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GENERAL HOSPITAL

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Risks and Potential Harms of Psychedelics

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MGH Psychiatry Academy, 5th Annual Psychedelics Conference

November 2025



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Psychiatric Risks

Psychedelics and Mental Health: A Population Study

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Abstract

Background: The classical serotonergic psychedelics LSD, psilocybin, mescaline are not known to cause brain damage and are regarded as non-addictive. Clinical studies do not suggest that psychedelics cause long-term mental health problems. Psychedelics have been used in the Americas for thousands of years. Over 30 million people currently living in the US have used LSD, psilocybin, or mescaline.

Objective: To evaluate the association between the lifetime use of psychedelics and current mental health in the adult population.

Method: Data drawn from years 2001 to 2004 of the National Survey on Drug Use and Health consisted of 130,152 respondents, randomly selected to be representative of the adult population in the United States. Standardized screening measures for past year mental health included serious psychological distress (K6 scale), mental health treatment (inpatient, outpatient, medication, needed but did not receive), symptoms of eight psychiatric disorders (panic disorder, major depressive episode, mania, social phobia, general anxiety disorder, agoraphobia, posttraumatic stress disorder, and non-affective psychosis), and seven specific symptoms of non-affective psychosis. We calculated weighted odds ratios by multivariate logistic regression controlling for a range of sociodemographic variables, use of illicit drugs, risk taking behavior, and exposure to traumatic events.

Results: 21,967 respondents (13.4% weighted) reported lifetime psychedelic use. There were no significant associations between lifetime use of any psychedelics, lifetime use of specific psychedelics (LSD, psilocybin, mescaline, peyote), or past year use of LSD and increased rate of any of the mental health outcomes. Rather, in several cases psychedelic use was associated with lower rate of mental health problems.

Conclusion: We did not find use of psychedelics to be an independent risk factor for mental health problems.

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Common trial exclusion criteria

- History of psychosis or mania (many studies also exclude if primary relative with these conditions)
- Active suicidal ideation or high risk for suicide
- Active substance use (~excepting mild to moderate cannabis use)
- Medical contraindications
- Are these generalizable?



Risk of psychosis and mania

- Anecdotal reports of prolonged psychosis going back to the 1960s
- Not seen in any modern clinical trials
- One 1960s study reported “psychosis > 24 hours” in subject whose twin had schizophrenia
- Most case reports finding association are obscured by comorbid heavy cannabis use

Longitudinal associations between psychedelic use and psychotic symptoms in the United States and the United Kingdom

Ludwig Honk ^a   , Cecilia U.D. Stenfors ^b , Simon B. Goldberg ^c , Peter S. Hendricks ^d ,

Walter Osika ^a , Haley Maria Dourron ^d , Alexander Lebedev ^e , Predrag Petrovic ^e ,

Otto Simonsson ^{a f}

Methods

- *9,732 participants enrolled*
- *Surveyed at T1 and T2 (2 months)*
- *T1: risk factors for psychosis and mania*
- *T1 & T2: symptoms of mania and psychosis*
- *T2: psychedelic use during study period?*

Highlights

- Longitudinal study with nationally representative samples on change in number of psychotic symptoms following psychedelic use.
- Psychedelic use was not generally associated with a change in the number of psychotic symptoms.
- In respondents with a personal or family history of bipolar disorders, psychedelic use was associated with an increase in the number of psychotic symptoms.
- In respondents with a personal history of psychotic disorders, psychedelic use was associated with a decrease in the number of psychotic symptoms.

Adolescent Psychedelic Use and Psychotic or Manic Symptoms

Otto Simonsson, PhD; Miriam A. Mosing, PhD; Walter Osika, MD, PhD; Fredrik Ullén, PhD; Henrik Larsson, PhD; Yi Lu, PhD; Laura W. Wesseldijk, PhD

- Sample of 16,255 adolescent twins
- Cross sectional evaluation of association between past psychedelic use and psychotic or manic symptoms
- Psychedelic use was associated with lower rates of psychotic sx when controlling for other drug use
- Higher risk for manic symptoms in individuals with higher genetic vulnerability for both schizophrenia and bipolar disorder



Hallucinogen Persisting Perceptual Disorder

- Re-experiencing perceptual distortions induced while under effects of a psychedelic with subsequent impairment or anxiety
- Has not occurred in any modern study
- Challenges: paucity of controlled data, recall bias
- Possible LSD > psilocybin (?)

Linszen et al, *Eur Neuropsychopharmacol* 2018
Halpern et al, *Curr Top Behav Neurosci* 2018



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Psychedelics and Suicide

Psychedelics not linked to mental health problems or suicidal behavior: A population study

Pål-Ørjan Johansen¹ and Teri Suzanne Krebs²

Journal of Psychopharmacology

2015, Vol. 29(3) 270–279

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DOI: [10.1177/0269881114568039](https://doi.org/10.1177/0269881114568039)

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A recent large population study of 130,000 adults in the United States failed to find evidence for a link between psychedelic use (lysergic acid diethylamide, psilocybin or mescaline) and mental health problems. Using a new data set consisting of 135,095 randomly selected United States adults, including 19,299 psychedelic users, we examine the associations between psychedelic use and mental health. After adjusting for sociodemographics, other drug use and childhood depression, we found no significant associations between lifetime use of psychedelics and increased likelihood of past year serious psychological distress, mental health treatment, suicidal thoughts, suicidal plans and suicide attempt, depression and anxiety. We failed to find evidence that psychedelic use is an independent risk factor for mental health problems. Psychedelics are not known to harm the brain or other body organs or to cause addiction or compulsive use; serious adverse events involving psychedelics are extremely rare. Overall, it is difficult to see how prohibition of psychedelics can be justified as a public health measure.

Psychedelics not linked to mental health problems or suicidal behavior: A population study

Pål-Ørjan Johansen¹ and Teri Suzanne Krebs²

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'Flying' on LSD, Student Plunges to Death in Greenwich Village

By ROBERT D. McFADDEN

A 20-year-old college student leaped four floors to his death Sunday from the roof of a Greenwich Village brownstone. Before he died, he told detectives that he had taken the hallucinogenic drug LSD and had "wanted to fly."

Dr. Michael Baden, an assistant medical examiner, said yesterday that records kept by the

City Medical Examiner indicated that there had been a dozen similar death plunges here under the influence of LSD in the last three years.

Sunday's victim was Walter

A. Gilchriest Jr. of Massena, N. Y., a junior majoring in social studies at the State Uni-

versity of New York at New Paltz. He had been in the city during the holidays visiting his sister, Cynthia, at 213 East 10th Street.

According to the police, the young man apparently walked to the roof of a building at 248 West 14th Street and jumped off at 2 A.M. He was found on the sidewalk in front of the building, suffering internal injuries.

Before he died at 4:27 A.M., he identified himself to the police and said he had leaped under the influence of lysergic acid diethylamide, known as LSD.

After an autopsy yesterday, Dr. Baden attributed the death to internal hemorrhaging re-

yesterday that Mr. Gilchriest

sulting from spleen laceration and a hip fracture.

Mr. Gilchriest's death recalled that of Diane Linkletter, the 20-year-old daughter of Art Linkletter, in a fall from the window of her Los Angeles apartment on Oct. 4. The entertainer later said Miss Linkletter had died during a "bad trip" on LSD.

Partly because of Miss Linkletter's death, President Nixon has said he will seek a \$17-million increase in the Federal appropriation for educational programs on drug abuse. The programs currently receive about \$23-million.

New Paltz State, in County, has an enrollment of about 4,700 students working for teaching

was a "better than student with grades just a B average. He was in courses that would have a teaching certificate."

He lived in an apartment room and worked part-time in a variety of jobs at the Union at New Paltz, paying his way through

Carl Martin, who directed Student Union as head of student activities, said yesterday that he was "shocked" by the death of Mr. Gilchriest. He described him as a "hospitable worker and student."

New Paltz State, in Ulster County, has an enrollment of about 4,700 students working for teaching

Linkletter Says Daughter Took LSD Before Death

HOLLYWOOD, Oct. 5 (UPI)—Art Linkletter said today that his 20-year-old daughter Diane jumped to her death from the window of her sixth floor apartment while under the influence of LSD.

The television entertainer said he knew for six months that she had been taking the drug. He said she was afraid of LSD but that he could not stop her from using it.

"It wasn't a suicide," Mr. Linkletter said, "because she wasn't herself."

"It was murder. She was murdered by the people who manufacture and sell LSD," he said.

Mr. Linkletter made the disclosure in an interview with The Los Angeles Times.

Friends Say Youth, Under Spell of LSD, Jumped to His Death

BERKELEY, Calif., July 31 (AP)—A 20-year-old Berkeley youth, reported by friends to be under the influence of the hallucinatory drug LSD for the first time, jumped from a third-story window to his death early today.

Vernon L. Cox took an oral dose of the drug at about 9 P. M. yesterday and jumped from an apartment window across the street from his home shortly after 1 A. M., his companions told the Berkeley police.

A witness to Mr. Cox's behavior under the influence of the drug, Ronald E. Ryer, 23, who lived in the building from which the youth jumped, said the dead youth and his roommate, Kenneth D. Tavalin, 19, were both having their first experience with LSD at the time.

Mr. Ryer said Mr. Cox became loud and violent after the drug began to take effect. He had hallucinations and had to be forcibly restrained from leaving the building several times, according to Mr. Ryer, who said Mr. Cox insisted he was taking a trip to Europe.

The last time Mr. Cox tried to leave and was stopped, he entered a room, slammed the door, ran to the window and jumped, the witnessess told the police.

The police were called to the scene. They rushed the youth to Herrick Hospital where he was pronounced dead.

Media reports from 1969 and Diane Linkletter



A suicide attempt following psilocybin ingestion in a patient with no prior psychiatric history

Eric N. Kramer^{#,*}, Kalyn Reddy[#], Bryan Shapiro

University of California Irvine Health, Orange, United States

- *A 30 year old man with no past psychiatric history presented to the emergency department after a suicide attempt by **multiple self-inflicted stab wounds to the neck with a 5-inch kitchen knife**....*
- *On interview [after], the patient denied any recent stressors and current or previous thoughts of self-harm. He expressed regret regarding the incident. He was unable to explain why he had attempted suicide, although he did confirm he had attempted suicide. Mental status exam was unremarkable.*
- *Ingestion of psilocybin-containing chocolates later revealed by patient's brother.*

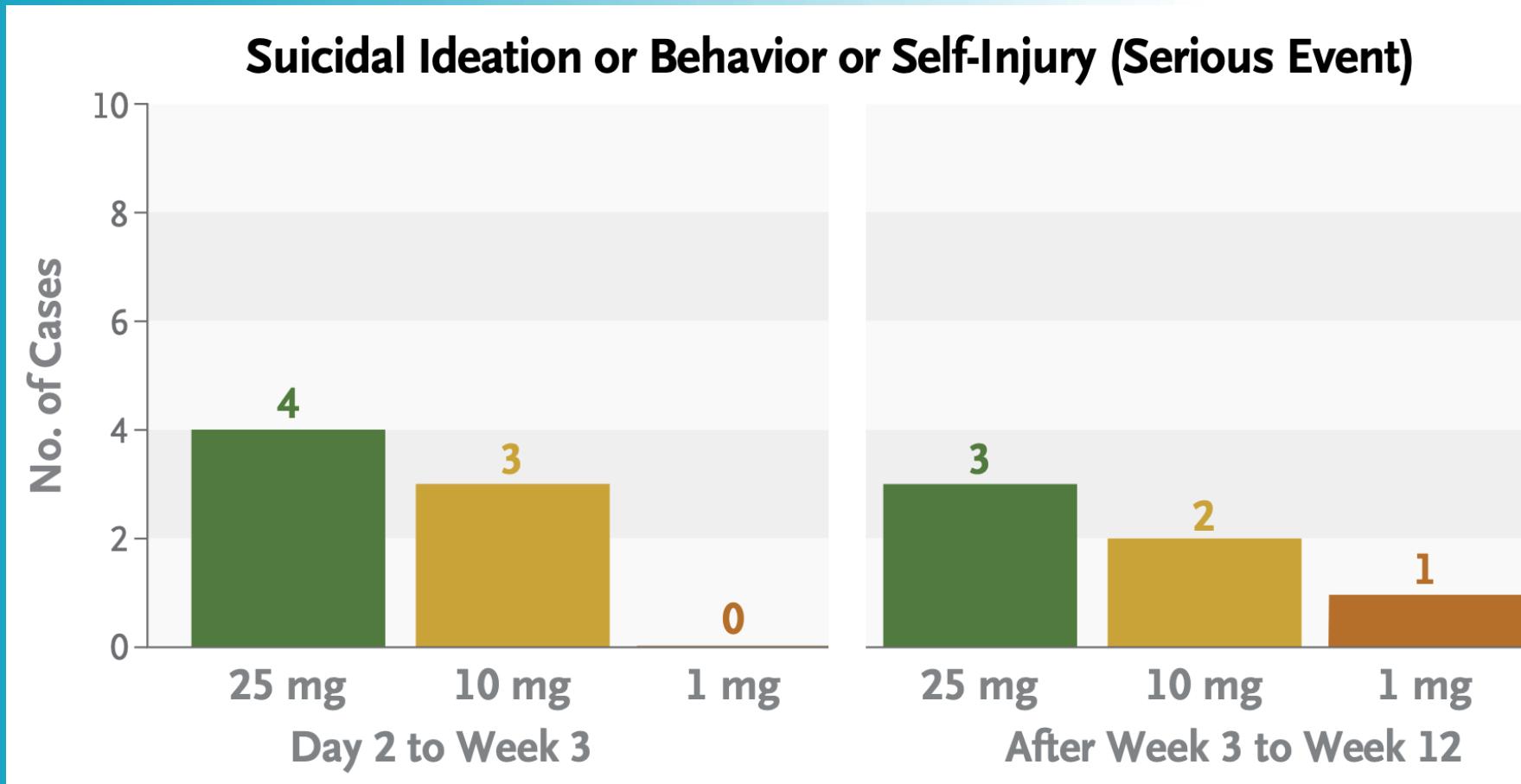


Psychedelic *therapy* and suicide

- Studies in modern era generally point toward reduction in symptoms of suicide and symptoms known to be risk factors for suicide (alcohol use, depression etc)
- Meta-analysis (2022) of 7 PAT trials found large effect sizes for reduction in “suicidality” relative to baseline, including “sustained” responses (1-8 weeks and 3-4 months), and medium effect sizes for reductions at 6 months
- However, authors noted significant limitations (small sample sizes, heterogeneity of interventions)
- Do psychedelics also carry a risk of suicide and/or suicidal ideation?

Zeifman et al, *J Clin Psychiatry*, 2022

Psilocybin for TRD, NEJM, 2022





Psychedelics and Ego Inflation

- “The trouble is, LSD attracts unstable therapists as much as it does the neurotic patient. It gives them an intoxicating sense of power to bestow such a fabulous experience on others.” Sidney Cohen, 1963
- Tendency of people who have had a psychedelic experience to seek to share it with others
- Association with pathological personalities (eg Manson)

Psychedelic medicine: safety and ethical concerns

Brian T Anderson, Alicia L Danforth, *Charles S Grob

those who do not have personal experience, we advise caution when evaluating the judgment of research and clinical colleagues who have only begun to take psychedelics within the past couple of years. Despite the association between psychedelic use and ego dissolution,⁷ grandiosity can loom large with initial psychedelic experiences, leading even conservative individuals to become wildly enthusiastic about the potentials of psychedelics to heal and transform. Although this enthusiasm tends to wane over time, the risks of ego inflation and grandiosity can persist in susceptible personality types. Conversely, people



Psychedelics, Suggestibility, and Vulnerability

- Long known that psychedelics induce a state of heightened suggestibility
- Psychedelic state itself is a highly vulnerable state
- This likely increases in correlation to the power of the experience itself
- Risk of fetishizing or aggrandizing therapist/s
- Power dynamic between patient and clinician
- Risk of abuse, manipulation or undue influence



Use of touch in psychedelic therapy

- Partly a legacy of Grof, designed in part based on extensive experience conducting LSD work
- Partly pragmatic: anxiety not uncommon and patients may ask for physical contact
- Most protocols allow for only limited touch, ie hand-holding or a hand on the shoulder
- Use of touch and patient preference always discussed beforehand
- Touch may be offered, but never done on therapists' own initiative
- Even if touch is beneficial, is modern mental healthcare prepared to know how to do this ethically and safely?



Ethical concerns around informed consent

- Risks of challenging experiences: seemingly low in controlled studies, but
- Survey of mushroom users: 39% reported their worst trip to be among the 5 most challenging experiences of their lives
- Potential to reactivate (or re-experience) trauma
- Some evidence showing enduring changes in personality, values, worldviews, and spirituality
- Need for “enhanced” informed consent?

Ethics and ego dissolution: the case of psilocybin

William R Smith,¹ Dominic Sisti²

worldview. Focusing on the case of psilocybin, we argue that the peculiar features of psychedelics pose certain novel risks, which warrant an enhanced informed consent process—one that is more comprehensive than what may be typical for other psychiatric medications. We highlight key issues that should be focused on during the consent process and suggest discussion prompts for enhanced consent in psychedelic psychiatry. Finally, we respond to



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