Psychedelic Treatment of Mental Illness

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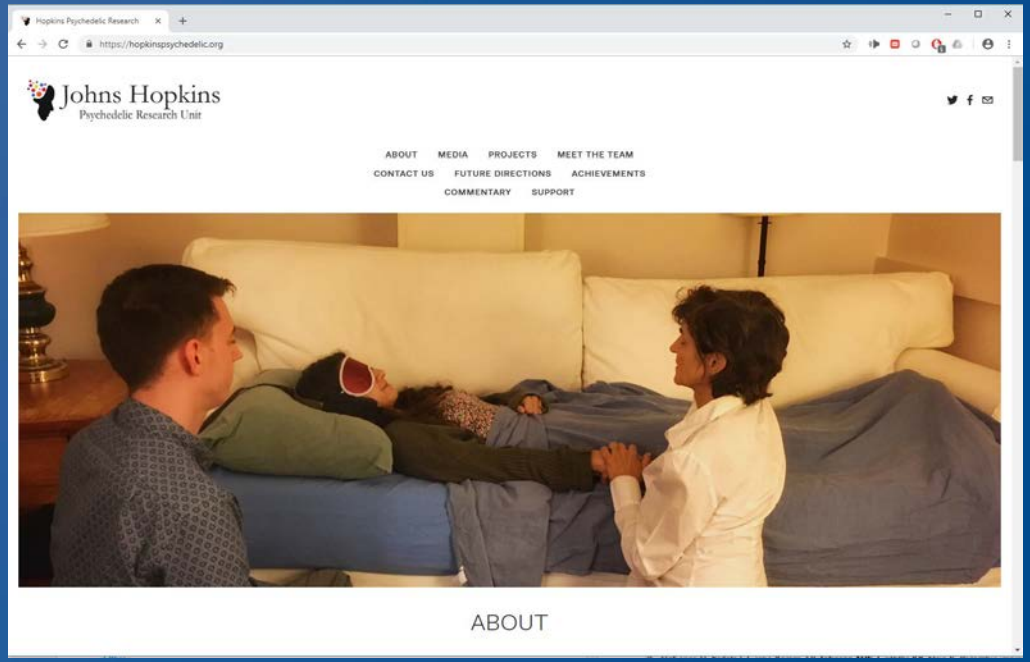
JOHNS HOPKINS MEDICINE



https://hopkinspsychedelic.org

Email: mwj@jhu.edu

- Funded by Steven and Alexandra Cohen Foundation, and the Tim Ferriss Collaborative
- World's largest center for psychedelic research
- Opioid addiction
- PTSD
- Anorexia
- fMRI study of alcoholism with comorbid depression
- Depression in Alzheimer's disease
- Mood symptoms of post-treatment Lyme disease
- Microdosing
- Creativity
- Genetics, biomarkers

The New York Times

Johns Hopkins Opens New Center for Psychedelic Research

The research center, with $17 million from donors, aims to give "psychedelic medicine" a long-sought foothold in the scientific establishment.

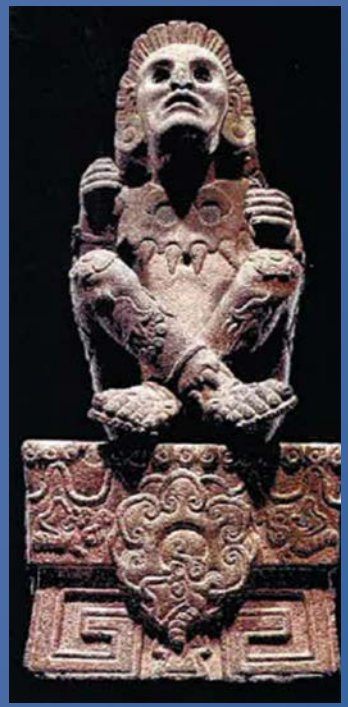
- Psilocybin in >200 mushroom species
- “Classic psychedelic”
  - Psilocybin
  - LSD
  - Mescaline (peyote)
  - DMT (ayahuasca)

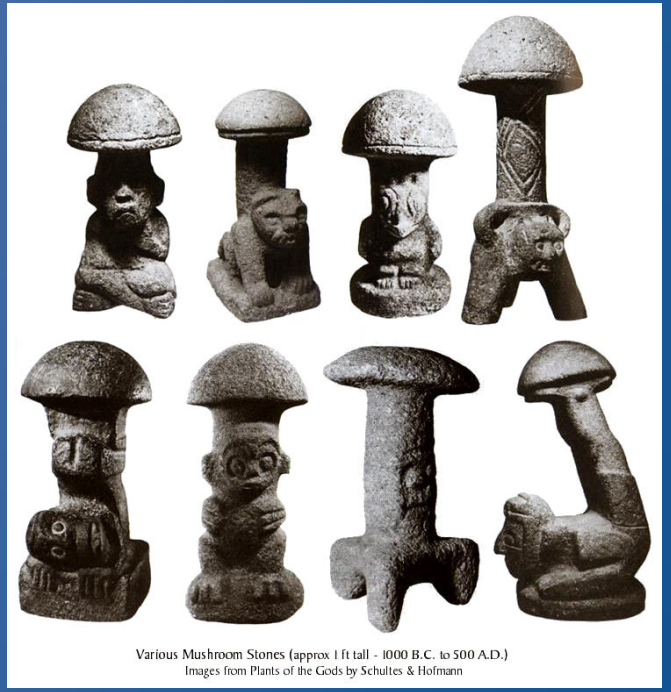
JOHNS HOPKINS MEDICINE

Primary Role for 5-HT_{2A}

- Classic psychedelics produce discriminative stimulus effects
  - Hirschhorn & Winter (1971)
- Antagonists 5-HT_{2A} antagonists block effects
  - e.g., Vollenweider et al. (1998); Winter et al. (2004)
- 5-HT_{2A} affinity well correlated with human potency
  - Glennon (1984)

Ritualistic use dates back many millennia





Various Mushroom Stones (approx 1 ft tall - 1000 B.C. to 500 A.D.)
Images from Plants of the Gods by Schultes & Hofmann

1940s – 1970s

- Psychedelics were intensely investigated as research tools and therapeutics
- Promising findings for:
  - Cancer-related distress
  - Alcoholism

The Dark Ages

- Despite promising preliminary findings, human research with psychedelics became largely dormant
- Dormancy largely a reaction to the association of LSD with the 1960s counterculture and casualties of reckless use outside of the clinic

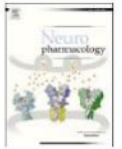
Abuse liability & Risks 2018

- Can cause harm in people with psychosis or predisposition
- For anybody, can cause fear, panic, confusion and potentially dangerous behavior
- Moderate elevations in pulse & blood pressure
- Headaches in day following use

Contents lists available at ScienceDirect

Neuropharmacology

journal homepage: www.elsevier.com/locate/neuropharm



Invited review

The abuse potential of medical psilocybin according to the 8 factors of the Controlled Substances Act

Matthew W. Johnson [a, *], Roland R. Griffiths [a, b], Peter S. Hendricks [c], Jack E. Henningfield [a, d]

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Keywords:
Psilocybin
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Controlled Substances Act
Depression
Anxiety
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ABSTRACT

This review assesses the abuse potential of medically-administered psilocybin, following the structure of the 8 factors of the US Controlled Substances Act (CSA). Research suggests the potential safety and efficacy of psilocybin in treating cancer-related psychiatric distress and substance use disorders, setting the occasion for this review. A more extensive assessment of abuse potential according to an 8-factor analysis would eventually be required to guide appropriate schedule placement.

Psilocybin, like other 5-HT2A agonist classic psychedelics, has limited reinforcing effects, supporting marginal, transient non-human self-administration. Nonetheless, mushrooms with variable psilocybin content are used illicitly, with a few lifetime use occasions being normative among users. Potential harms include dangerous behavior in unprepared, unsupervised users, and exacerbation of mental illness in those with or predisposed to psychotic disorders. However, scope of use and associated harms are low compared to prototypical abused drugs, and the medical model addresses these concerns with dose control, patient screening, preparation and follow-up, and session supervision in a medical facility.

Conclusions: (1) psilocybin has an abuse potential appropriate for CSA scheduling if approved as medicine; (2) psilocybin can provide therapeutic benefits that may support the development of an approvable New Drug Application (NDA) but further studies are required which this review describes; (3) adverse effects of medical psilocybin are manageable when administered according to risk management approaches; and (4) although further study is required, this review suggests that placement in Schedule IV may be appropriate if a psilocybin-containing medicine is approved.

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Psilocybin Can Cause Temporary Headaches 2012

- Typically mild – moderate
- Might be a clue to understanding how psilocybin can treat cluster headaches

Drug and Alcohol Dependence 123 (2012) 132–140

Contents lists available at SciVerse ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Psilocybin dose-dependently causes delayed, transient headaches in healthy volunteers

Matthew W. Johnson[a,*], R. Andrew Sewell[b,c], Roland R. Griffiths[a,d]

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Psilocybin
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Cluster headache
Migraine
Classic hallucinogen
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ABSTRACT

Background: Psilocybin is a well-characterized classic hallucinogen (psychedelic) with a long history of religious use by indigenous cultures, and nonmedical use in modern societies. Although psilocybin is structurally related to migraine medications, and case studies suggest that psilocybin may be efficacious in treatment of cluster headache, little is known about the relationship between psilocybin and headache.
Methods: This double-blind study examined a broad range of psilocybin doses (0, 5, 10, 20, and 30 mg/70 kg) on headache in 18 healthy participants.
Results: Psilocybin frequently caused headache, the incidence, duration, and severity of which increased in a dose-dependent manner. All headaches had delayed onset, were transient, and lasted no more than a day after psilocybin administration.
Conclusions: Possible mechanisms for these observations are discussed, and include induction of delayed headache through nitric oxide release. These data suggest that headache is an adverse event to be expected with the nonmedical use of psilocybin-containing mushrooms as well as the administration of psilocybin in human research. Headaches were neither severe nor disabling, and should not present a barrier to future psilocybin research.

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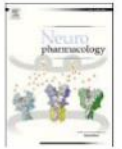
Abuse liability & Risks 2018

- Can cause harm in people with psychosis or predisposition
- For anybody, can cause fear, panic, confusion and potentially dangerous behavior
- Moderate elevations in pulse & blood pressure
- Headaches in day following use
- Persisting perceptual changes
- Data suggest no addiction

Contents lists available at ScienceDirect

Neuropharmacology

journal homepage: www.elsevier.com/locate/neuropharm



Invited review

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Conclusions: (1) psilocybin has an abuse potential appropriate for CSA scheduling if approved as medicine; (2) psilocybin can provide therapeutic benefits that may support the development of an approvable New Drug Application (NDA) but further studies are required which this review describes; (3) adverse effects of medical psilocybin are manageable when administered according to risk management approaches; and (4) although further study is required, this review suggests that placement in Schedule IV may be appropriate if a psilocybin-containing medicine is approved.

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Safety Guidelines 2008

- Assisted in the approval of psychedelic studies by new scientists and universities

Original Papers

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10.1177/0269881108093587

Human hallucinogen research: guidelines for safety

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WA Richards *Johns Hopkins Bayview Medical Center, Baltimore, MD, USA.*
RR Griffiths *Department of Psychiatry and Behavioral Sciences, Johns Hopkins University, School of Medicine, Baltimore, MD, USA; Department of Neuroscience, Johns Hopkins University, School of Medicine, Baltimore, MD, USA.*

Abstract

There has recently been a renewal of human research with classical hallucinogens (psychedelics). This paper first briefly discusses the unique history of human hallucinogen research, and then reviews the risks of hallucinogen administration and safeguards for minimizing these risks. Although hallucinogens are relatively safe physiologically and are not considered drugs of dependence, their administration involves unique psychological risks. The most likely risk is overwhelming distress during drug action ('bad trip'), which could lead to potentially dangerous behaviour such as leaving the study site. Less common are prolonged psychoses triggered by hallucinogens. Safeguards against these risks include the exclusion of volunteers with personal or family history of psychotic disorders or other severe psychiatric disorders, establishing trust and rapport between session monitors and volunteer before the session, careful volunteer preparation, a safe physical session environment and interpersonal support from at least two study monitors during the session. Investigators should probe for the relatively rare hallucinogen persisting perception disorder in follow-up contact. Persisting adverse reactions are rare when research is conducted along these guidelines. Incautious research may jeopardize participant safety and future research. However, carefully conducted research may inform the treatment of psychiatric disorders, and may lead to advances in basic science.

Key words

5-HT$_{2A}$ agonists; adverse reactions; DMT; entheogens; hallucinogens; human research; LSD; mescaline; psilocybin; psychedelics; safety guidelines

JOHNS HOPKINS
MEDICINE

Mystical Experiences & Lasting Benefit 2006 & 2008

- Safe in this structured setting
- Among the 5 most meaningful life experiences for majority of people
- Improvements in mood and quality of life >1 year after sessions

Psychopharmacology (2006) 187:268–283
DOI 10.1007/s00213-006-0457-5

ORIGINAL INVESTIGATION

Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance

Original Papers

Psychopharm

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22(6) (2008) 621–632
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10.1177/0269881108094300

Mystical-type experiences occasioned by psilocybin mediate the attribution of personal meaning and spiritual significance 14 months later

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R Jesse *Council on Spiritual Practices, San Francisco, CA, USA.*

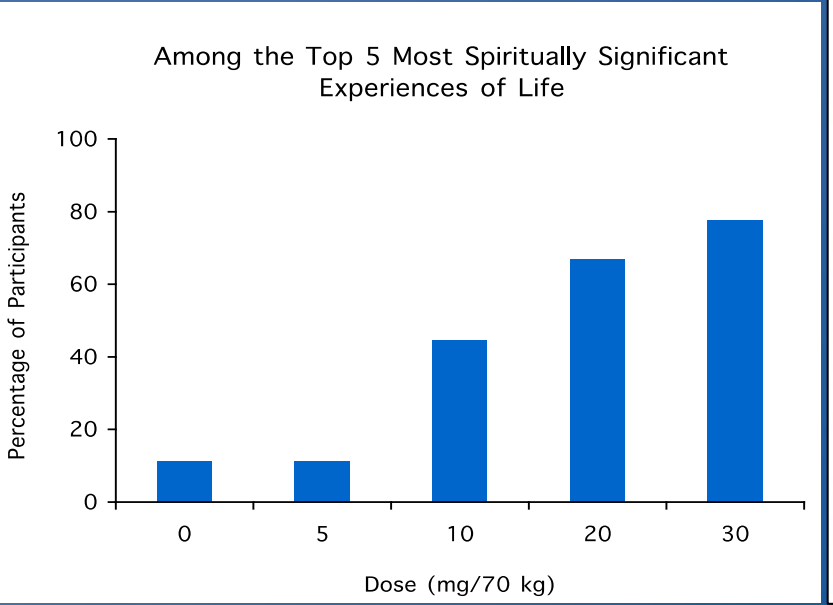
Abstract

Psilocybin has been used for centuries for religious purposes; however, little is known scientifically about its long-term effects. We previously reported the effects of a double-blind study evaluating the psychological effects of a high psilocybin dose. This report presents the 14-month follow-up and examines the relationship of the follow-up results to data

satisfaction; 58% met criteria for having had a 'complete' mystical experience. Correlation and regression analyses indicated a central role of the mystical experience assessed on the session day in the high ratings of personal meaning and spiritual significance at follow-up. Of the measures of personality, affect, quality of life and spirituality assessed across the

Psilocybin Dose Effects 2011

- Increasing psilocybin dose has an orderly effect on mystical experience, challenging experience, and long term positive attribution



Psychopharmacology (2011) 218:649–665
DOI 10.1007/s00213-011-2358-5

ORIGINAL INVESTIGATION

Psilocybin occasioned mystical-type experiences: immediate and persisting dose-related effects

Roland R. Griffiths · Matthew W. Johnson · William A. Richards · Brian D. Richards · Una McCann · Robert Jesse

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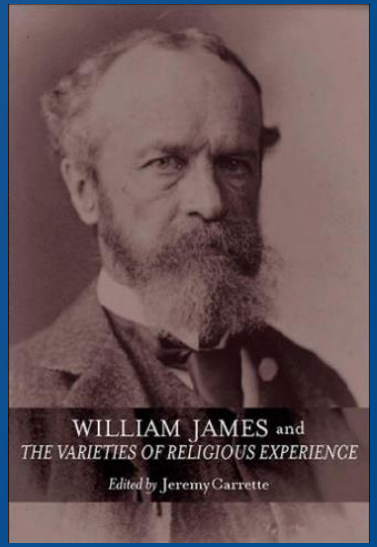
© Springer-Verlag 2011

Abstract
Rationale This dose-effect study extends previous observations showing that psilocybin can occasion mystical-type experiences having persisting positive effects on attitudes, mood, and behavior.
Objectives This double-blind study evaluated psilocybin (0, 5, 10, 20, 30 mg/70 kg, p.o.) administered under supportive conditions.
Methods Participants were 18 adults (17 hallucinogen-naïve). Five 8-h sessions were conducted individually for each participant at 1-month intervals. Participants were randomized to receive the four active doses in either ascending or descending order (nine participants each). Placebo was scheduled quasi-randomly. During sessions, volunteers used eyeshades and were instructed to direct their attention inward. Volunteers completed questionnaires assessing effects immediately after and 1 month after each session, and at 14 months follow-up.
Results Psilocybin produced acute perceptual and subjective effects including, at 20 and/or 30 mg/70 kg, extreme anxiety/fear (39% of volunteers) and/or mystical-type experience (72% of volunteers). One month after sessions at the two highest doses, volunteers rated the psilocybin experience as having substantial personal and spiritual significance, and attributed to the experience sustained positive changes in attitudes, mood, and behavior, with the ascending dose sequence showing greater positive effects. At 14 months, ratings were undiminished and were consistent with changes rated by community observers. Both the acute and persisting effects of psilocybin were generally a monotonically increasing function of dose, with the lowest dose showing significant effects.

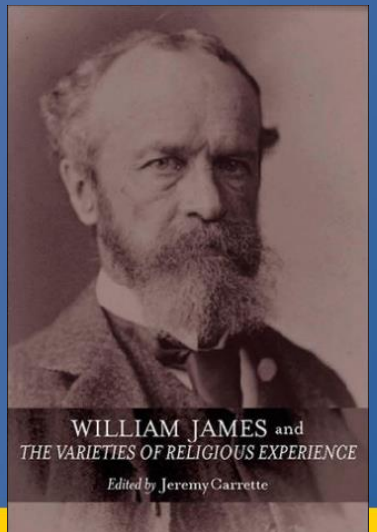
Mystical Experience

- About 60% of participants in both studies met criteria for a “complete” mystical experience
  - Unity
  - Noetic quality
  - Sacredness
  - Sense of transcending time and space
  - Positive mood
  - Ineffability



Mystical Experience Scale "MEQ30" 2012 & 2015

- First validated scale to assess mystical experiences from drugs or other specific experiences
- Factors: unity, positive mood, transcendence of time/space, ineffability



JOURNAL FOR THE SCIENTIFIC STUDY OF RELIGION
JSSR

Factor Analysis of the Mystical Experience Questionnaire: A Study of Experiences Occasioned by the Hallucinogen Psilocybin

Original Paper

Validation of the revised Mystical Experience Questionnaire in experimental sessions with psilocybin

Frederick S Barrett[1], Matthew W Johnson[1] and Roland R Griffiths[1,2]

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Abstract

The 30-item revised Mystical Experience Questionnaire (MEQ30) was previously developed within an online survey of mystical-type experiences occasioned by psilocybin-containing mushrooms. The rated experiences occurred on average eight years before completion of the questionnaire. The current paper validates the MEQ30 using data from experimental studies with controlled doses of psilocybin. Data were pooled and analyzed from five laboratory experiments in which participants (n=184) received a moderate to high oral dose of psilocybin (at least 20 mg/70 kg). Results of confirmatory factor analysis demonstrate the reliability and internal validity of the MEQ30. Structural equation models demonstrate the external and convergent validity of the MEQ30 by showing that latent variable scores on the MEQ30 positively predict persisting change in attitudes, behavior, and well-being attributed to experiences with psilocybin while controlling for the contribution of the participant-rated intensity of drug effects. These findings support the use of the MEQ30 as an efficient measure of individual mystical experiences. A method to score a "complete mystical experience" that was used in previous versions of the mystical experience questionnaire is validated in the MEQ30, and a stand-alone version of the MEQ30 is provided for use in future research.

Keywords

Psilocybin, hallucinogens, entheogen, psychedelic, spiritual, mystical experience, factor analysis, structural equation modeling, psychometrics

Psilocybin Increases Openness 2011

- First experimental study to change a personality dimension
- Driven by mystical experience

Original Paper

Mystical experiences occasioned by the hallucinogen psilocybin lead to increases in the personality domain of openness

Katherine A MacLean[1], Matthew W Johnson[1] and Roland R Griffiths[1,2]

Psychopharm

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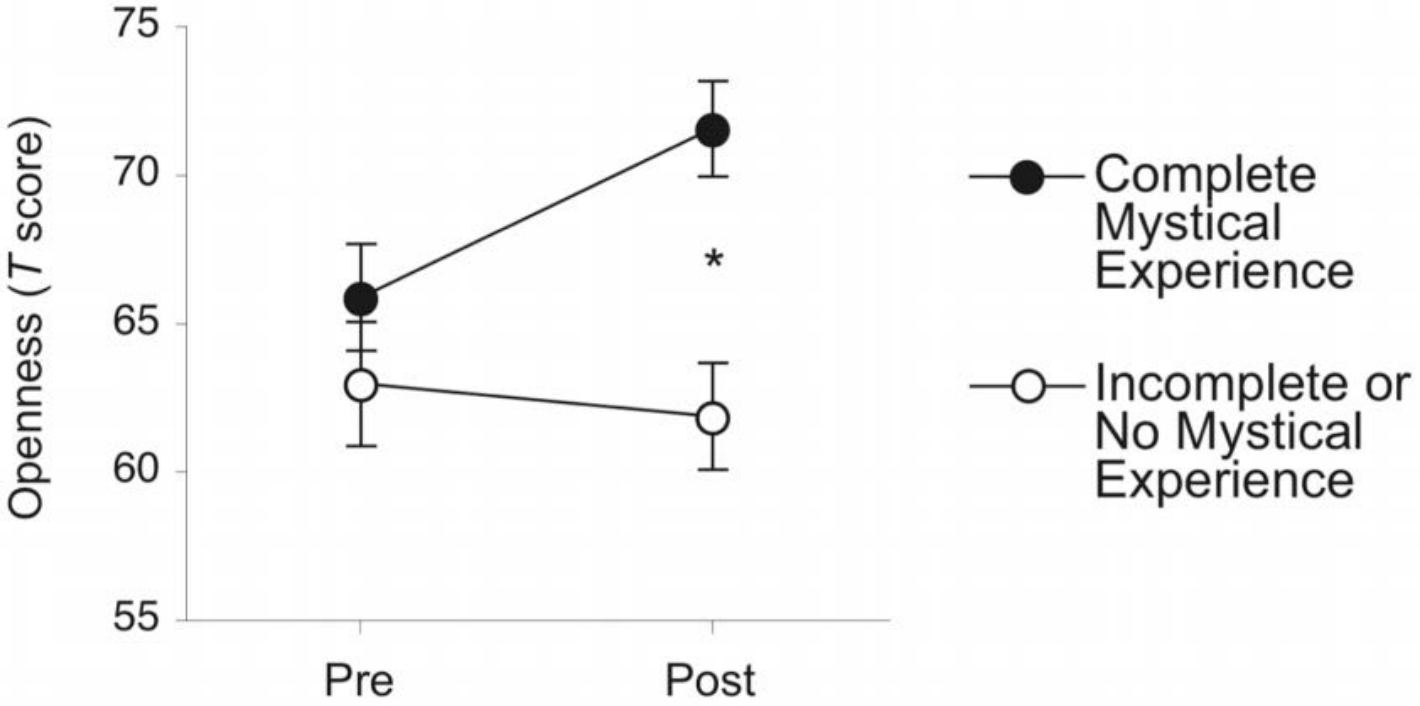
Abstract

A large body of evidence, including longitudinal analyses of personality change, suggests that core personality traits are predominantly stable after age 30. To our knowledge, no study has demonstrated changes in personality in healthy adults after an experimentally manipulated discrete event. Intriguingly, double-blind controlled studies have shown that the classic hallucinogen psilocybin occasions personally and spiritually significant mystical experiences that predict long-term changes in behaviors, attitudes and values. In the present report we assessed the effect of psilocybin on changes in the five broad domains of personality – Neuroticism, Extroversion, Openness, Agreeableness, and Conscientiousness. Consistent with participant claims of hallucinogen-occasioned increases in aesthetic appreciation, imagination, and creativity, we found significant increases in Openness following a high-dose psilocybin session. In participants who had mystical experiences during their psilocybin session, Openness remained significantly higher than baseline more than 1 year after the session. The findings suggest a specific role for psilocybin and mystical-type experiences in adult personality change.

Keywords

Hallucinogen, mystical experience, openness, personality, psilocybin, psychedelic

Driven by Mystical Experience



JOHNS HOPKINS
MEDICINE

Cancer Existential Distress 2016

- 51 patients
- Life threatening cancer
- Depression and/or anxiety disorder

Original Paper

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 Johnson[1], Michael A Carducci[3], Annie Umbricht[1], William A Richards[1], Brian D Richards[1], Mary P Cosimano[1] and Margaret A Klinedinst[1]

Psychopharm

Journal of Psychopharmacology
1–17
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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.

Trial Registration

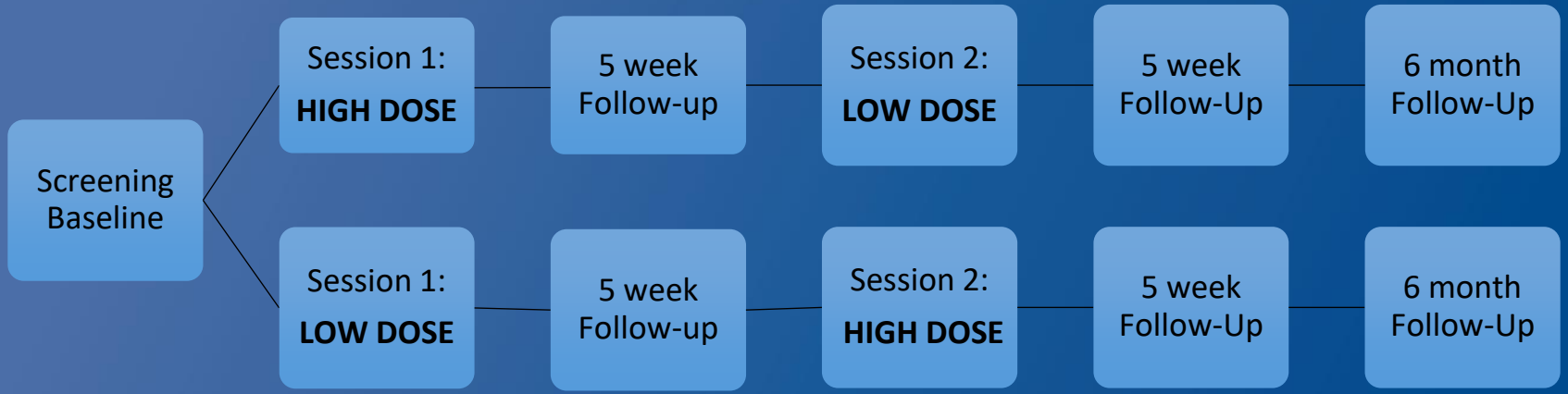
ClinicalTrials.gov identifier: NCT00465595

Keywords

Psilocybin, hallucinogen, cancer, anxiety, depression, symptom remission, mystical experience

Study Design

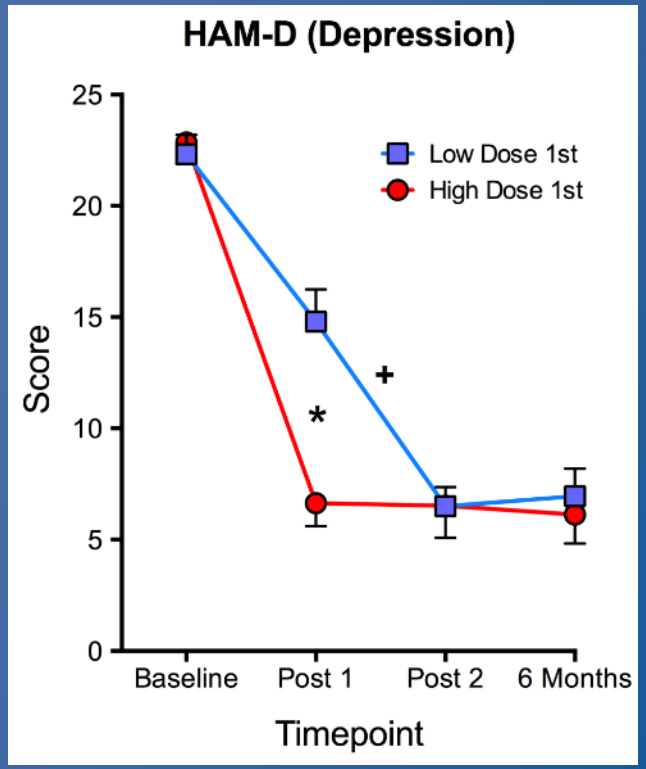
- Two psilocybin sessions 5 weeks apart
- 1 (or 3) mg/70 kg versus 22 (or 30) mg/70 kg



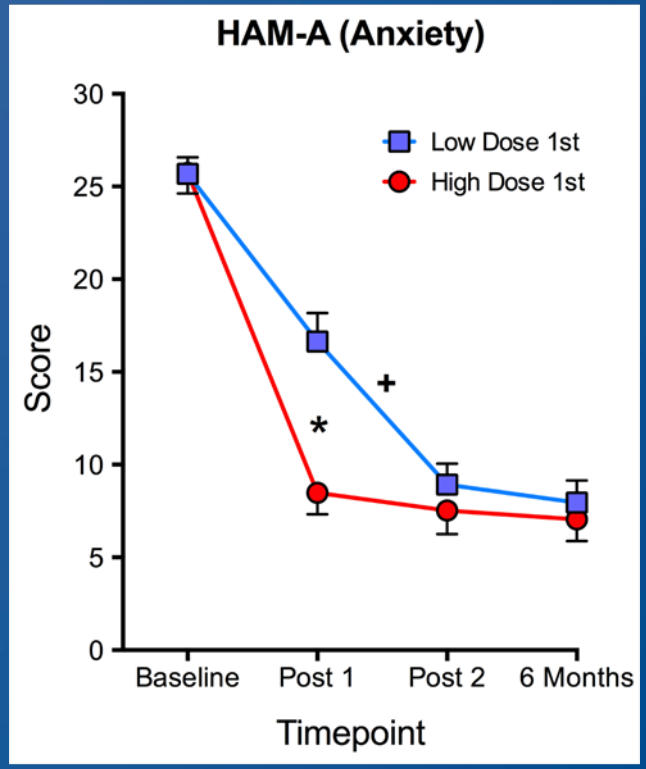
Serious adverse events

- No serious adverse events attributable to psilocybin

Lasting Antidepressant & Anti-Anxiety



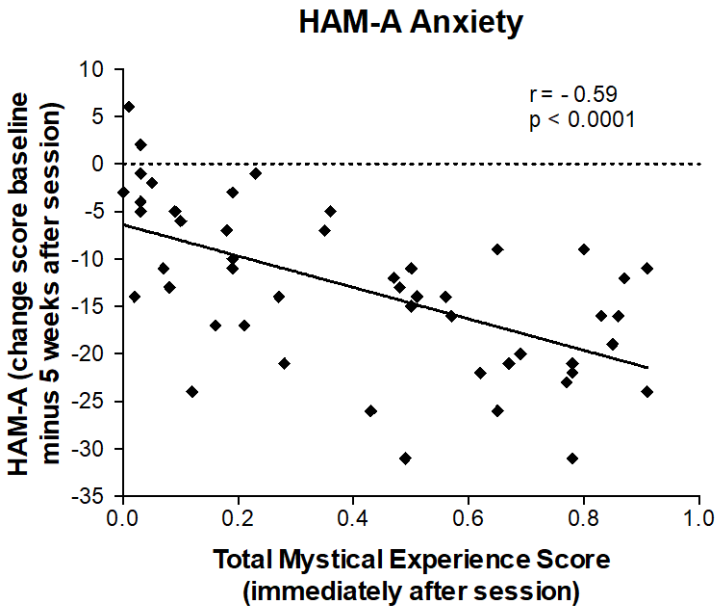
* Cohen's d= 1.30
+ Cohen's d= 3.08

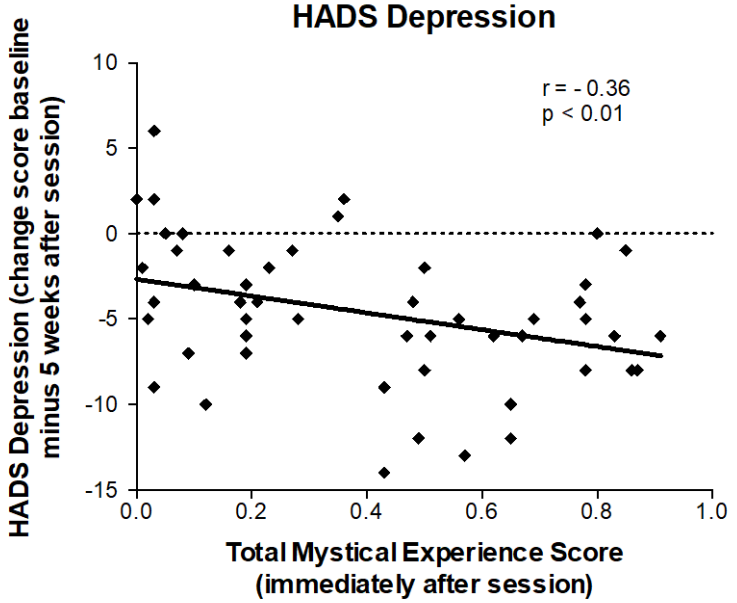


* Cohen's d= 1.22
+ Cohen's d= 3.71

Mystical Experience Correlated with Therapeutic Effects

JOHNS HOPKINS MEDICINE



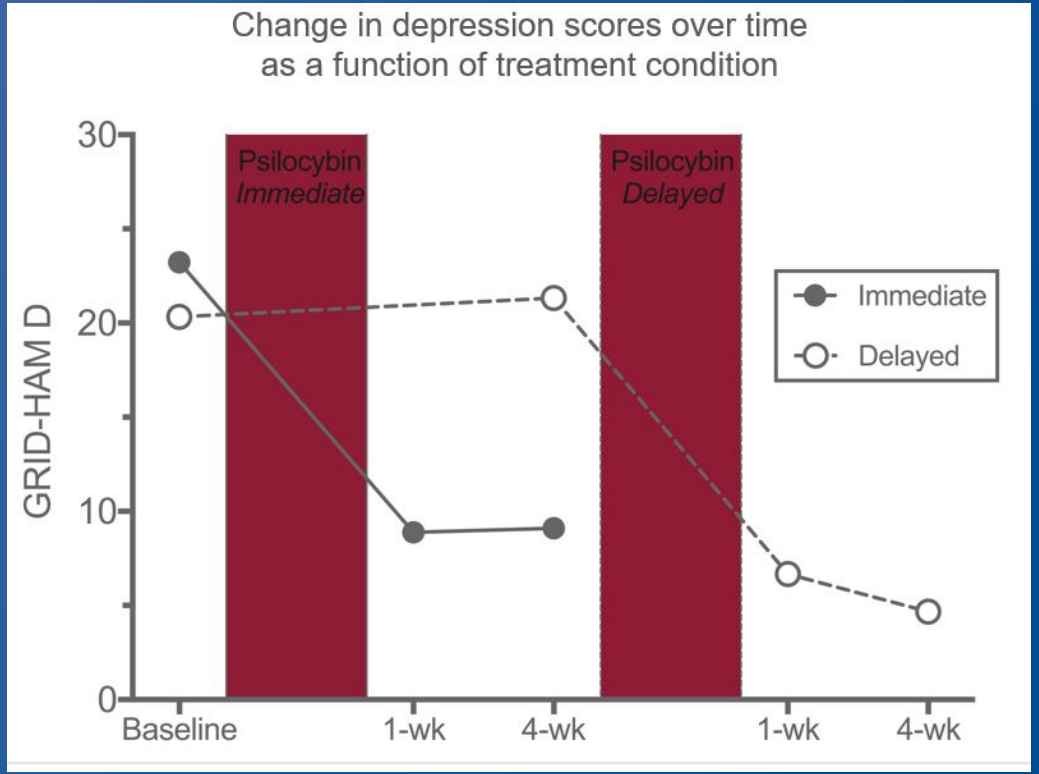


Consistent findings

- Cancer patients:
  - Grob et al., 2011
  - Ross et al., 2016
- Outside of cancer:
  - Carhart-Harris et al., 2016

Depression Pilot

- Wait-list control study
- Current n=12

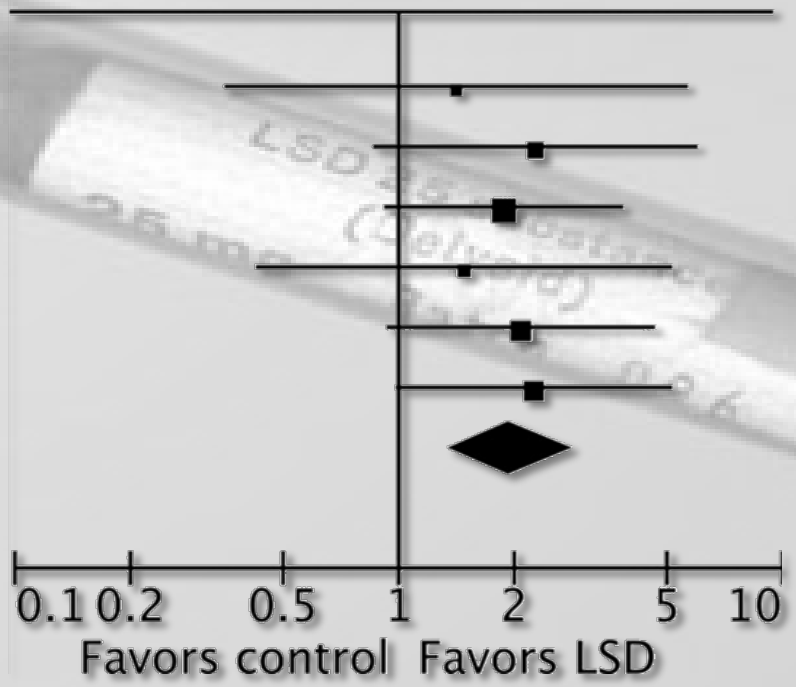


Addiction Treatment

- Classic psychedelics can be misused but are not addictive

Krebs & Johansen (2012)

Across studies, LSD nearly doubled the odds that alcoholic patients would be improved at the 1st follow up (N=536)



Ceremonial psychedelic use linked with addiction recovery

- Peyote and the Native American Church
  - Albaugh & Anderson, 1974; Bergman, 1971; Blum et al., 1977; Calabrese, 1997; Garrity, 2000; Menninger, 1971; Pascarosa et al., 1976; Roy, 1973
- Ayahuasca ceremonies in South America and South American Religions
  - Dobkin de Rios et al., 2002; Halpern et al., 2008

Smoking Cessation Pilot 2014

- Feasibility and safety

Original Paper

Pilot study of the 5-HT$_{2A}$R agonist psilocybin in the treatment of tobacco addiction

Psychopharm

Matthew W Johnson[1], Albert Garcia-Romeu[1], Mary P Cosimano[1] and Roland R Griffiths[1,2]

Journal of Psychopharmacology
1–10
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THE AMERICAN JOURNAL OF DRUG AND ALCOHOL ABUSE
http://dx.doi.org/10.3109/00952990.2016.1170135

Taylor & F
Taylor & Francis G

ORIGINAL ARTICLE

Long-term follow-up of psilocybin-facilitated smoking cessation

Matthew W. Johnson, PhD[a], Albert Garcia-Romeu, PhD[a], and Roland R. Griffiths, PhD[a,b]

[a]Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD, USA; [b]Departme
Neuroscience, Johns Hopkins University School of Medicine, Baltimore, MD, USA

ABSTRACT

Background: A recent open-label pilot study ($N = 15$) found that two to three moderate to high doses (20 and 30 mg/70 kg) of the serotonin 2A receptor agonist, psilocybin, in combination with cognitive behavioral therapy (CBT) for smoking cessation, resulted in substantially higher 6-month smoking abstinence rates than are typically observed with other medications or CBT alone. *Objectives*: To assess long-term effects of a psilocybin-facilitated smoking cessation program at ≥12 months after psilocybin administration. *Methods*: The present report describes biologically verified smoking abstinence outcomes of the previous pilot study at ≥12 months, and related data on subjective effects of psilocybin. *Results*: All 15 participants completed a 12-month follow-up, and 12 (80%) returned for a long-term (≥16 months) follow-up, with a mean interval of 30 months (range = 16–57 months) between target-quit date (i.e., first psilocybin session) and long-term follow-up. At 12-month follow-up, 10 participants (67%) were confirmed as smoking abstinent. At long-term follow-up, nine participants (60%) were confirmed as smoking abstinent. At 12-month follow-up 13 participants (86.7%) rated their psilocybin experiences among the five most personally meaningful and spiritually significant experiences of their lives. *Conclusion*: These results suggest that in the context of a structured treatment program, psilocybin holds considerable promise in promoting

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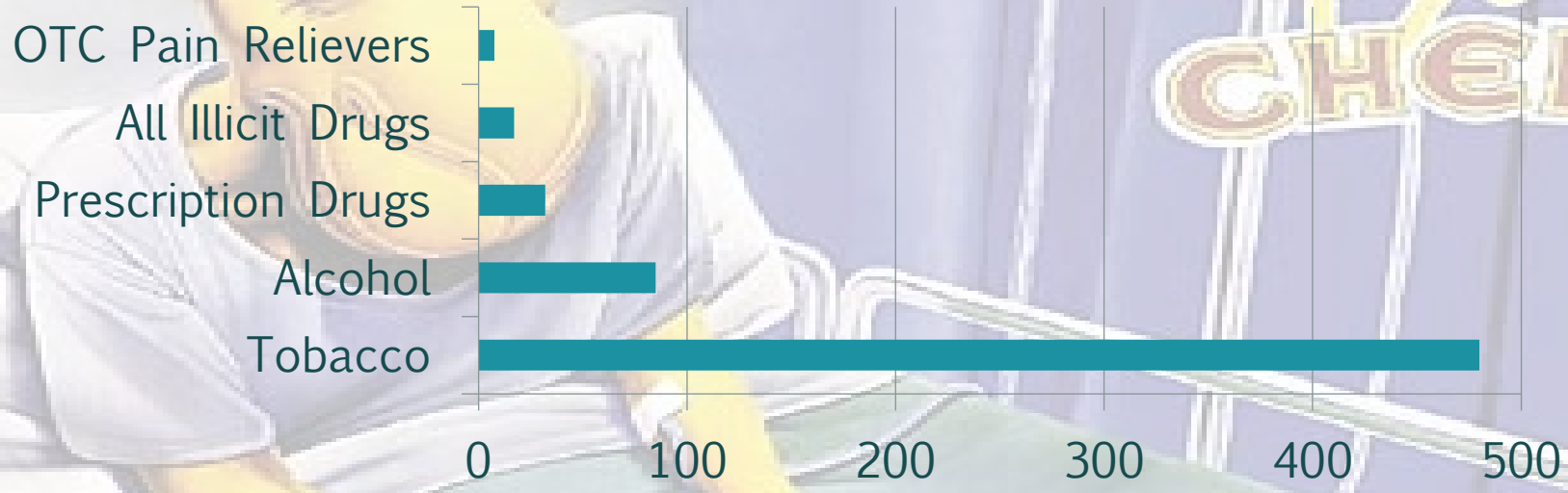
KEYWORDS
Hallucinogen; tobac
smoking cessation;
addiction; psilocybi
psychedelic; mystic
experience; spiritua

U.S. Drug Related Deaths Per Year (Thousands)

(Mokdad et al., 2004; UN Office on Drugs & Crime, 2009; US DHHS, 2014)



- ~5 millions deaths per year world wide (WHO, 2009)
- ~69% of U.S. smokers want to quit (CDC, 2011)
- Even effective medications (Chantix, Zyban, NRT) fail to help ~70-80% of patients remain smoke free for a year

TECH & SCIENCE

Kick Your Smoking Habit With...Magic Mushrooms?

BY PAULA MEJIA 9/11/14 AT 5:42 PM

MARTIN BOND/ALAMY

Table 1. Demographic and smoking characteristics, *N*=15.

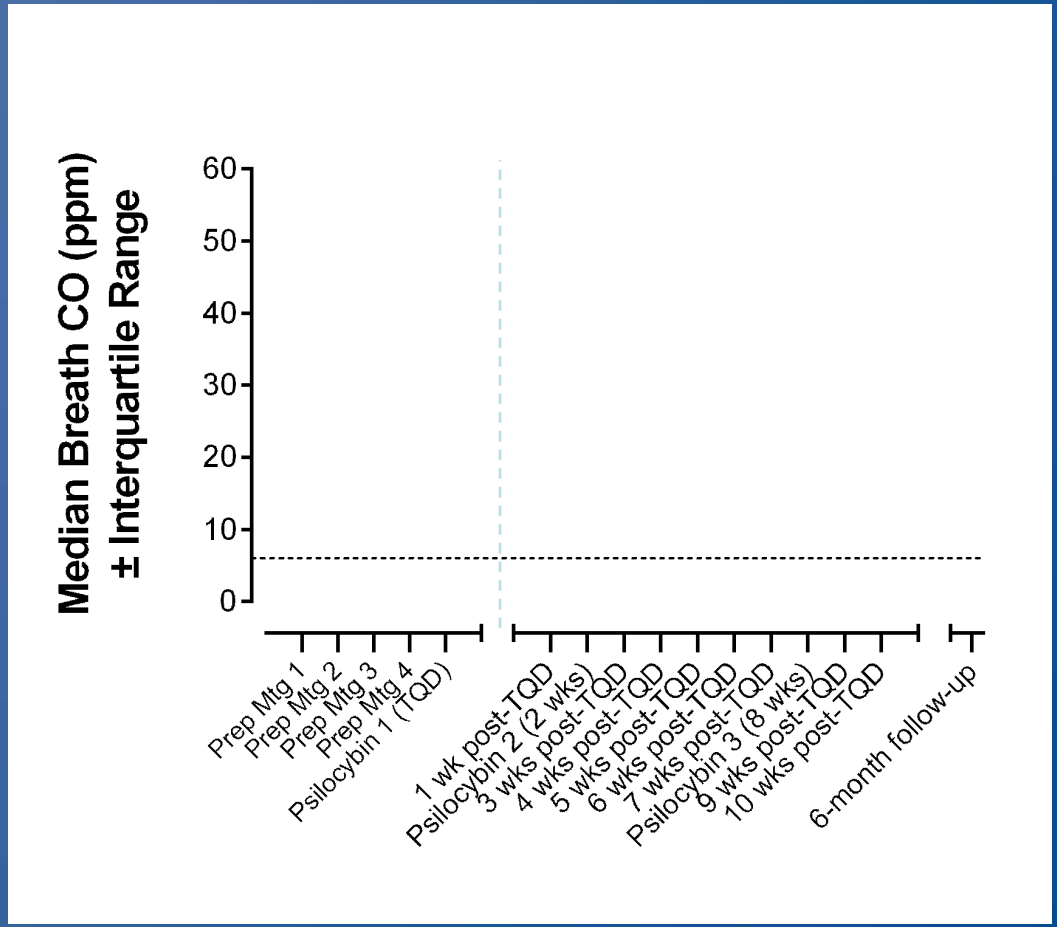
Categories	Mean (SD)	Range
Sex [a]	10 M, 5 F	
Age (years)	51 (10.5)	26-65
Education [b]		
Some college	4 (26.7)	
Bachelor's degree	7 (46.7)	
Graduate degree	4 (26.7)	
Cigarette dependence (FTCD) [c]	5.3 (1.3)	3-8
Years smoking	31 (9.9)	10-49
Previous quit attempts	6 (3.6)	2-12
Cigarettes/day at intake	19 (2.9)	15-25
Breath CO at intake	30 (9.9)	13-53
Urine cotinine at intake	1676 (594)	841-3212

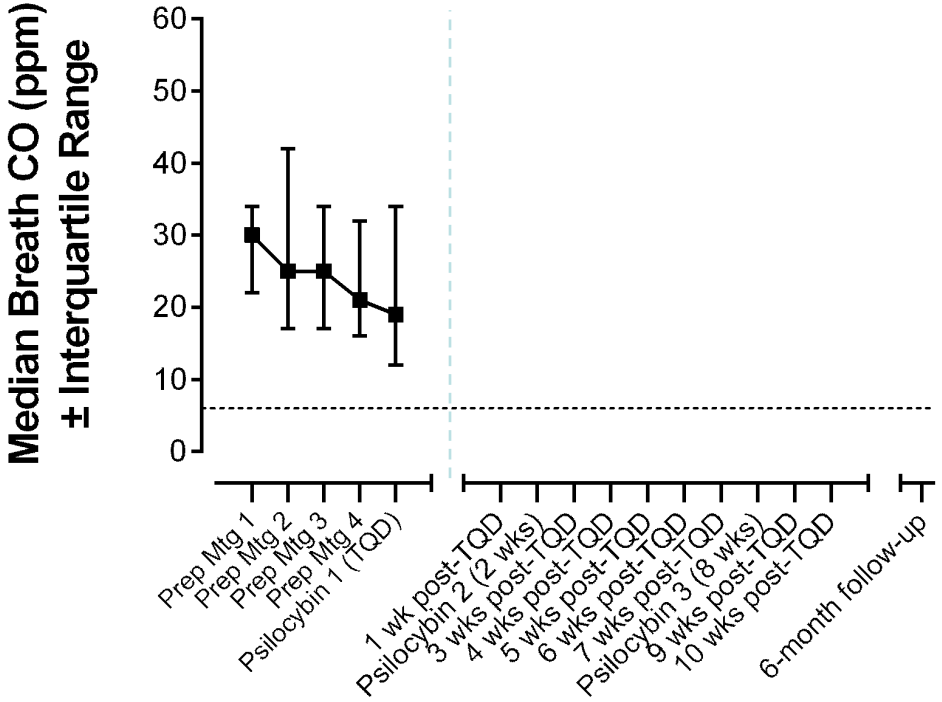
Pilot Study Timeline

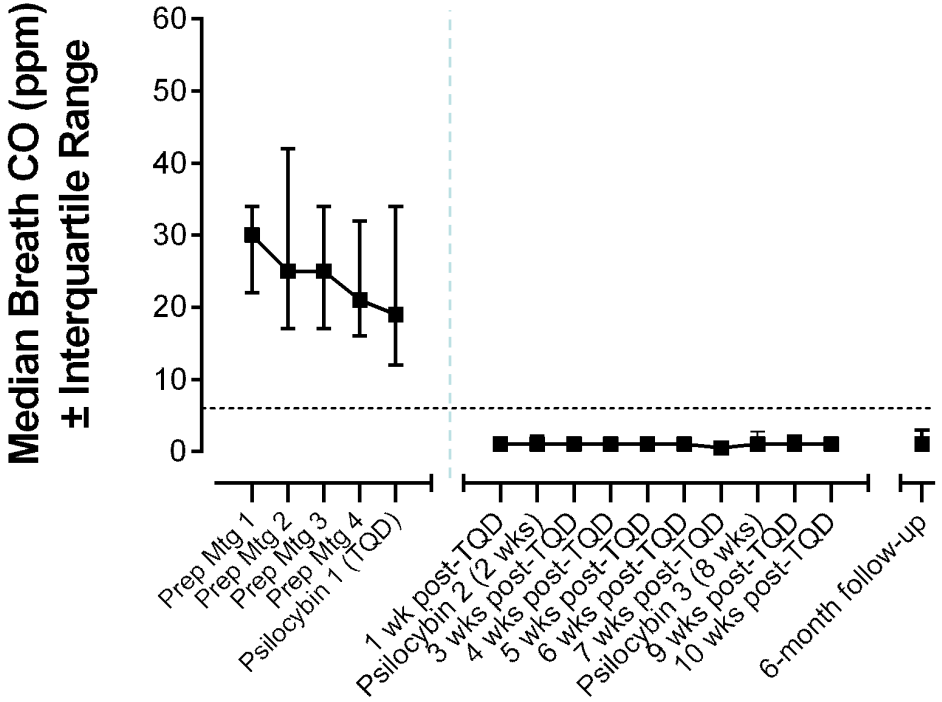
- 15 week protocol with weekly meetings
- Cognitive behavioral therapy
- 3 psilocybin sessions over 8 weeks (20-30 mg/70 kg)
- 1st Psilocybin session on target quit date

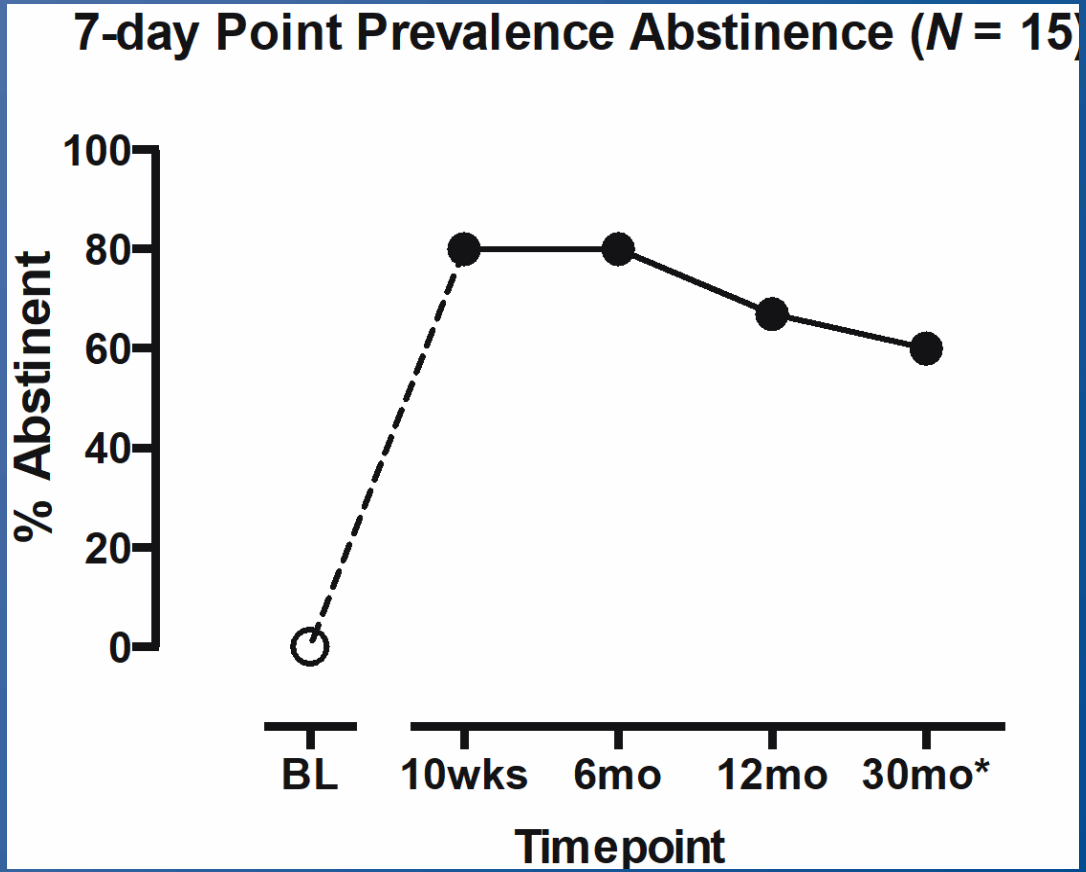
Serious adverse events

- No serious adverse events attributable to psilocybin


Median Breath CO (ppm)
± Interquartile Range
60
50
40
30
20
10
0
Prep Mtg 1
Prep Mtg 2
Prep Mtg 3
Prep Mtg 4
Psilocybin 1 (TQD)
1 wk post-TQD
Psilocybin 2 (2 wks)
3 wks post-TQD
4 wks post-TQD
5 wks post-TQD
6 wks post-TQD
7 wks post-TQD
Psilocybin 3 (8 wks)
9 wks post-TQD
10 wks post-TQD
6-month follow-up

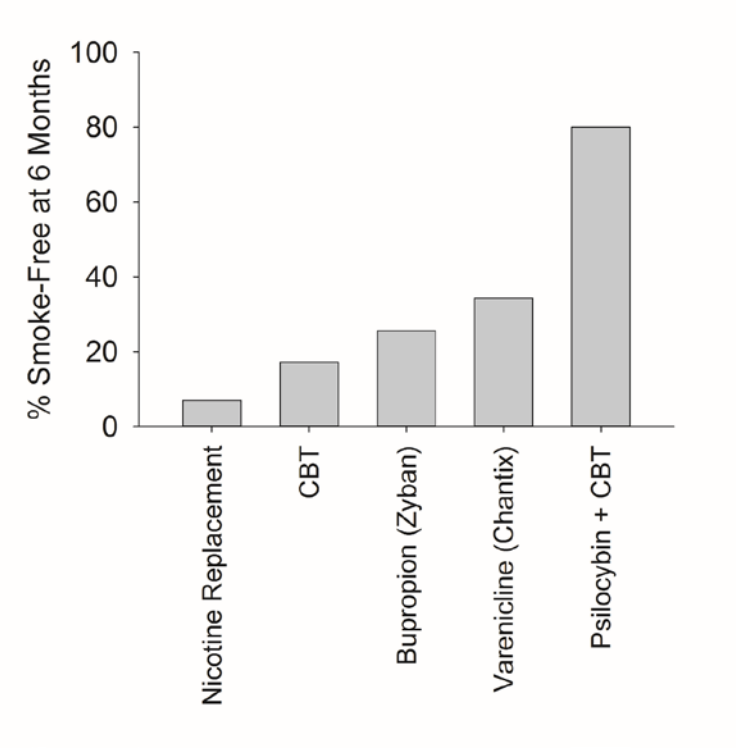

Median Breath CO (ppm)
± Interquartile Range
60
50
40
30
20
10
0
Prep Mtg 1
Prep Mtg 2
Prep Mtg 3
Prep Mtg 4
Psilocybin 1 (TQD)
1 wk post-TQD
Psilocybin 2 (2 wks)
3 wks post-TQD
4 wks post-TQD
5 wks post-TQD
6 wks post-TQD
7 wks post-TQD
Psilocybin 3 (8 wks)
9 wks post-TQD
10 wks post-TQD
6-month follow-up


Median Breath CO (ppm)
± Interquartile Range
60
50
40
30
20
10
0
Prep Mtg 1
Prep Mtg 2
Prep Mtg 3
Prep Mtg 4
Psilocybin 1 (TQD)
1 wk post-TQD
Psilocybin 2 (2 wks)
3 wks post-TQD
4 wks post-TQD
5 wks post-TQD
6 wks post-TQD
7 wks post-TQD
Psilocybin 3 (8 wks)
9 wks post-TQD
10 wks post-TQD
6-month follow-up


7-day Point Prevalence Abstinence (N = 15)
% Abstinent
100
80
60
40
20
0
BL
10wks
6mo
12mo
30mo*
Timepoint

Success Rates Substantially Higher than Typical

(Hughes et., 2003; Jorenby et al., 2006; Sykes & Marks, 2001)



Mystical Experience in Smoking Cessation 2015

- Greater success in those who had mystical experience
- Mystical experience associated with craving reduction

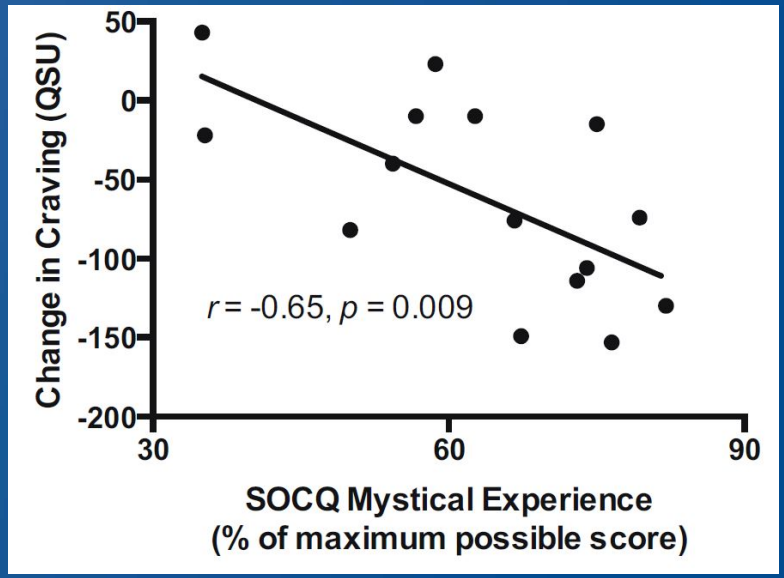
Current Drug Abuse Reviews, 2014, *7*, 157-164

Psilocybin-Occasioned Mystical Experiences in the Treatment of Tobacco Addiction

Albert Garcia-Romeu[1], Roland R. Griffiths[1,2] and Matthew W. Johnson[*,1]

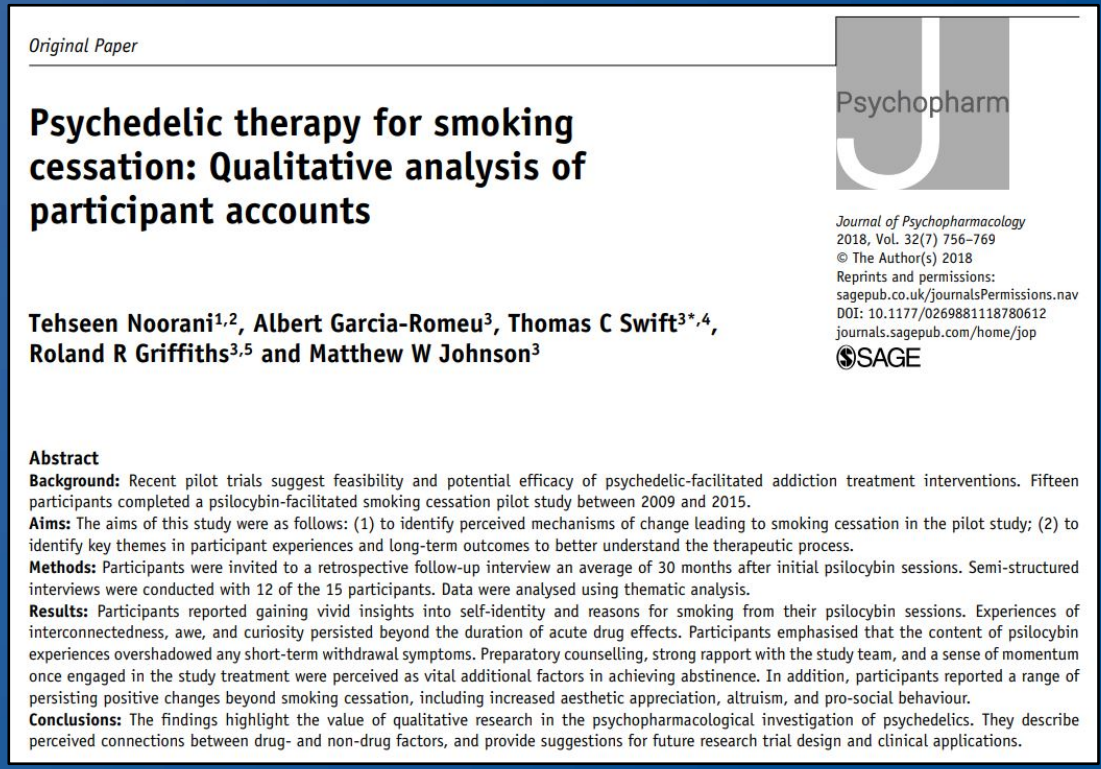
[1]*Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD, USA*

[2]*Department of Neuroscience, Johns Hopkins University School of Medicine, Baltimore, MD, USA*



Qualitative analysis: Smoking Cessation, 2018

- Persisting sense of interconnectedness, awe, curiosity
- Reduced smoking withdrawal symptoms compared with previous quit attempts
- Other positive changes: Altruism, appreciation for aesthetics
- Insights: self-identity, smoking reasons



Original Paper

Psychedelic therapy for smoking cessation: Qualitative analysis of participant accounts

Tehseen Noorani[1,2], Albert Garcia-Romeu[3], Thomas C Swift[3*,4], Roland R Griffiths[3,5] and Matthew W Johnson[3]

Psychopharm

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Abstract

Background: Recent pilot trials suggest feasibility and potential efficacy of psychedelic-facilitated addiction treatment interventions. Fifteen participants completed a psilocybin-facilitated smoking cessation pilot study between 2009 and 2015.

Aims: The aims of this study were as follows: (1) to identify perceived mechanisms of change leading to smoking cessation in the pilot study; (2) to identify key themes in participant experiences and long-term outcomes to better understand the therapeutic process.

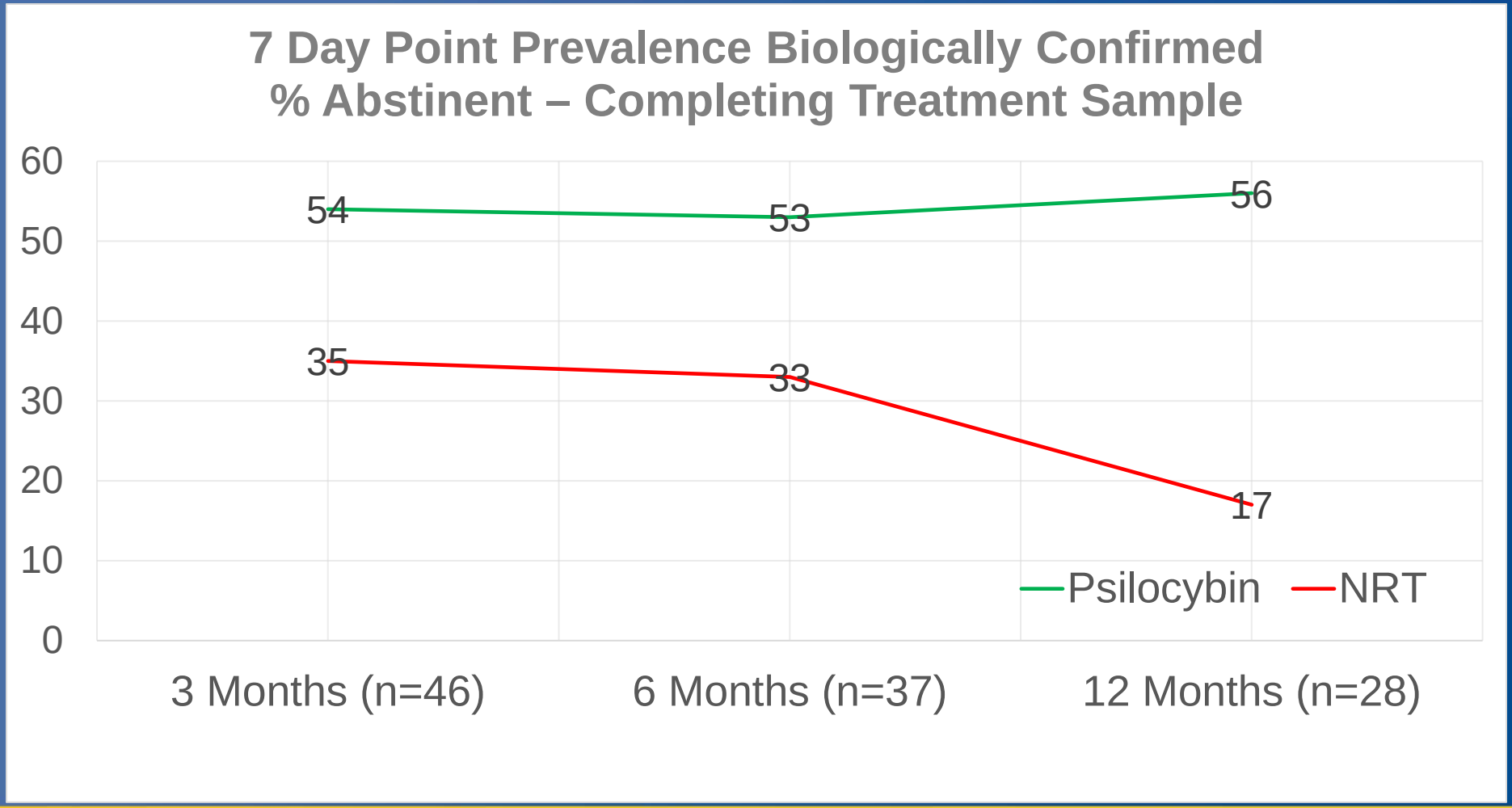
Methods: Participants were invited to a retrospective follow-up interview an average of 30 months after initial psilocybin sessions. Semi-structured interviews were conducted with 12 of the 15 participants. Data were analysed using thematic analysis.

Results: Participants reported gaining vivid insights into self-identity and reasons for smoking from their psilocybin sessions. Experiences of interconnectedness, awe, and curiosity persisted beyond the duration of acute drug effects. Participants emphasised that the content of psilocybin experiences overshadowed any short-term withdrawal symptoms. Preparatory counselling, strong rapport with the study team, and a sense of momentum once engaged in the study treatment were perceived as vital additional factors in achieving abstinence. In addition, participants reported a range of persisting positive changes beyond smoking cessation, including increased aesthetic appreciation, altruism, and pro-social behaviour.

Conclusions: The findings highlight the value of qualitative research in the psychopharmacological investigation of psychedelics. They describe perceived connections between drug- and non-drug factors, and provide suggestions for future research trial design and clinical applications.

Randomized Comparative Efficacy Trial

- 80 treatment-resistant smokers
- Randomized to psilocybin or nicotine patch
- Same cognitive behavior therapy
- 1 psilocybin session


7 Day Point Prevalence Biologically Confirmed
% Abstinent – Completing Treatment Sample
60
50
40
30
20
10
0
54
53
56
35
33
17
Psilocybin
NRT
3 Months (n=46)
6 Months (n=37)
12 Months (n=28)

Psilocybin improves cognitive control and downregulates parietal cortex in treatment-seeking smokers

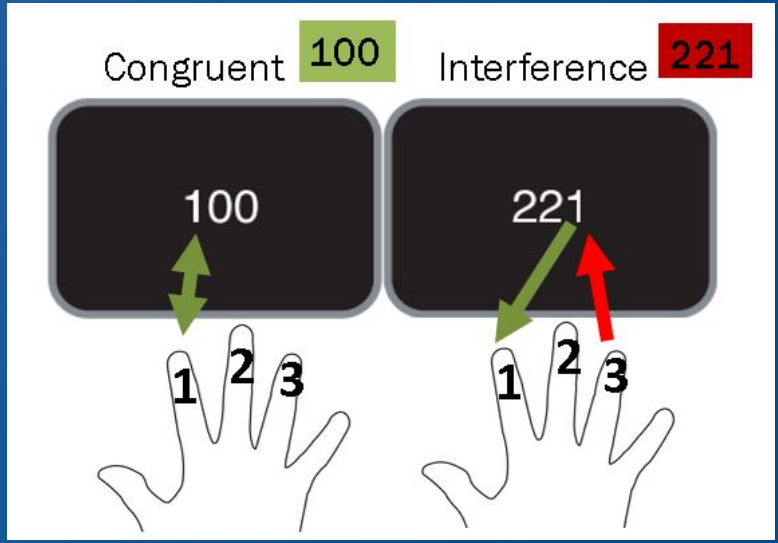
NIH National Institute on Drug Abuse

M. R. McKenna[1], J. R. Fedota[1], A. Garcia-Romeu[2], R. R. Griffiths[2], M. W. Johnson[2], and E. A. Stein[1]

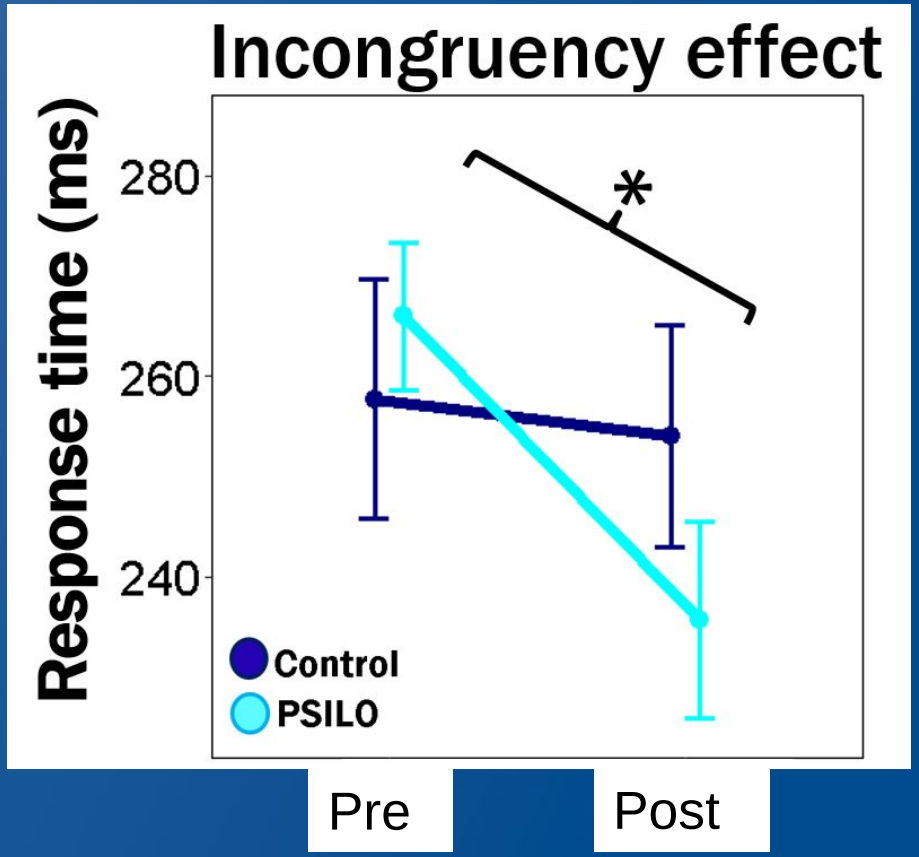
Neuroimaging Research Branch, National Institute on Drug Abuse, Intramural Research Program, National Institutes of Health, Baltimore, MD[1]
Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD[2]

Preliminary Cognitive and fMRI Results (17 Psilocybin, 10 NRT)

- Multi-Source Interference Task (MSIT) (Bush & Shin, 2006)
  - Cognitive interference
  - Congruency effect:
    - Reaction time of incongruent – congruent trials



Psilocybin group shows less “cognitive interference” the day after quitting



Alcohol Dependence Pilot

- 10 alcohol-dependent participants
- Motivational Enhancement Therapy
- 2 sessions of .3 mg/kg and .4 mg/kg psilocybin

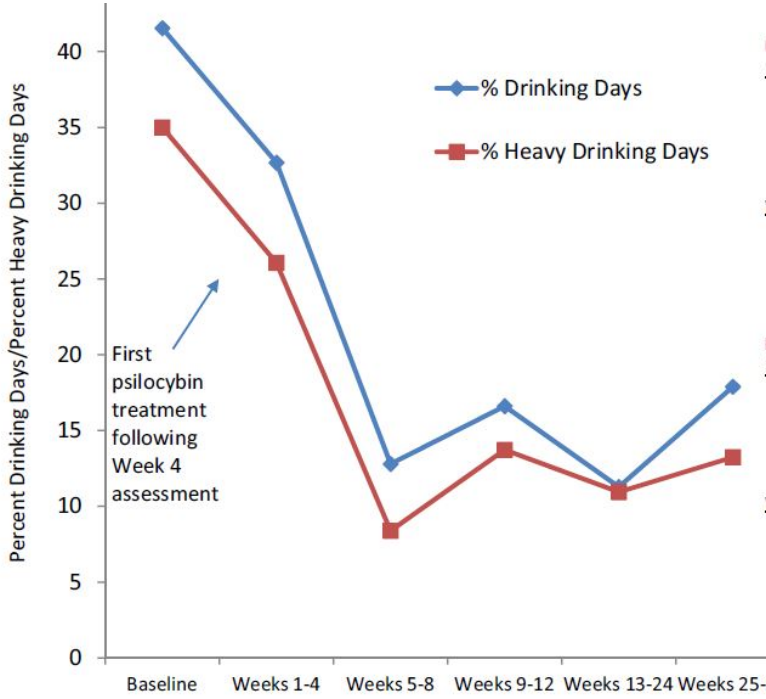
Original Paper

Psychopharm

Journal of Psychopharmacology
2015, Vol. 29(3) 289–299

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

Michael P Bogenschutz[1], Alyssa A Forcehimes[1], Jessica A Pommy[1], Claire E Wilcox[1], PCR Barbosa[2] and Rick J Strassman[1]

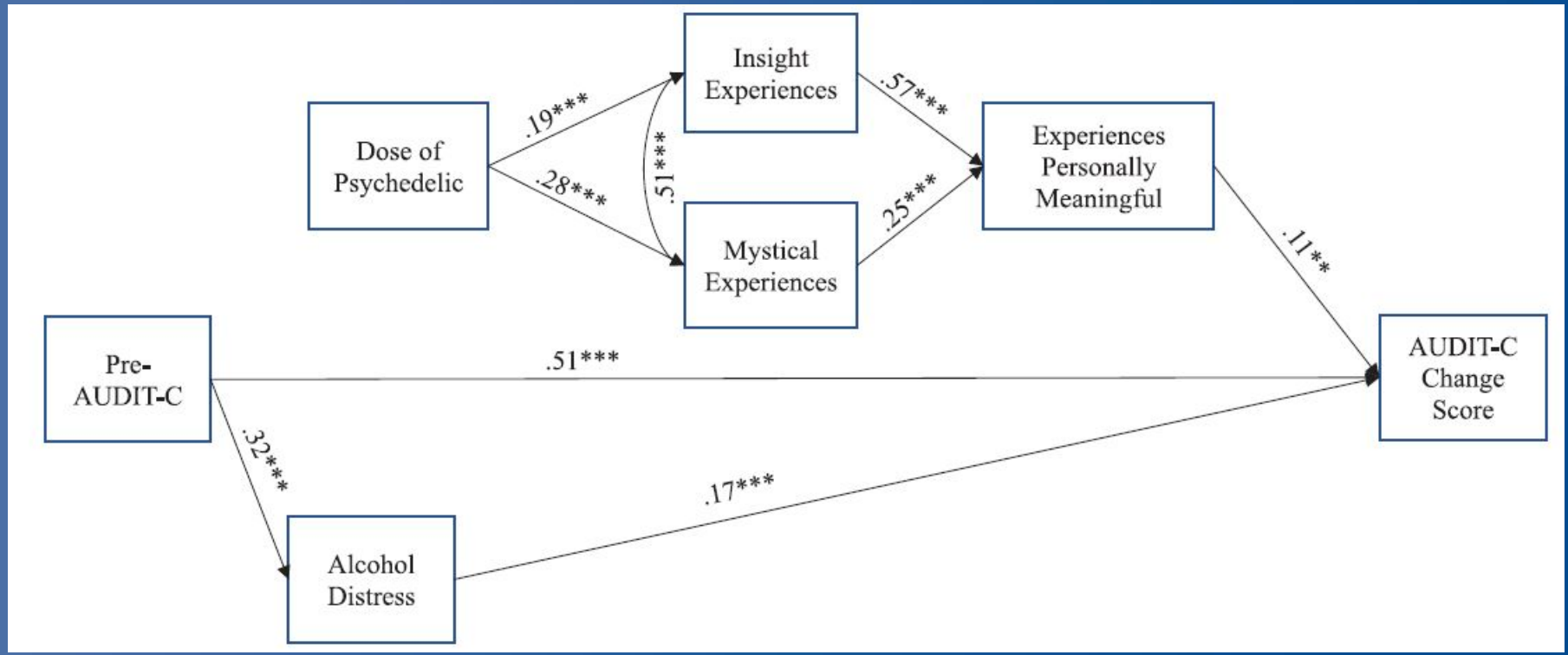


Drinking Days

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	$p = .018$	$d = 1.040$


Insight Experiences
Dose of Psychedelic
Mystical Experiences
Experiences Personally Meaningful
Pre-AUDIT-C
AUDIT-C Change Score
Alcohol Distress
.19***
.28***
.51***
.57***
.25***
.11**
.51***
.32***
.17***

Understanding Psychedelic Behavior Change

Common Mechanisms?

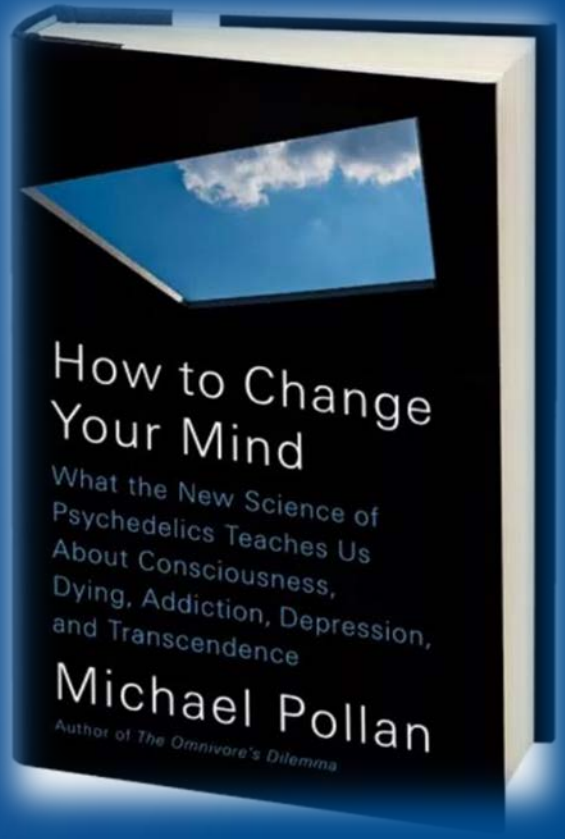
- Narrowing of behavioral and mental repertoire
  - Addiction broadly defined
  - Supported by overly rigid brain networks

Endogenous role for 5-HT2A receptors in modulating meaning and mental/behavioral plasticity?

The Dope Slap Effect

JOHNS HOPKINS MEDICINE

“Matt Johnson believes that psychedelics can be used to change all sorts of behaviors, not just addiction. The key, in his view, is their power to occasion a sufficiently dramatic experience to ‘dope-slap people out of their story...’ Psychedelics open a window of mental flexibility in which people can let go of the mental models we use to organize reality.’”



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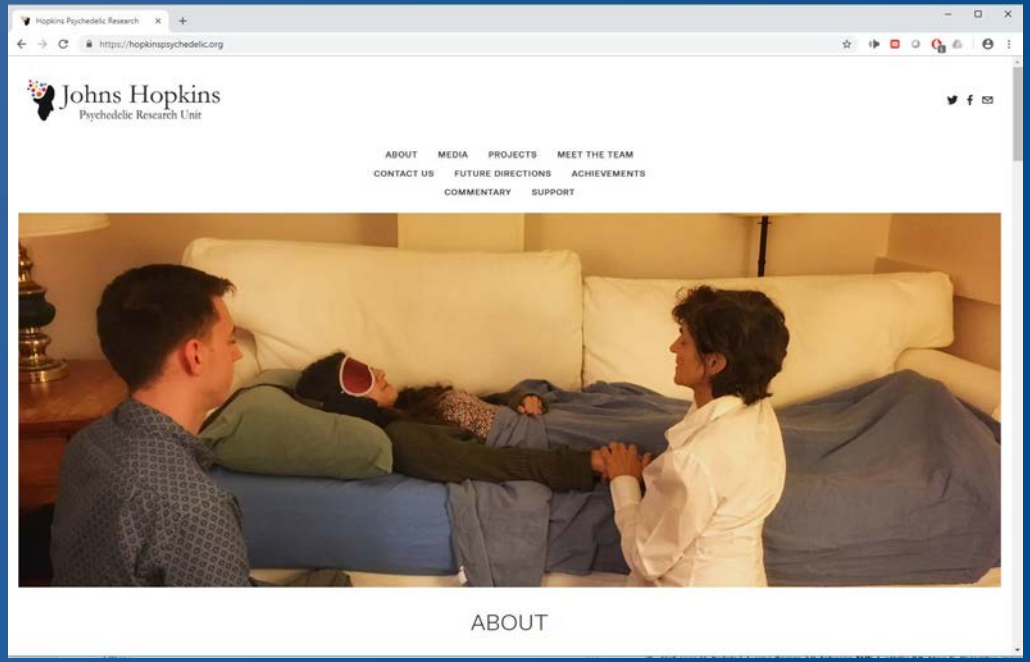

https://hopkinspsychedelic.org

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