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Psychedelic-Assisted Psychotherapy

Dr. Joe Flanders

Mindspace

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Dr. Joe Flanders is the Founder and Director of Mindspace Wellbeing and the Vice-President of Psychology at Numinus Wellness. He is a licensed psychologist and an Assistant Professor (Professional) at McGill University. He has an active practice as a psychotherapist, psychedelic-assisted psychotherapist, and mindfulness teacher—in addition to his role as the head of Practitioner Relations at Numinus. He appears frequently in the media as an expert in mental health, mindfulness, and psychedelics.

Disclosures/Conflicts of Interest



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- Employee of and shareholder in Numinus Wellness, a corporation developing psychedelic compounds, conducting research on psychedelic-assisted psychotherapy and providing psychedelic-assisted psychotherapy services.
- Mindspace Wellbeing is a subsidiary of Numinus Wellness.



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Learning Objectives

- Describe the history of psychedelic therapies in the West
- List the most common psychedelic compounds
- Discuss the key studies driving the psychedelic renaissance
- Explain current hypotheses about the mechanisms of action in psychedelic therapy

The problem



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There is a mounting crisis in mental health

Instances of anxiety, depression and other mental health disorders have been on a steady rise for the last 30 years, and coronavirus pandemic has now created an even greater crisis; prescriptions for anti-anxiety and anti-depression medication have spiked 20% during the lockdown.

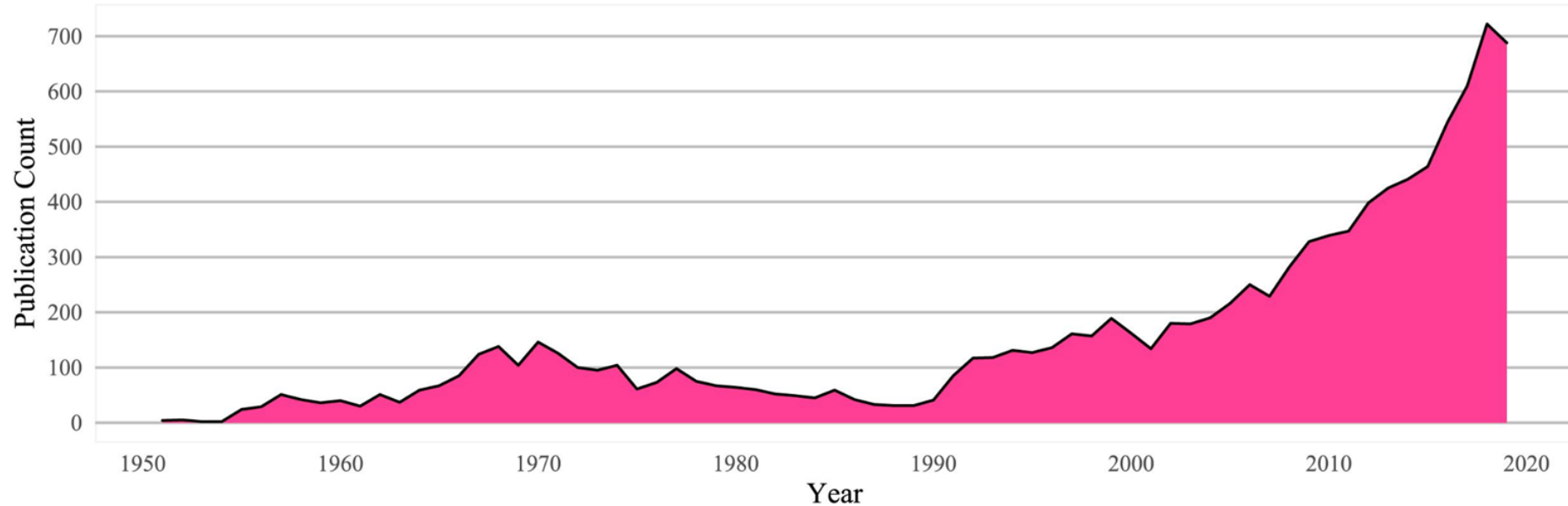
Unfortunately, there have been very few new developments with medication in this time span, with increasing evidence that existing treatments are ineffective (with high relapse rates), or worse, simply exacerbate the problem, turning potentially treatable issues into long-term chronic conditions at a huge cost to society's collective well-being.

The Psychedelic Renaissance



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Web of science psychedelic publication count by year, searching for
"LSD," "PSILOCYBIN," "PSYCHEDELICS," or "HALLUCINOGENS"

Psychedelic research



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Psilocybin-assisted Psychotherapy

- Smoking cessation
- Alcohol use disorder
- Cocaine use disorder
- OCD
- Anxiety & depression in patients with advanced-stage cancer
- Treatment-resistant depression
- Distress associated with loss due to HIV/AIDS

MDMA-assisted Psychotherapy

- Treatment-resistant PTSD
- Anxiety related to end of life
- Social anxiety in Autism Spectrum Disorder
- Alcohol use disorder

Ketamine

- Alcohol use disorder
- Treatment resistant depression
- Heroin use disorder

Wellness

- Creativity
- Spirituality
- Meditation
- Religious professionals
- Prosocial attitudes & behaviours
- Train openness

Planned trials

- Anorexia Nervosa (psilocybin)
- Opioid use disorder (psilocybin)
- Emotional distress in early Alzheimers (psilocybin)
- Group therapy
- Microdosing

Recent FDA Breakthrough Therapies in Psychiatry (150 total)



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April 2016: Pimavanserin for Parkinson's Disease Psychosis

April 2017: Valbenazine for Tardive Dyskinesia

August 2017: Deutetrabenazine for Tardive Dyskinesia

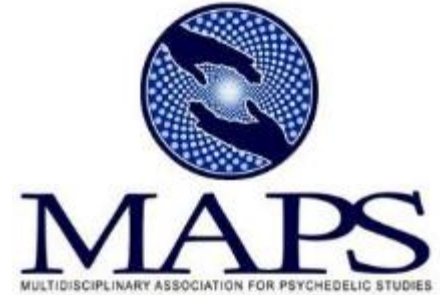
August 2017: MDMA-assisted psychotherapy for PTSD

October 2018: Psilocybin (COMPASS) for treatment-resistant depression

March 2019: Brexanolone for postpartum depression

March 2019: Esketamine for treatment-resistant depression

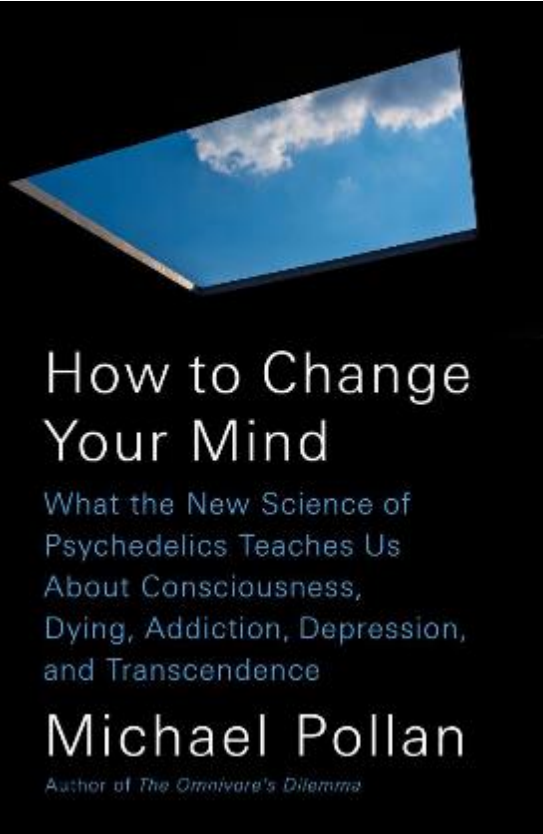
November 2019: Psilocybin (Usona) for major depressive disorder





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JOHNS HOPKINS
**Center for Psychedelic &
Consciousness Research**

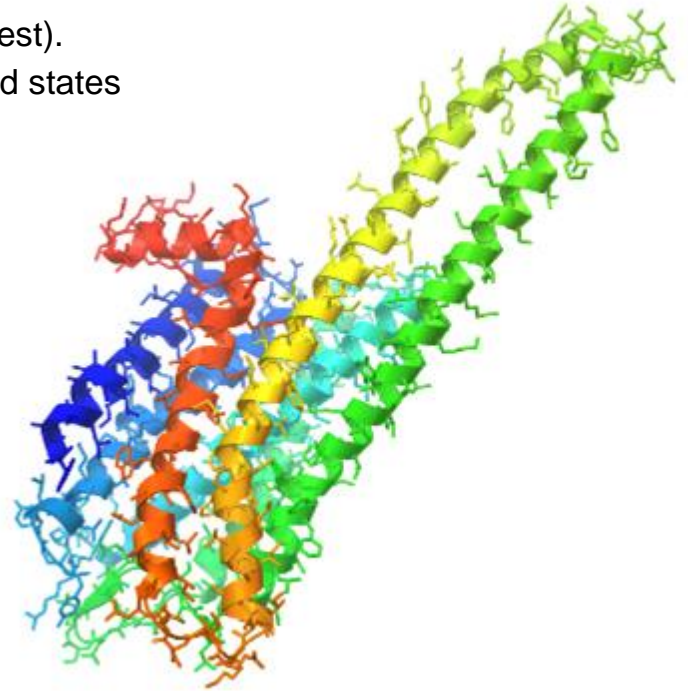
Psychedelics: definition



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- Coined in 1953 by Canadian psychiatrist Humphrey Osmond
- From the Greek *psyche* (mind/soul) and *delos* (reveal/manifest).
- A diverse group of molecules that produce profoundly altered states of consciousness
- Classical Psychedelics:
 - LSD, psilocybin, ayahuasca (DMT + MAOI), peyote
 - 5-HT_{2A} agonists
- Empathogens: MDMA
- Others:
 - Ketamine/Esketamine
 - Ibogaine
 - Cannabinoids?
- Origins can be traced variously to:
 - 6,000 BC North Africa
 - Aztec Rituals
 - 20th Century Switzerland



Mechanism of action



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Biological

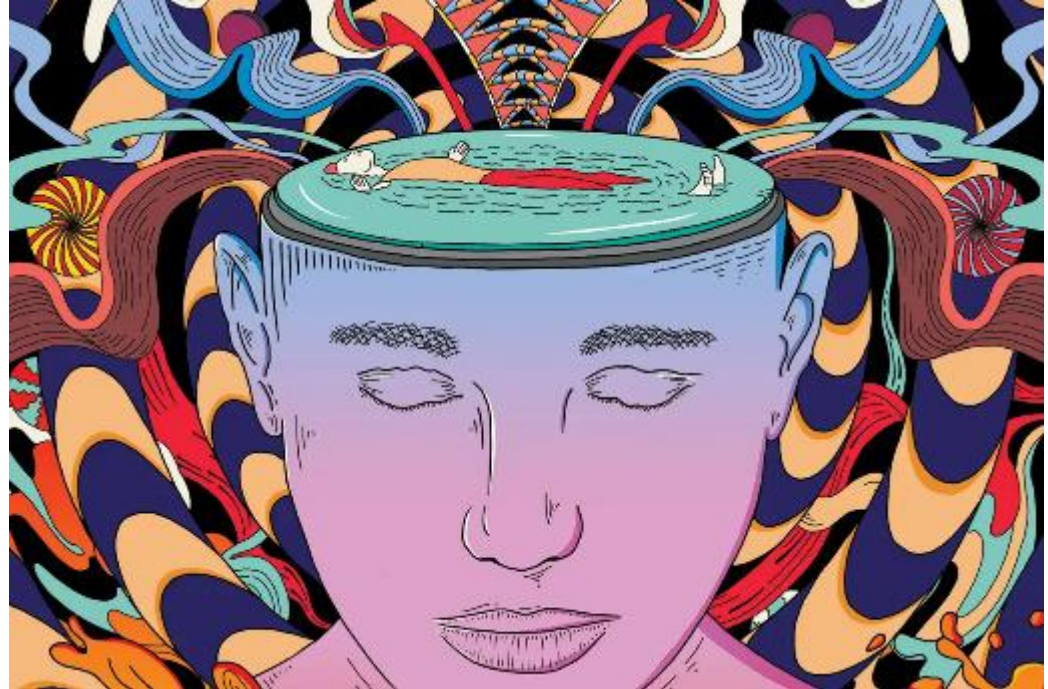
- 5HT2A receptor action
- Anti-inflammatory effects
- Oxytocin release

Psychological

- Sense of awe
- Interconnectedness
- Positive mood
- Autobiographical memory access
- Emotional release

Interaction

- Set & setting
- PAP



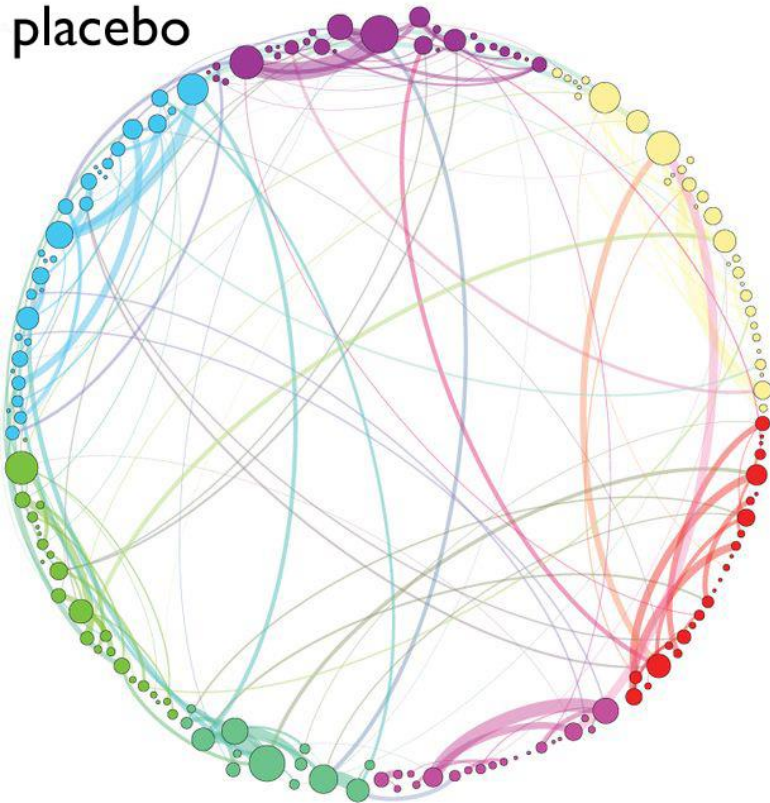
Entropic brain hypothesis



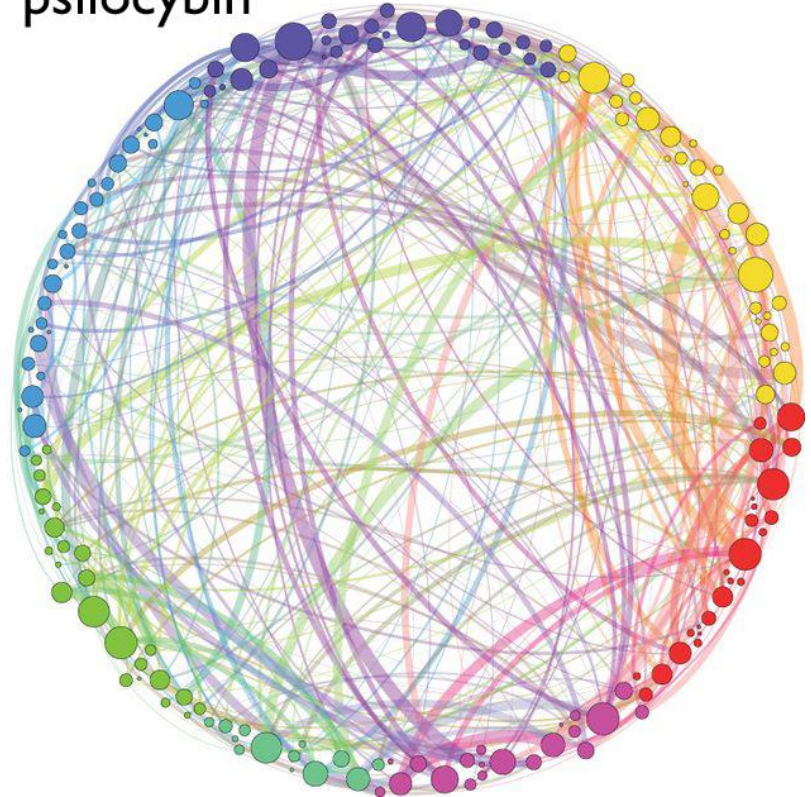
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placebo



psilocybin



Use & Risks



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Lifetime prevalence:

- 32 million in US in 2010
- 17% of people 21-64 years
- Highest rate among 30-34 year olds (20%; 26% male, 15% female)
- Jump from 4% to 8% of US college students

Recognized risks:

- Hallucinogen Persisting Perception Disorder
- Substance (Hallucinogen) Induced Psychosis

Anecdotal evidence

- Increased anxiety
- Lower mood
- Dramatic shifts in relationships and value systems
- Somatic symptoms
- “Psychedelic Trauma”



Harm profile



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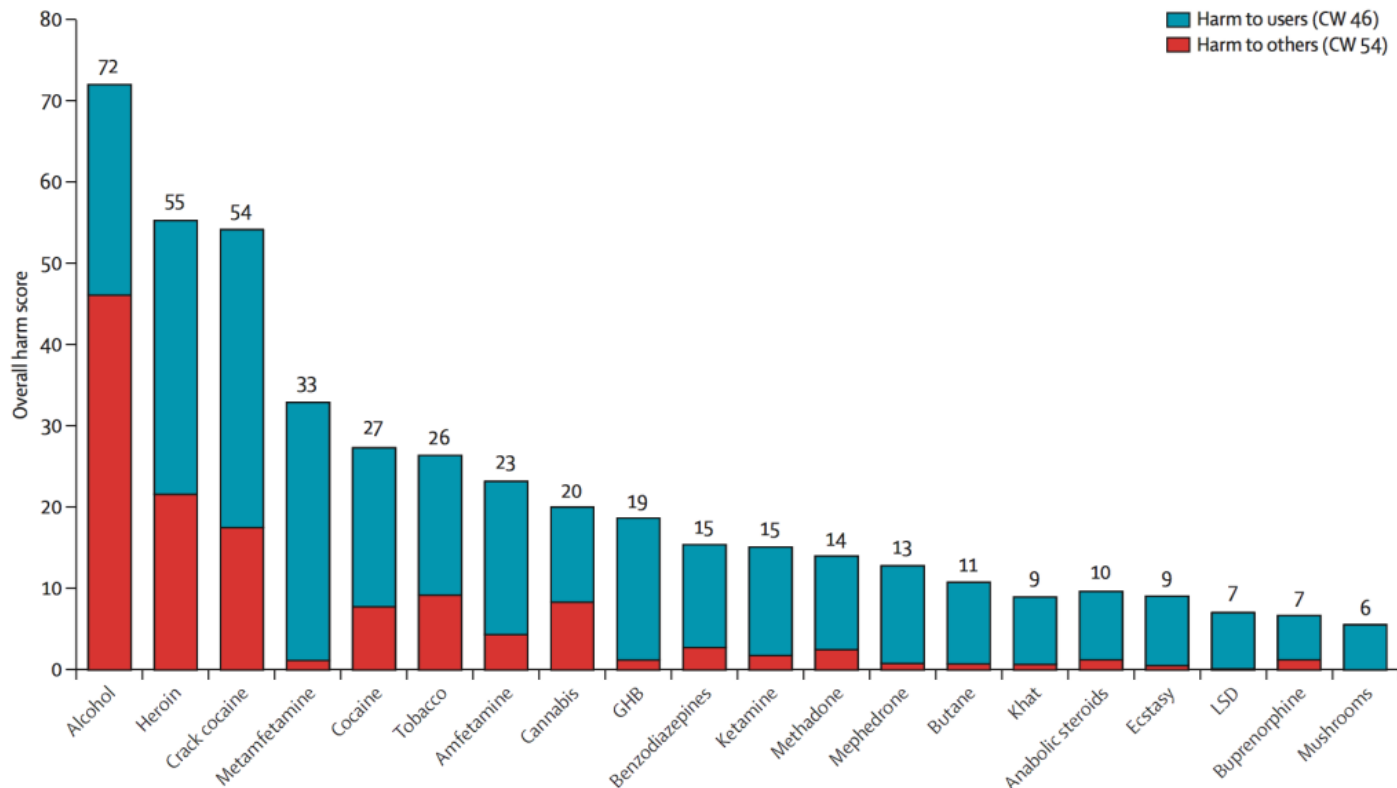


Image credit: The 2010 Lancet study's official rankings. Alcohol is by far the most dangerous drug. Nutt et al./Lancet

The history of psychedelics

Earliest evidence

DMT

2130 BCE - Earliest evidence of **DMT** usage in form of **entheogenic Yopo snuffs** derived from *Anadenanthera* seeds in NW Argentina.
1931 - DMT is first synthesized by Richard Manske.

MDMA

1912 - MDMA first synthesized and patented by the German pharmaceutical company Merck in Darmstadt.

Peyote

3800 BCE - Earliest evidence of suspected **Peyote cacti** usage in North America.
1897 - German chemist Arthur Heffter isolated **Mescaline** from Peyote.

Salvia

Little is known about its traditional use as an entheogen.
1938 - Jean B. Johnson wrote about **Salvia divinorum** (*Hierba Maria*) in his publications about the Mazatec shamans.

Ayahuasca

1851 - "English botanist Richard Spruce encountered the use of an intoxicating beverage among Tukano Natives of the Rio Uapés in Brazil" this was the first non-published scientific discovery of **Ayahuasca**.

LSD

1938 - Swiss chemist Albert Hofmann working at Sandoz Pharmaceuticals first synthesized **LSD**.
1943 - Hofmann accidentally discovered its psychedelic properties.

Psilocybin

7000 to 9000 BCE - N. Africa
Psilocybin use traces back to very prehistoric times.
6000 BCE - Spain
Earliest murals of suspected **Psilocybin** Mushroom rituals.

Iboga

Possibly used for thousands of years. Roots of **Iboga** are used during initiation rites in the Bwiti Religion in Gabon, Africa.

1950's and 1960's scientific research

over
1000
scientific
papers

Dr. Oscar Janiger
psychiatrist in Los Angeles
substance: **LSD**
period: **1954 till 1962**.
participants: **900**

around
40.000
patients

period: **45 years** participants: **45**
Conclusion: LSD can be safely administered in controlled doses to healthy humans by researchers trained in psychotherapy.

6
international
conferences

Expansion of the hippie movement, which promoted the use of psychedelic drugs such as marijuana and LSD as harmless and non-addictive, in order to explore the altered states of consciousness.

Mid 1960s prohibition

All scientific psychedelic research on humans banned in U.S.

Summer of Love - San Francisco
Around **100,000 people** gathered, influenced by the movement and lifestyle.

Second Summer of Love - Britain
A renaissance of acid house music and rave parties. Supported **MDMA** and **LSD** use.

october
1966

LSD was considered as having a negative impact on the values of the Western middle class and declared a controlled substance in California.
The rest of the world followed.
After that, the **LSD** black market emerged.

october
1970

The **Controlled Substances Act** declares that these drugs have "**no currently accepted medical use**". However, researchers were unable to further explore their therapeutic potential because they are banned.

1967

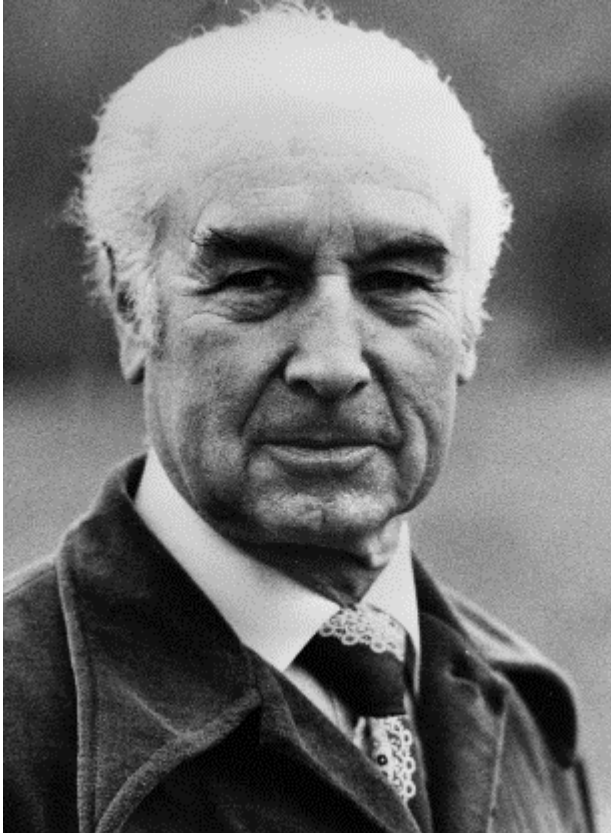
1986

Lysergic Acid Diethylamide (LSD)



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Albert Hofmann synthesizes LSD for the first time in 1938

- Ergot a fungus growing on rye
- Discovers psychoactive properties in 1943
- Distributed widely by Sandoz
- Research took off in the 1950s
 - Exploring psychosis
 - Adjunct for psychotherapy

Harvard Psilocybin Project (1960-62)



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Psilocybin research

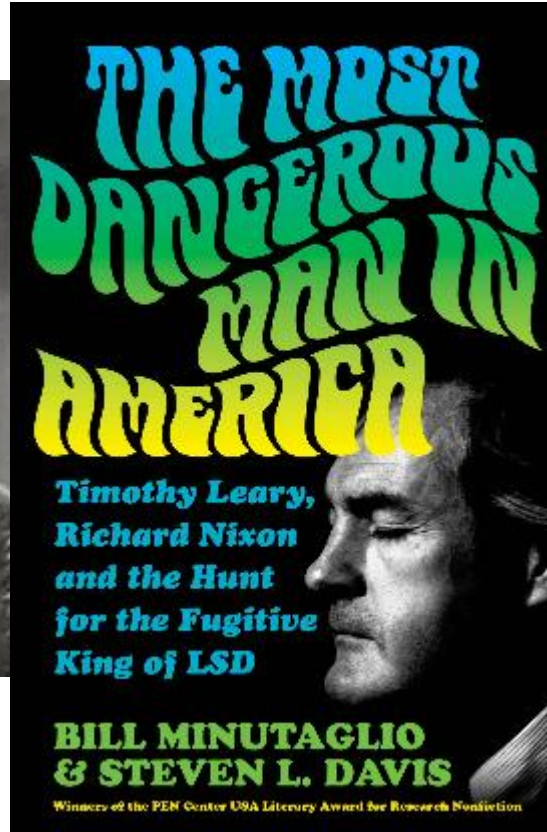
- Timothy Leary & Richard Alpert
- Concord Prison Experiment & Marsh Chapel Experiment
- Ethics controversy
- Fired from Harvard in 1963
- Set & Setting
- “Turn on, tune in, drop out”

Prohibition



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Psychedelics go underground

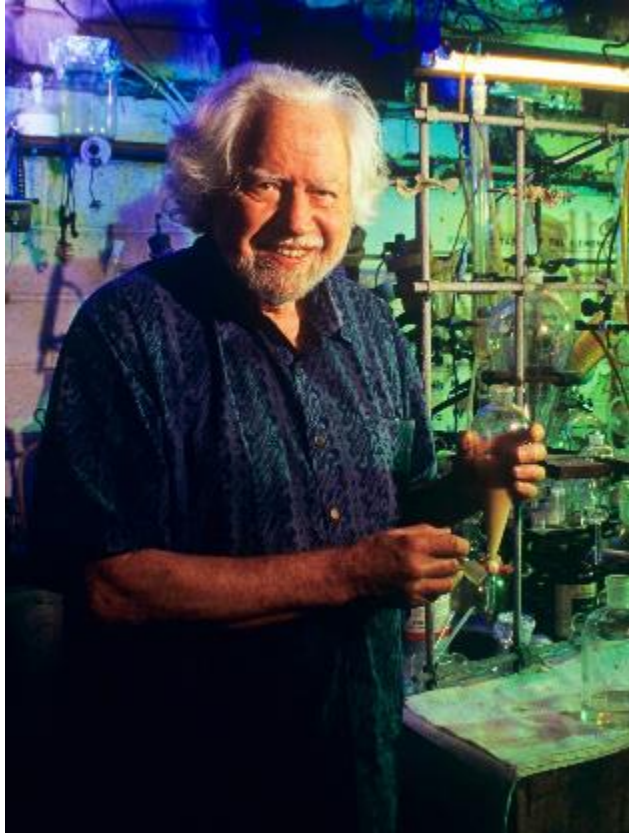
- 1962 FDA starts regulating research
- 1963 LSD hits the streets
- 1970 Controlled Substances Act
- 1976 research comes to a halt

3,4-methylenedioxymethamphetamine (MDMA)



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Alexander Shulgin synthesizes MDMA in 1976

- Tried it himself
- Introduced it to psychotherapists who used it for anxiety, trauma & couples therapy
- 70s & 80s “Ecstasy”/”Molly” becomes a popular street/rave drug
- 1985 it was added to Schedule I



MAPS



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Multidisciplinary Association for Psychedelic Science (MAPS)

- Founded by Rick Doblin in 1986
- To organize and mobilize the response to the DEA's restrictions on MDMA through research
- 2017 FDA grants "breakthrough stats" for MDMA-assisted treatment of PTSD
- 3 trials underway

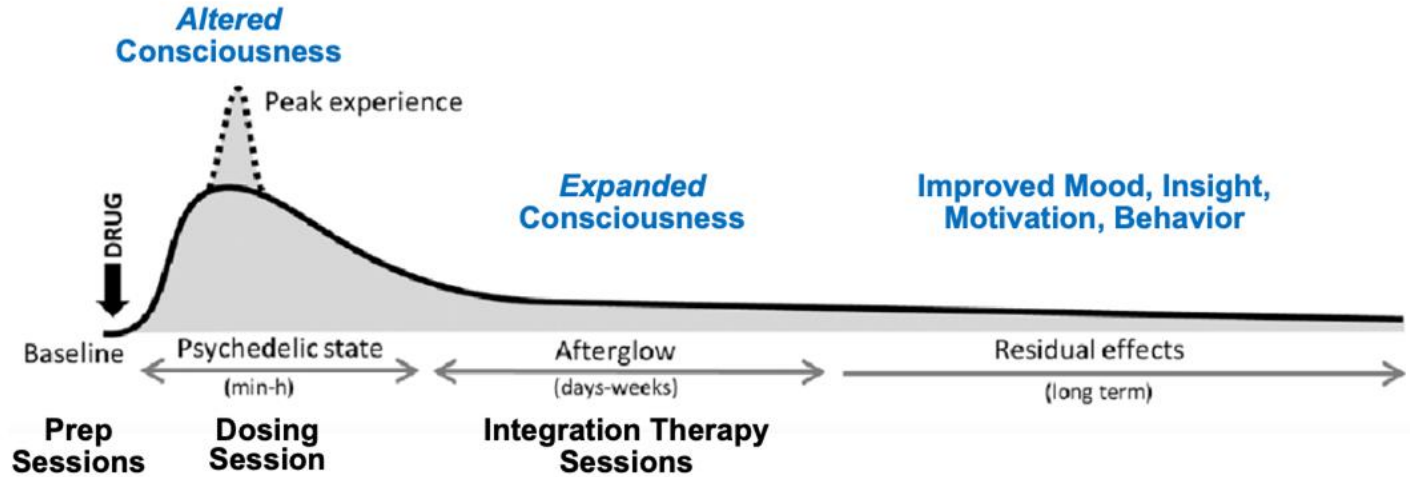


Psychedelic-Assisted Psychotherapy



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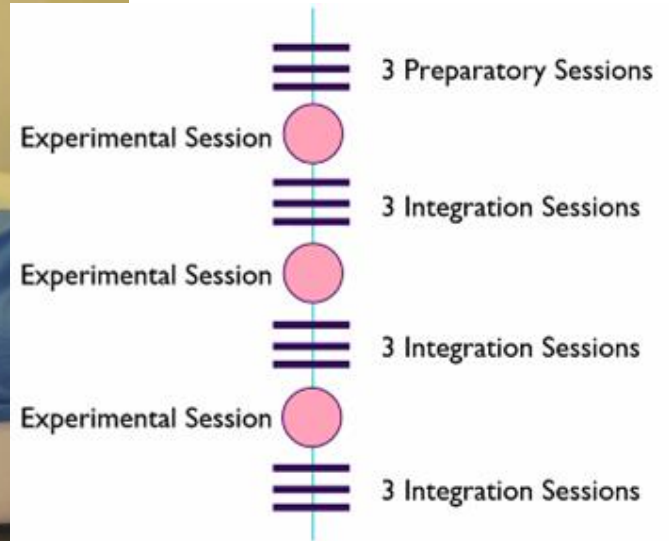


- The utilisation of a psychedelic molecule in order to facilitate psychotherapy
- Characterized by:
 - Several preparatory psychotherapy sessions
 - 1-3 treatment (“high-dose”) sessions creating non-ordinary states of consciousness
 - “Journeys” are characterized by heightened internal and external environmental sensitivity
 - 3-12 integration sessions debriefing the experience, consolidating insights, aiming for lasting change
 - Trust of patient’s “inner healing intelligence”



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MDMA-Assisted Psychotherapy for PTSD









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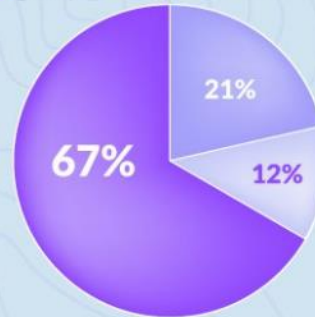
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TREATING PTSD WITH MDMA-ASSISTED THERAPY

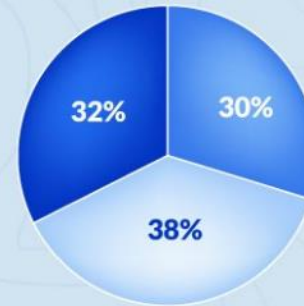
Phase 3 Trial Results Published

67% of participants in the **MDMA-assisted therapy** group
no longer had PTSD after 3 sessions, compared to
32% in the **placebo with therapy** group.

-   Lost PTSD diagnosis
-   Clinically meaningful response
-   No response



MDMA-ASSISTED THERAPY



PLACEBO WITH THERAPY

Mitchell 2021, *Nature Medicine*



The Multidisciplinary Association for Psychedelic Studies (MAPS) is a 501(c)(3) non-profit research organization working to develop MDMA-assisted therapy into an FDA-approved prescription treatment. The safety and efficacy of MDMA-assisted therapy is currently under investigation. It has not yet been approved by the FDA, does not work for everyone, and carries risks even in therapeutic settings. Learn more about our research at maps.org.



Psilocybin-Assisted Psychotherapy for Depression



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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 Johnson¹, Michael A Carducci³,
Annie Umbricht¹, William A Richards¹, Brian D Richards¹,
Mary P Cosimano¹ and Margaret A Klinedinst¹



Randomized, double-blind, cross-over trial

- Psilocybin administered to 51 cancer patients with life-threatening diagnoses and symptoms of depression and/or anxiety.
- Very low dose vs. high dose
- 5 weeks between sessions



Psilocybin-Assisted Psychotherapy for Depression



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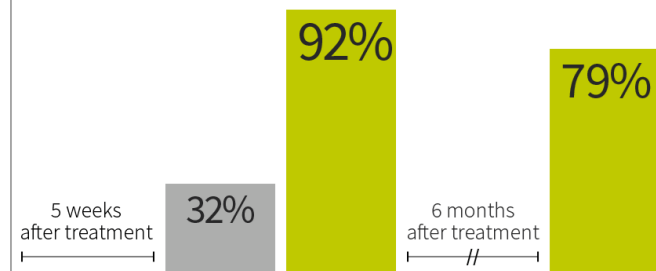
- Large decreases: in clinician- *and* self-rated measures of **depressed mood** and **anxiety**
- Increases in
 - quality of life
 - life meaning
 - optimism
 - Peace with death
- At 6-month follow-up:
 - 80% of participants show clinically significant decreases in depressed mood and anxiety



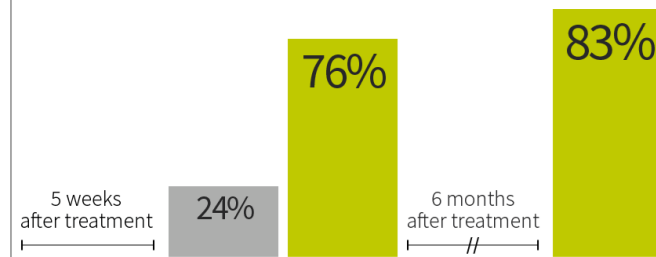
Improvements in Depression

...were treated with either a high dose of psilocybin or an active placebo

■ Control group
■ Psilocybin group



Improvements in Anxiety



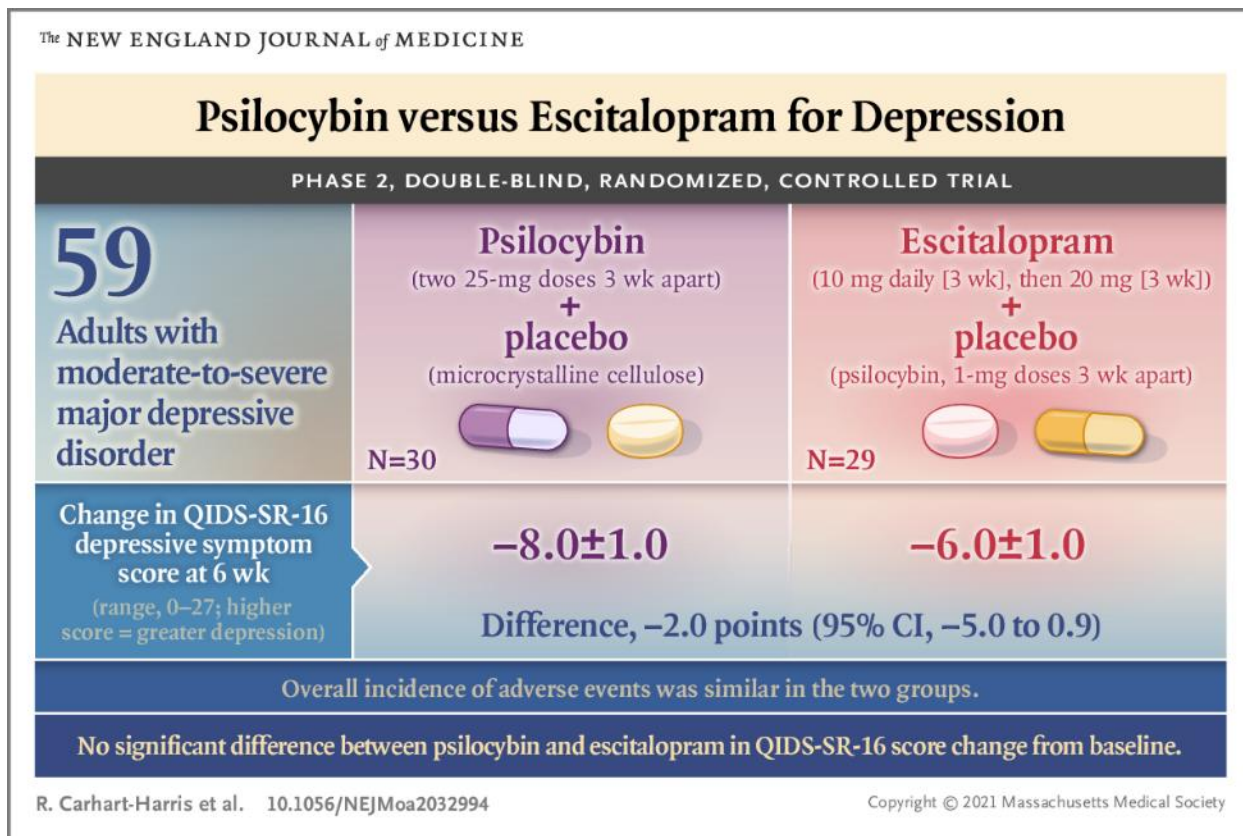
Griffiths, R.R., Johnson, M.W., Carducci, M.A., Umbricht, A., Richards, W.A.
substantial and sustained decreases in depression and anxiety in patients wi

Psilocybin-Assisted Psychotherapy for Depression



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Ketamine

- “Dissociative” anesthetic
- Extremely popular ER drug for sedation since 1990s
- Scheduled in 1999 by FDA following widespread use as club drug
- First used for TRD in 2000



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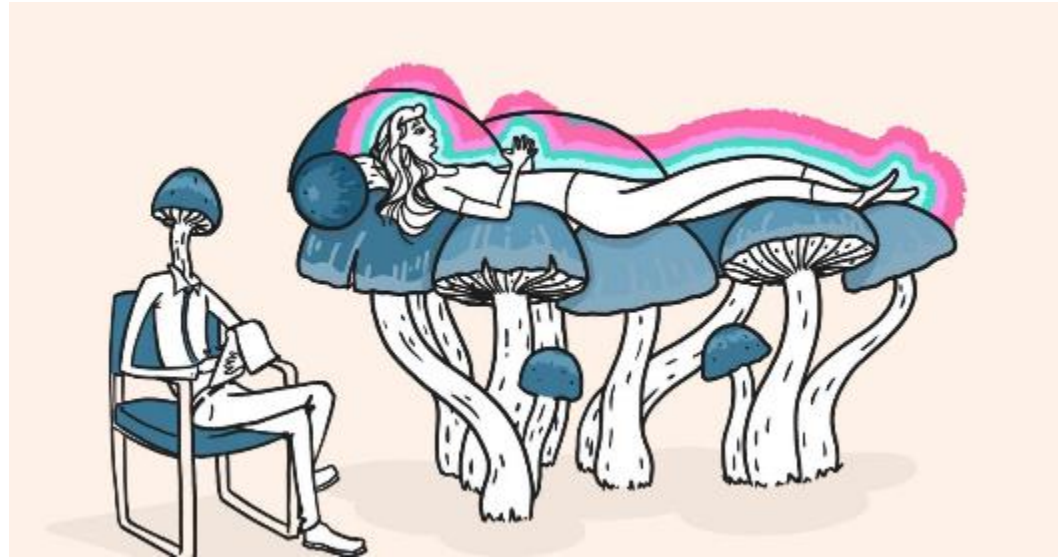
Takeaways



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- Psychedelics are powerful molecules that can create non-ordinary states of consciousness.
- The effects of these NOSCs can range from profoundly healing to traumatizing. Use with care.
- Early research into psychedelic-assisted psychotherapy suggests enormous potential for helping alleviate the current mental health crisis in our society. And perhaps more...





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References/Citations

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- Carhart-Harris, R. Giribaldi, B. Watts, R. *et al.* (2021). Trial of Psilocybin versus Escitalopram for Depression. *New England Journal of Medicine*. 384:1402-1411.
- Additional references available upon request.

Q&A



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- We will now discuss questions that were submitted via the Q&A feature throughout the presentation.
- Due to time constraints, we will not be able to address every question asked.



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Thanks for your attention.



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