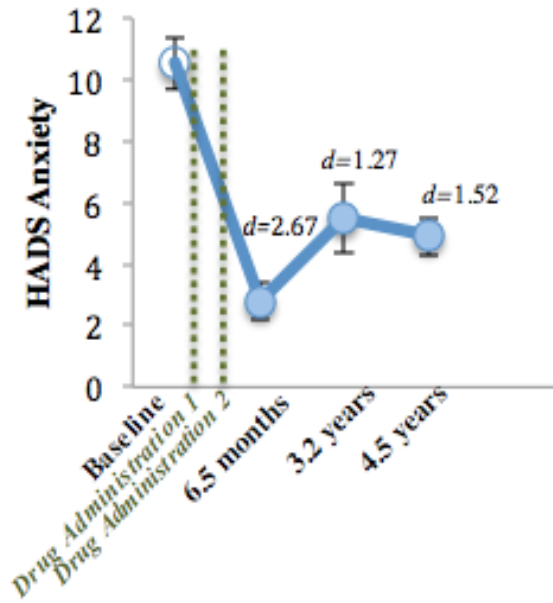
**Methods:** The present study is a long-term within-subjects follow-up analysis of self-reported symptomatology involving a subset of participants that completed the parent trial. All 16 participants who were still alive were contacted, and 15 participants agreed to participate at an average of 3.2 and 4.5 years following psilocybin administration.

**Results:** Reductions in anxiety, depression, hopelessness, demoralization, and death anxiety were sustained at the first and second follow-ups. Within-group effect sizes were large. At the second (4.5 year) follow-up approximately 60–80% of participants met criteria for clinically significant antidepressant or anxiolytic responses. Participants overwhelmingly (71–100%) attributed positive life changes to the psilocybin-assisted therapy experience and rated it among the most personally meaningful and spiritually significant experiences of their lives.

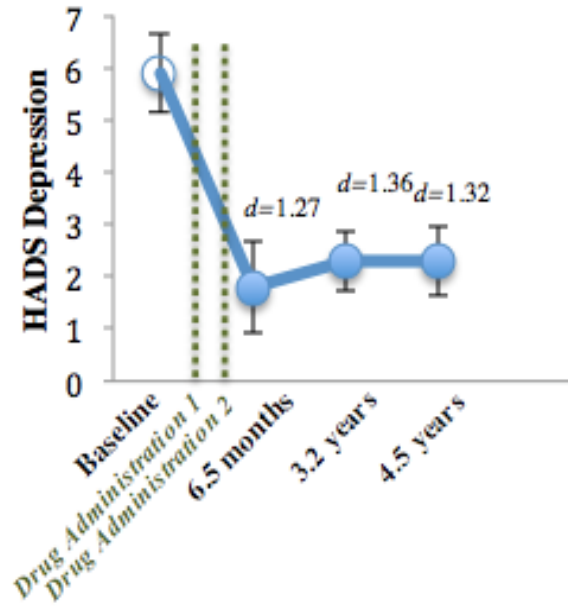
**Conclusion:** These findings suggest that psilocybin-assisted psychotherapy holds promise in promoting long-term relief from cancer-related psychiatric distress. Limited conclusions, however, can be drawn regarding the efficacy of this therapy due to the crossover design of the parent study. Nonetheless, the present study adds to the emerging literature base suggesting that psilocybin-facilitated therapy may enhance the psychological, emotional, and spiritual well-being of patients with life-threatening cancer.

# Long-term sustained improvements in depression and anxiety following single-dose psilocybin intervention

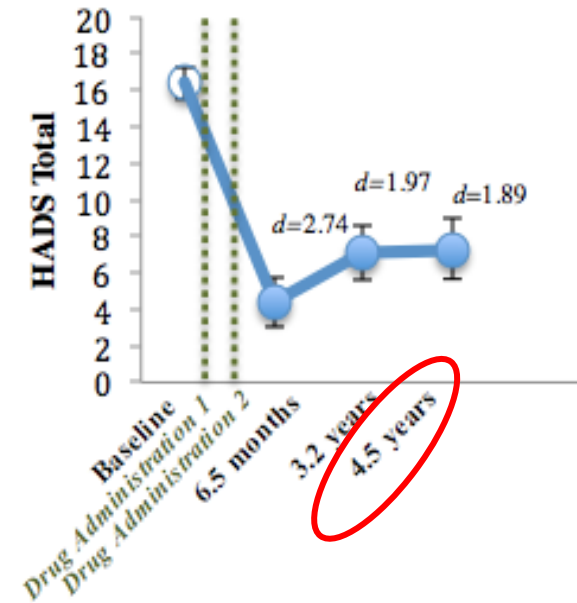
### HADS Anxiety



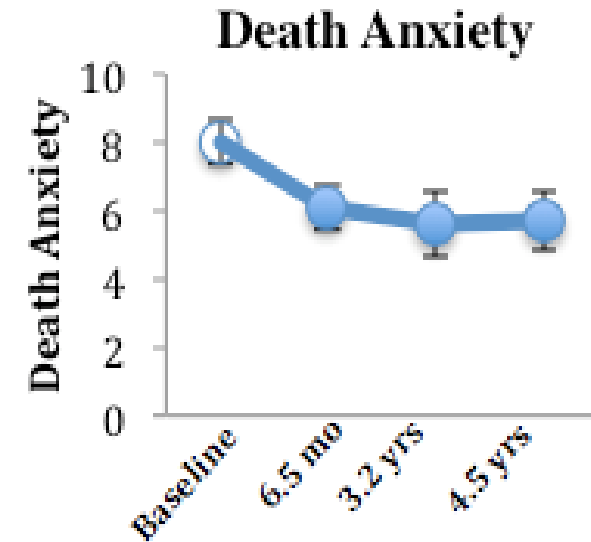
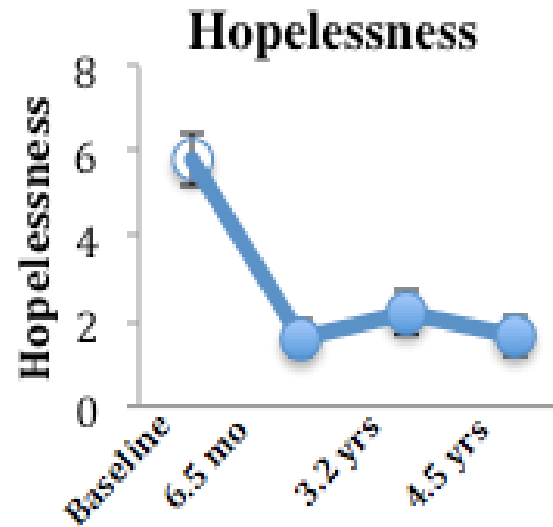
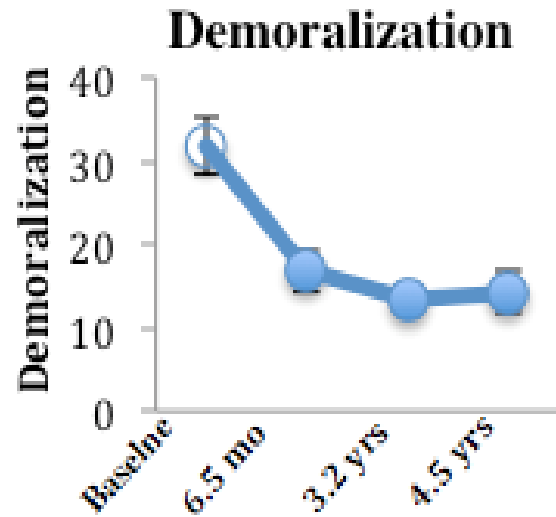
### HADS Depression



### HADS Total



# Long-term sustained improvements in existential distress following single-dose psilocybin intervention



<u>PEQ (% of max score)</u>	Psilo attribution <u>6.5 months</u> post dose-2 <sup>a</sup>	Psilo attribution <u>4.5 years</u> post dose-2 <sup>a</sup>
	N=23	N=14
Top 5 <u>most meaningful</u> , including single most (%)	<b>70</b>	<b>71</b>
Top 5 most <u>spiritually</u> <u>significant</u> , including single most (%)	<b>52</b>	<b>96</b>
Increased <u>well-being</u> moderately or very much (%)	<b>87</b>	<b>86</b>

# Acute and Sustained Reductions in Loss of Meaning and Suicidal Ideation Following Psilocybin-Assisted Psychotherapy for Psychiatric and Existential Distress in Life-Threatening Cancer

Stephen Ross,\* Gabrielle Agin-Liebes, Sharon Lo, Richard J. Zeifman, Leila Ghazal, Julia Benville, Silvia Franco Corso, Christian Bjerre Real, Jeffrey Guss, Anthony Bossis, and Sarah E. Mennenga

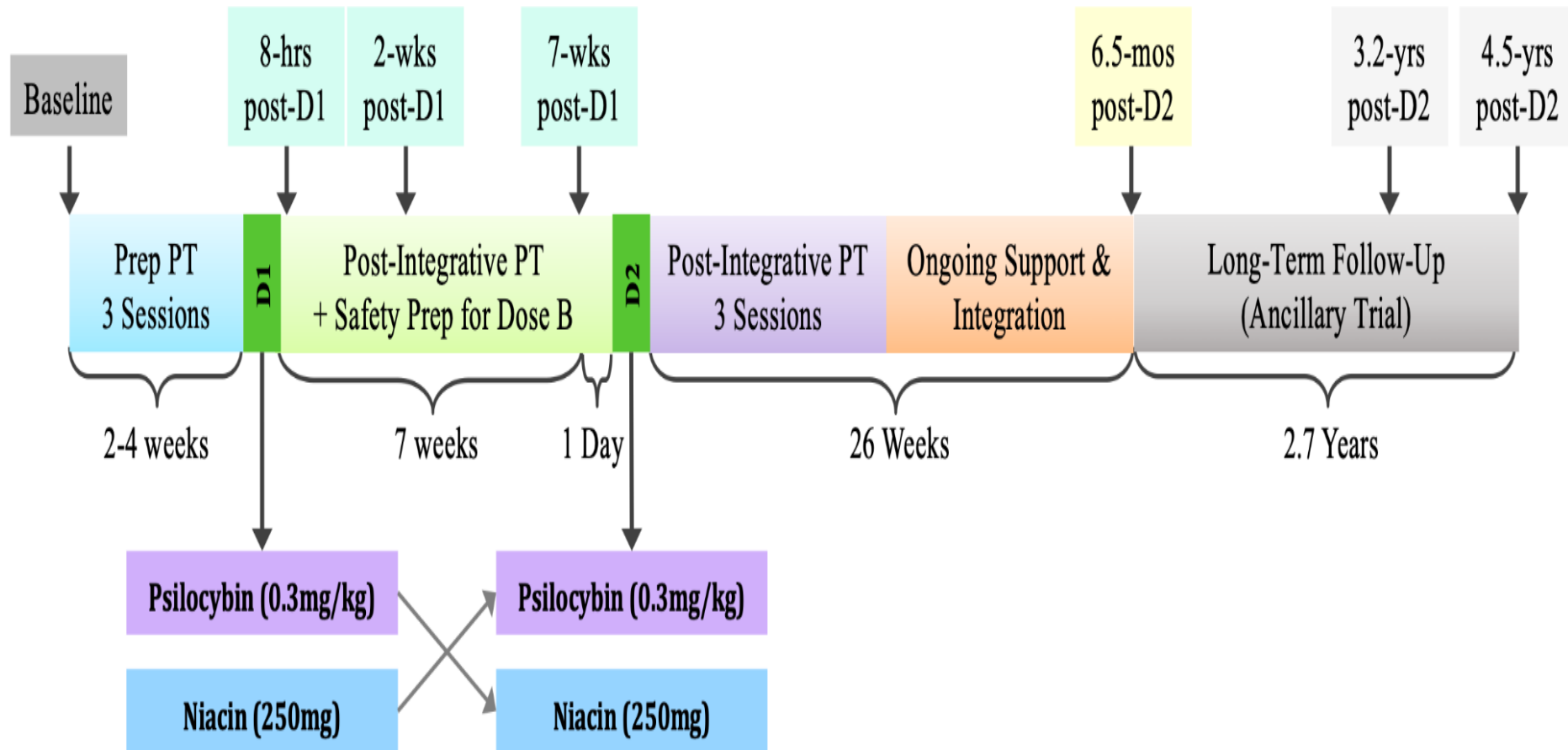


Cite This: <https://doi.org/10.1021/acsptscl.1c00020>

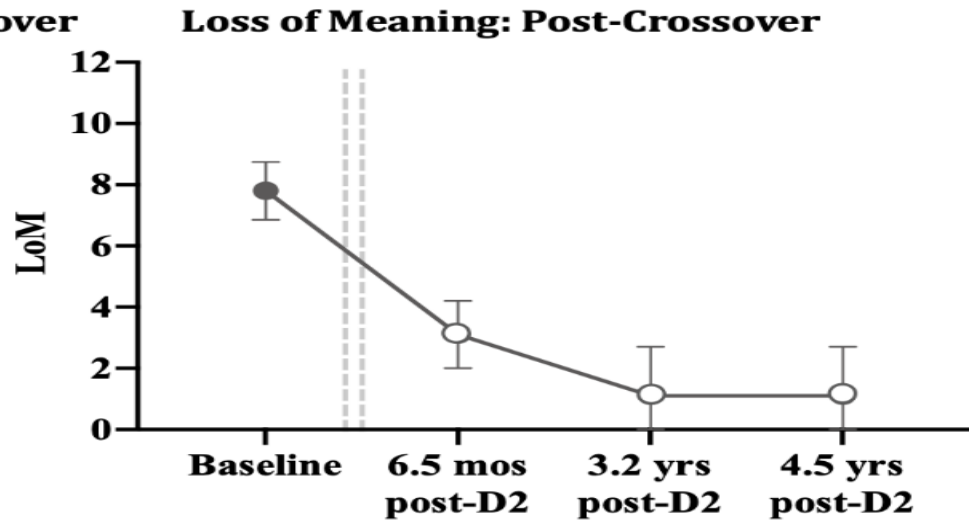
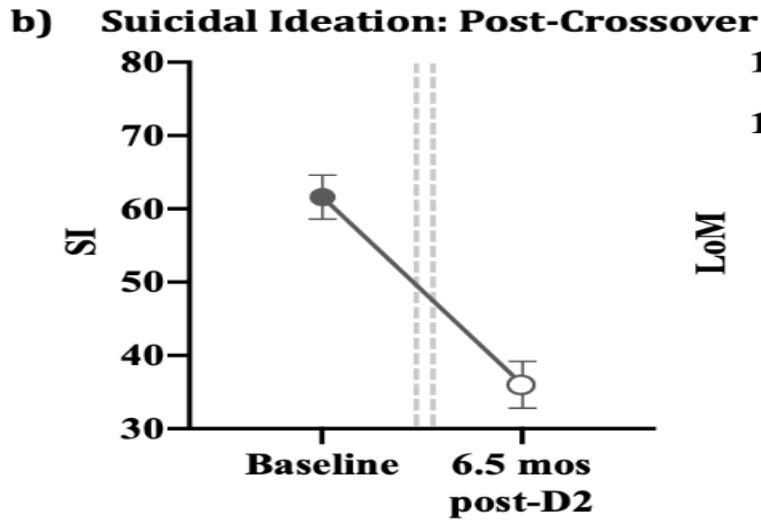
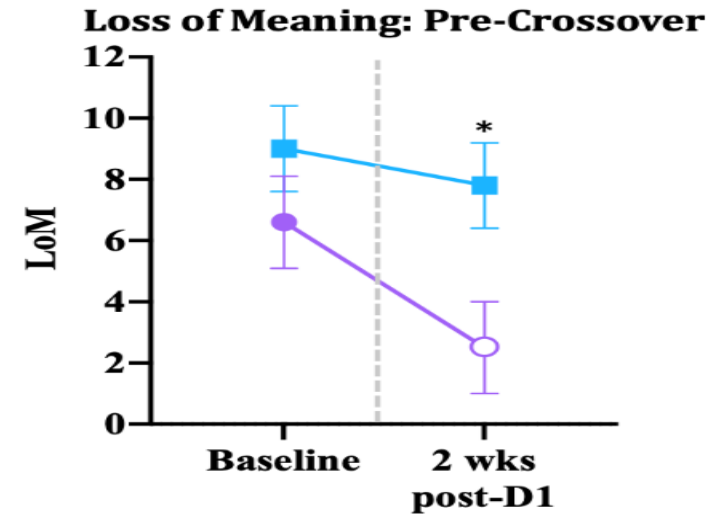
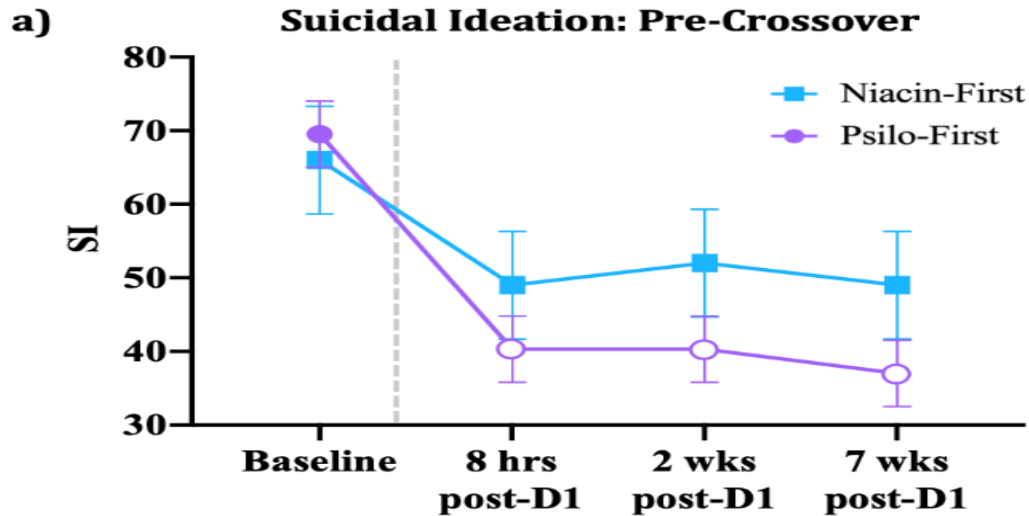


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# Suicidality: Secondary Analyses

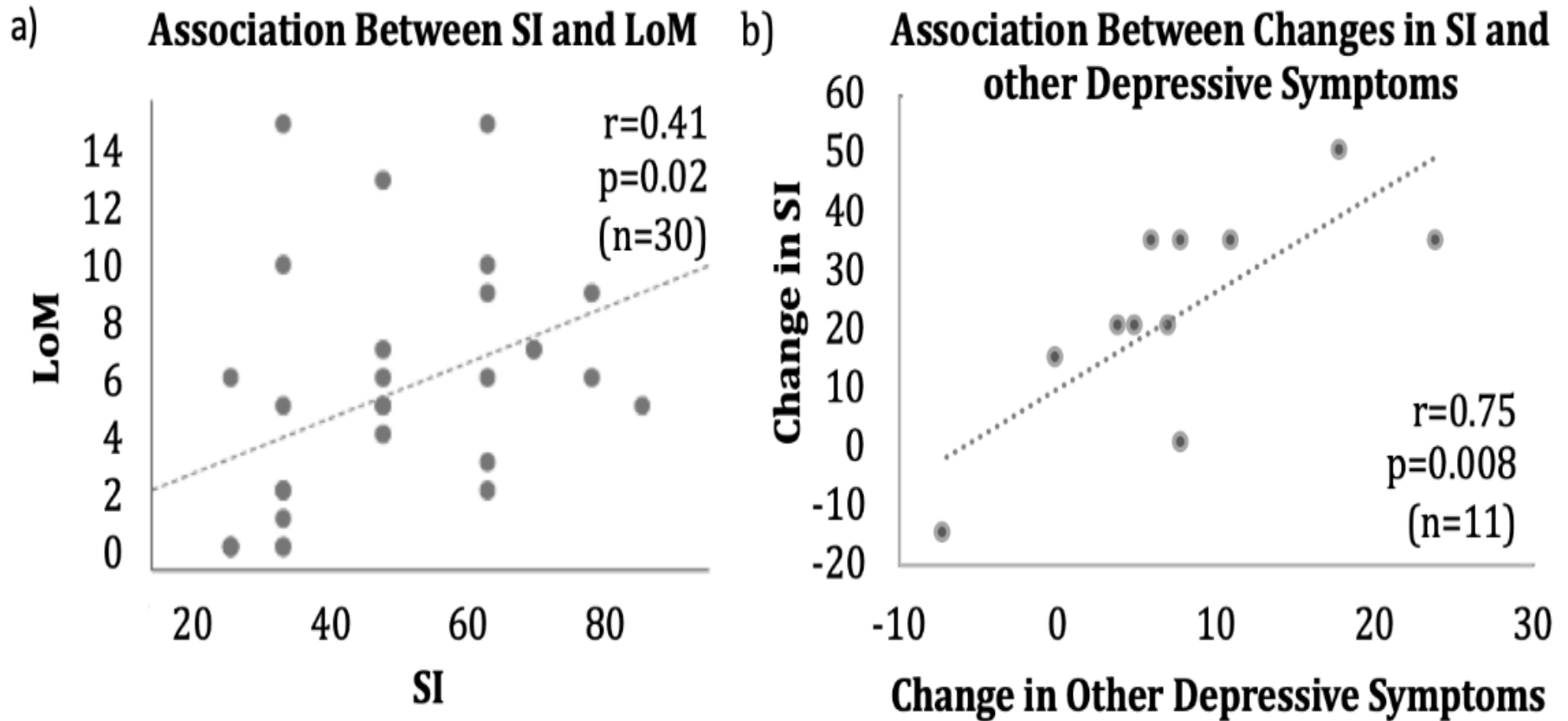






- Mean ( $\pm$ SE) changes in primary outcome variables (SI & Loss of Meaning) pre-crossover in two treatment groups (psilocybin-first  $n=6$ , niacin-first  $n=5$ ) across
- **Loss of Meaning** correlated with **Desire for Hastened Death**

# Link between Loss of Meaning & Suicidal Ideation



**Figure 4.** Relationships between Suicidal Ideation (SI), Loss of Meaning (LoM), and Other Depressive Symptoms.

- a) Correlation between LoM and SI scores collapsed across assessment timepoint
- b) Correlation between change from baseline to 2-weeks post-dose 1 in SI.

# Summary of Phase 2 findings

- Safety & feasibility established
- Rapidly acting anxiolytic
- Rapidly acting anti-depressant
- Highly significant clinical outcomes
- Sustained anti-depressant & anxiolytic effects
  - Several months to several years from single dose intervention
- Potential rapid and sustained anti-suicidal effects

# Summary of Phase 2 findings

- ↓ Existential distress
  - Demoralization
  - Hopelessness
  - Death Anxiety
- ↑ Quality of Life (QoL)
- Highly spiritually significant & meaningful experiences
- Mystical experience as potential psychological mechanism of action

# The New York Times

A Dose of a Hallucinogen From a 'Magic Mushroom,' and Then Lasting Peace

12/1/2016



# Impact

- NYU and JHU articles co-published 12/1/16 in Journal of Psychopharmacology
  - Front page of the NY Times
- Accompanied by a dozen supporting articles by key opinion leaders internationally
  - **2 former presidents of the American Psychiatric Association**
  - Palliative care
  - Psycho-oncology
  - Molecular psychopharmacology
  - Addiction
  - Regulatory
- Overwhelmingly positive response from public/media
  - Press release > **1.7 billion** views internationally

# Future: next steps

- Phase IIb/III RCTs PAP to treat psychiatric & existential distress in **advanced cancer**
- Phase II RCTs of PAP targeting fear of recurrence and existential distress in **early stage cancer**
- Open-label & phase II RCTs PAP to treat psychiatric & existential distress across life-threatening or end-of-life medical & neurologic illnesses & **palliative care** settings
- Open-label and phase II RCTs of psychedelic therapy for **cancer pain syndromes**

# Upcoming/Planned studies

- PAP in **advanced cancer** anxiety, depression & demoralization syndrome
  - Funding: NCI RO1 pending
  - NYU Langone Center for Psychedelic Medicine + NYU Perlmutter Cancer Center + UC Denver
  - N=200; Phase 2/3
  - Multi-center
- PAP in cancer **demoralization syndrome**
  - Funding: Biotech (Reset pharma)
  - Dose-response study
  - N=100; Phase 2/3
  - Pre-IND meeting Nov 2021
  - Multi-center with NYU as lead site



# Upcoming/Planned studies

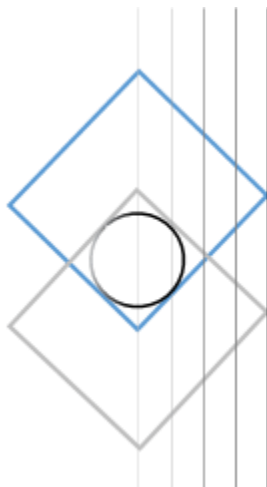
- PAP in early stage breast cancer to treat fear of recurrence and existential distress
  - Funding: NCI RO1 in process + philanthropic support
  - Collaboration between NYU Langone Center for Psychedelic Medicine & NYU Perlmutter Breast Cancer Center
  - N=200; Phase 2/3
- PAP to treat demoralization syndrome in palliative care cohort
  - Funding: UCLA-Harbor Lundquist Institute
  - Collaboration with Charles Grob of UCLA and Anthony Bossis of NYU Langone Center for Psychedelic Medicine
  - N=100; Phase 2
  - Multi-center
  - In parallel: Open-label study PAP in palliative care: Dana Farber (Y Beaussant)

# Upcoming/Planned studies

- **LSD-assisted therapy** in advanced **cancer pain** on **chronic opioid therapy**
- Funding:
  - NYU Langone Center for Psychedelic Medicine
  - Grant submitted to NINDS EPPIC-NET for multi-site study (N=100)
  - Biotech
- Phase 1/2
- Primary outcome: Pain
- Secondary outcomes
  - Opioid sparing
  - Psychiatric & existential distress

# Funding

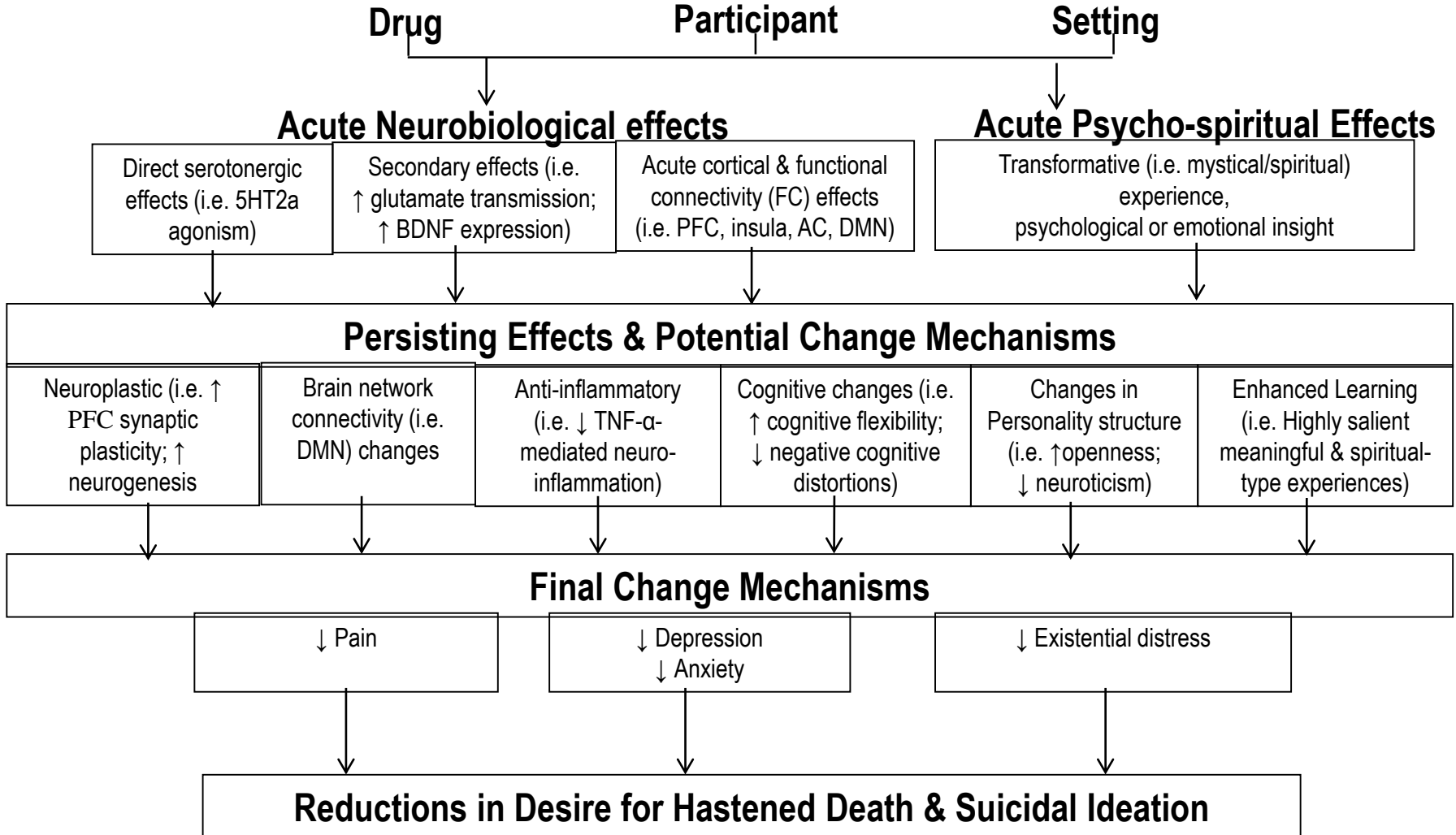
- Philanthropy
- Non-Profit
- NIH
- Biotech/Pharma



Center for  
Psychedelic  
Medicine



# Design trials to assess mechanisms of action



# Re-scheduling, Implementation & Dissemination

- Re-scheduling from 1 → ? (2-3) based on abuse potential assessment
- Regulatory framework → optimize safety & efficacy & establish best clinical practices
  - FDA REMS program
  - Therapist qualifications and training
  - Quality control oversight (ie JCAHO)
- Settings
  - Hospice
  - Palliative Care
  - Cancer Centers
- Re-imburement & insurance coverage
- Justice principle Belmont Report
  - Equity of care dissemination

**nurse**  
**care**  
**hospice**  
**heart**  
**love**  
**respect**  
**end-of-life**  
**personalized**  
**local**  
**calm**  
**honor**  
**peace**  
**soul**  
**quality**  
**unity**  
**accessibility**  
**journey**  
**servant**  
**stress-relief**  
**professionalism**  
**help**  
**companionship**  
**understanding**  
**comfort**  
**spirit**  
**family**  
**passion**





# Classic psychedelics to treat addiction





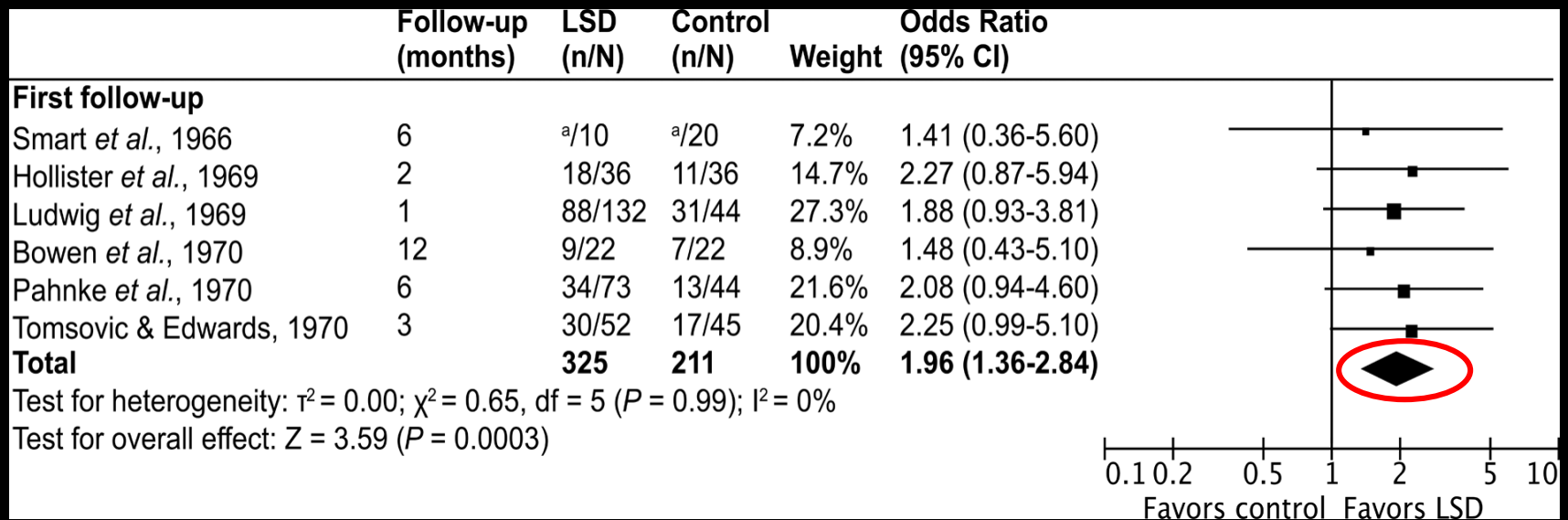
# Current Status Psychedelic Treatment Studies for Addiction

- NYU Langone Center for Psychedelic Medicine & Bellevue Hospital
  - Michael Bogenschutz (PI) & Stephen Ross (co-PI)
  - **RCT Psilocybin-assisted MI for AUD**
  - Heffter funded
- Johns Hopkins Center for Psychedelic & Consciousness Research
  - Matthew Johnson PI
  - **RCT Psilocybin-assisted CBT for tobacco addiction**
    - Comparative efficacy: Psilocybin to NRT
    - Following completed small open-label trial
  - Heffter & NIDA funded
- University of Alabama
  - Peter Hendricks PI
  - **RCT Psilocybin therapy for cocaine addiction**
  - Heffter funded
- University of Wisconsin Madison
  - Randy Brown PI
  - **Open-label psilocybin therapy for opioid addiction on suboxone**
  - Heffter funded

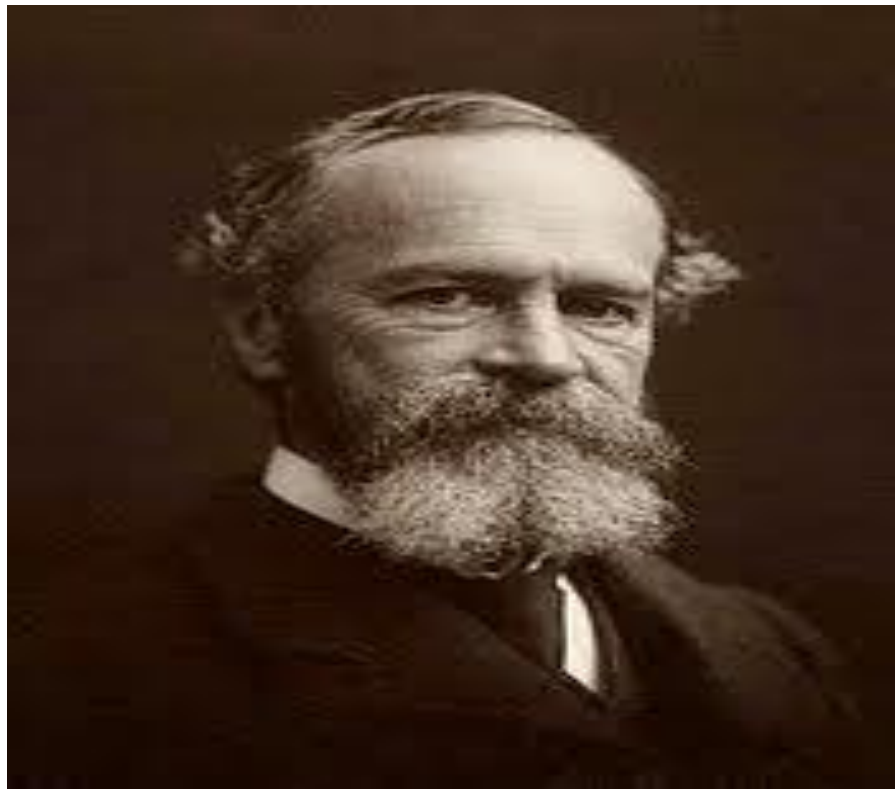
# Meta-analysis of randomized trials

Krebs and Johansen 2012: consistent medium sized effect across 6 randomized trials, 536 participants.

Rates of abstinence or marked improvement at first follow-up



Number needed to treat = 6-7 for drinking outcomes at first post-treatment follow-up.



‘Religiomania is the best cure for  
dipsomania’

# CHARLES B. TOWNS HOSPITAL

293 Central Park West New York, New York

## For ALCOHOLISM and DRUG ADDICTION



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Across from Central Park

*This advertisement  
for the facility where  
A.A. cofounder Bill W.  
received treatment  
ran in the same issue  
of the Journal of the  
American Medical  
Association as a  
review praising the  
newly published  
Big Book.*



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15338-600-60 1



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

Michael P Bogenschutz<sup>1</sup>, Alyssa A Forcehimes<sup>1</sup>, Jessica A Pommy<sup>1</sup>,  
Claire E Wilcox<sup>1</sup>, PCR Barbosa<sup>2</sup> and Rick J Strassman<sup>1</sup>

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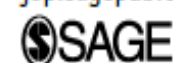
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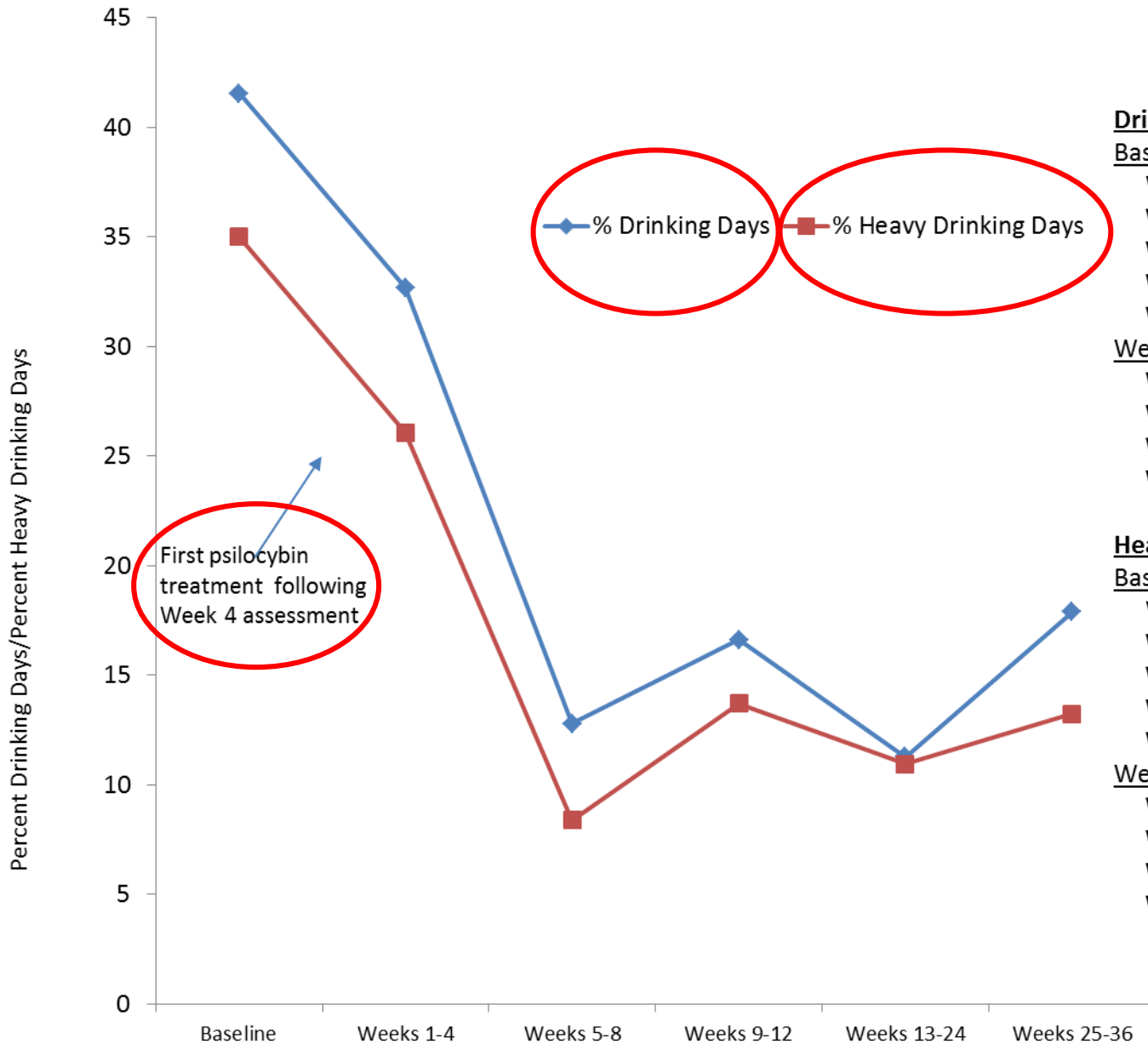
## Abstract

Several lines of evidence suggest that classic (5HT<sub>2A</sub> agonist) hallucinogens have clinically relevant effects in alcohol and drug addiction. Although recent studies have investigated the effects of psilocybin in various populations, there have been no studies on the efficacy of psilocybin for alcohol dependence. We conducted a single-group proof-of-concept study to quantify acute effects of psilocybin in alcohol-dependent participants and to provide preliminary outcome and safety data. Ten volunteers with DSM-IV alcohol dependence received orally administered psilocybin in one or two supervised sessions in addition to Motivational Enhancement Therapy and therapy sessions devoted to preparation for and debriefing from the psilocybin sessions. Participants' responses to psilocybin were qualitatively similar to those described in other populations. Abstinence did not increase significantly in the first 4 weeks of treatment (when participants had not yet received psilocybin), but increased significantly following psilocybin administration ( $p < 0.05$ ). Gains were largely maintained at follow-up to 36 weeks. The intensity of effects in the first psilocybin session (at week 4) strongly predicted change in drinking during weeks 5–8 ( $r = 0.76$  to  $r = 0.89$ ) and also predicted decreases in craving and increases in abstinence self-efficacy during week 5. There were no significant treatment-related adverse events. These preliminary findings provide a strong rationale for controlled trials with larger samples to investigate efficacy and mechanisms.

# Design and Aims

- Single group pilot study (**N = 10**)
- Participants receive **2 psilocybin sessions** in the context of
- 12 weeks of psychosocial treatment (**Motivational Interviewing**) and are
- Followed: 9 months
- Doses:
  - 0.3mg/kg (21 mg/70 kg)
  - 0.4 mg/kg (28 mg/70kg)
- Aims:
  - Safety
  - Feasibility
  - Evaluate **pre-post changes in drinking**
  - Evaluate mediators
    - Motivation, self-efficacy, craving, depression, anxiety, and spirituality

# Drinking Outcomes and Effect Sizes



## Drinking Days

### Baseline vs.

Weeks 1-4	p = .164	d = 0.490
Weeks 5-8	p = .009	d = 1.194
Weeks 9-12	p = .015	d = 1.033
Weeks 13-24	p = .006	d = 1.332
Weeks 25-36	p = .007	d = 1.187

### Weeks 1-4 vs.

Weeks 5-8	p = .016	d = 1.109
Weeks 9-12	p = .033	d = 0.869
Weeks 13-24	p = .014	d = 1.163
Weeks 25-36	p = .013	d = 1.036

## Heavy Drinking Days

### Baseline vs.

Weeks 1-4	p = .158	d = 0.492
Weeks 5-8	p = .007	d = 1.249
Weeks 9-12	p = .019	d = 0.985
Weeks 13-24	p = .010	d = 1.161
Weeks 25-36	p = .004	d = 1.383

### Weeks 1-4 vs.

Weeks 5-8	p = .022	d = 1.046
Weeks 9-12	p = .059	d = 0.750
Weeks 13-24	p = .038	d = 0.876
Weeks 25-36	p = .018	d = 1.040

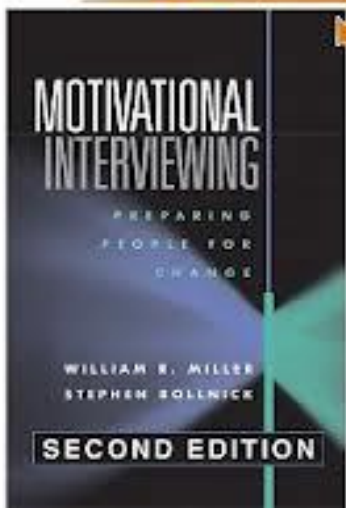


# ALCOHOLISM

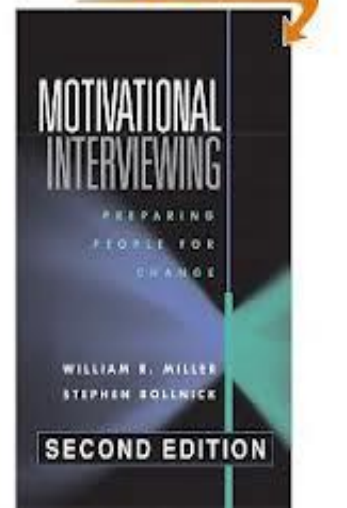
The first step is admitting you have a problem.



Click to **LOOK INSIDE!**



Click to **LOOK INSIDE!**





**Figure 2: Overview of study design**

Study period	Week	Treatment		Assessment		
<b>Period 1</b>	<b>-4 to -1</b>			<b>Screening</b>		
<b>Pre-treatment</b>	<b>-1 to 0</b>			<b>Baseline</b>		
<b>Period 2</b>	<b>0</b>	<b>1 (META)</b>				
<b>Pre-Randomization</b>	<b>1</b>	<b>2 (META)</b>				
	<b>2</b>	<b>3 (PSI)</b>				
	<b>3</b>	<b>4 (PSI)</b>				
<b>Period 3</b> <b>Double-blind</b> <b>Phase</b>	<b>4</b>	<b>Psilocybin 25mg/70kg</b>	<b>5 (PSI)</b>	<b>Diphenhydramine 50 mg</b>	<b>4 weeks</b>	
	<b>4.1</b>		<b>6 (PSI)</b>			
	<b>5</b>		<b>7 (META)</b>		<b>5 weeks</b>	
	<b>6</b>		<b>8 (META)</b>			
	<b>7</b>		<b>9 (PSI)</b>			
	<b>8</b>	<b>Psilocybin 25-40mg/70kg*</b>	<b>10 (PS1)</b>	<b>Diphenhydramine 50-100 mg*</b>	<b>8 weeks</b>	
	<b>8.1</b>		<b>11 (PSI)</b>			
	<b>9</b>		<b>12 (META)</b>		<b>9 weeks</b>	
	<b>10</b>		<b>13 (META)</b>			
	<b>12</b>		<b>14 (META/PSI)</b>		<b>12 weeks</b>	
		<b>24</b>				<b>24 weeks</b>
		<b>36</b>				<b>36 weeks</b>
<b>Period 4</b> <b>Open-label</b> <b>Extension phase</b>	<b>37</b>		<b>15 (PSI)</b>			
	<b>38</b>	<b>Psilocybin 25-40mg/70kg*</b>	<b>16 (PSI)</b>	<b>Psilocybin 25mg/70kg</b>	<b>38 weeks</b>	
	<b>38.1</b>		<b>17 (PSI)</b>			
	<b>39</b>		<b>18 (META/PSI)</b>		<b>39 weeks</b>	
	<b>42</b>		<b>19 (META/PSI)</b>		<b>42 weeks</b>	
	<b>54</b>				<b>54 weeks</b>	

\*Dose titrated based on response in prior session, see section 3.3.8.1.3

# Design

- 2013-2021
- Double-blind RCT (n = 95 randomized, 93 received medication)
- Participants age 25-65 with DSM-IV alcohol dependence
- Submitted for peer review

# Assessment & Outcomes

- Screening & Baseline
- Post-medication sessions
  - Acute medication effects (e.g., mystical experience, self-compassion)
- Longitudinal Monitoring
  - EtOH use (TLFB, urine and hair)
  - Safety (adverse events, abuse potential)
  - Other persisting effects
    - Motivation, self-efficacy, craving
    - Mood, anxiety
    - Personality, values, self-compassion, spirituality
- 1° endpoint: Week 36
- 1° outcome measure: % Heavy Drinking Days during weeks 4-36

# Acknowledgements



**Thank you!**