



The New Paradigm of Psychedelic Medicine

Scott Shannon, MD DFAACAP
Wholeness

Disclosures

- I have published two textbooks on Integrative Psychiatry and books on pediatric mental health, and I receive royalties
- I have received research support from MAPS/Lykos, Mind Med and Beckley Psytech
- Grant support from the Flourish Trust for research



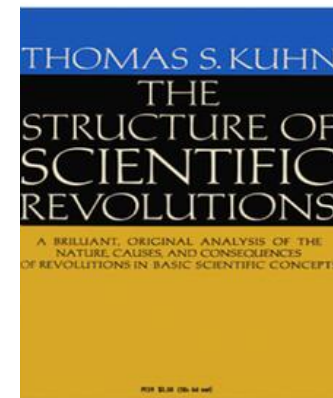
Agenda

- Overview
- Paradigms
- The Psychedelic Framework
- MDMA
- Psilocybin
- Ketamine
- The Goal



The Shift of Paradigms

- Thomas Kuhn: *The Structure of Scientific Revolutions* (1962)
- Discontinuous breaks in our understanding of data
- A paradigm shift: A limited view shifts to a more expansive view
- “One funeral at a time” Max Planck



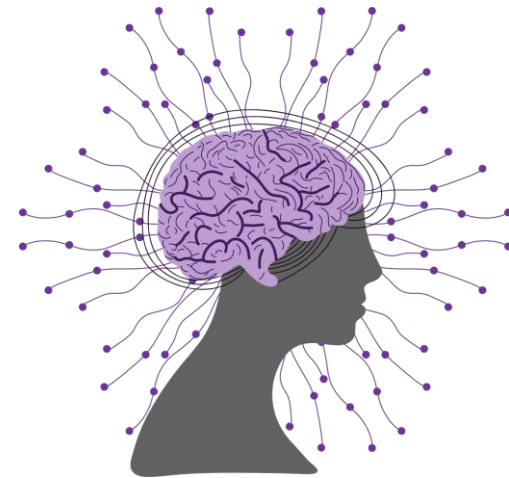
From Mechanism to Systems

Traditional Psychiatry

- Symptoms are isolated malfunctions: reductionism
- Focus on discrete biological targets
- Linear cause → treatment → symptom reduction

Emerging Systems View

- Mental illness reflects constrained system organization
- Brain, body, trauma, relationships, behavior, and meaning interact dynamically
- Symptoms may represent stable “attractor states”



Key Insight: Health reflects flexibility, coherence, and adaptive capacity.

Shannon, S and Weil, A. *Frontiers in Psychiatry*, 2026.

Healing Through Reorganization

Clinical change often unfolds sequentially in phases:

1. Stabilization
2. Perturbation
3. Reorganization
4. Consolidation

Psychedelic Medicine.

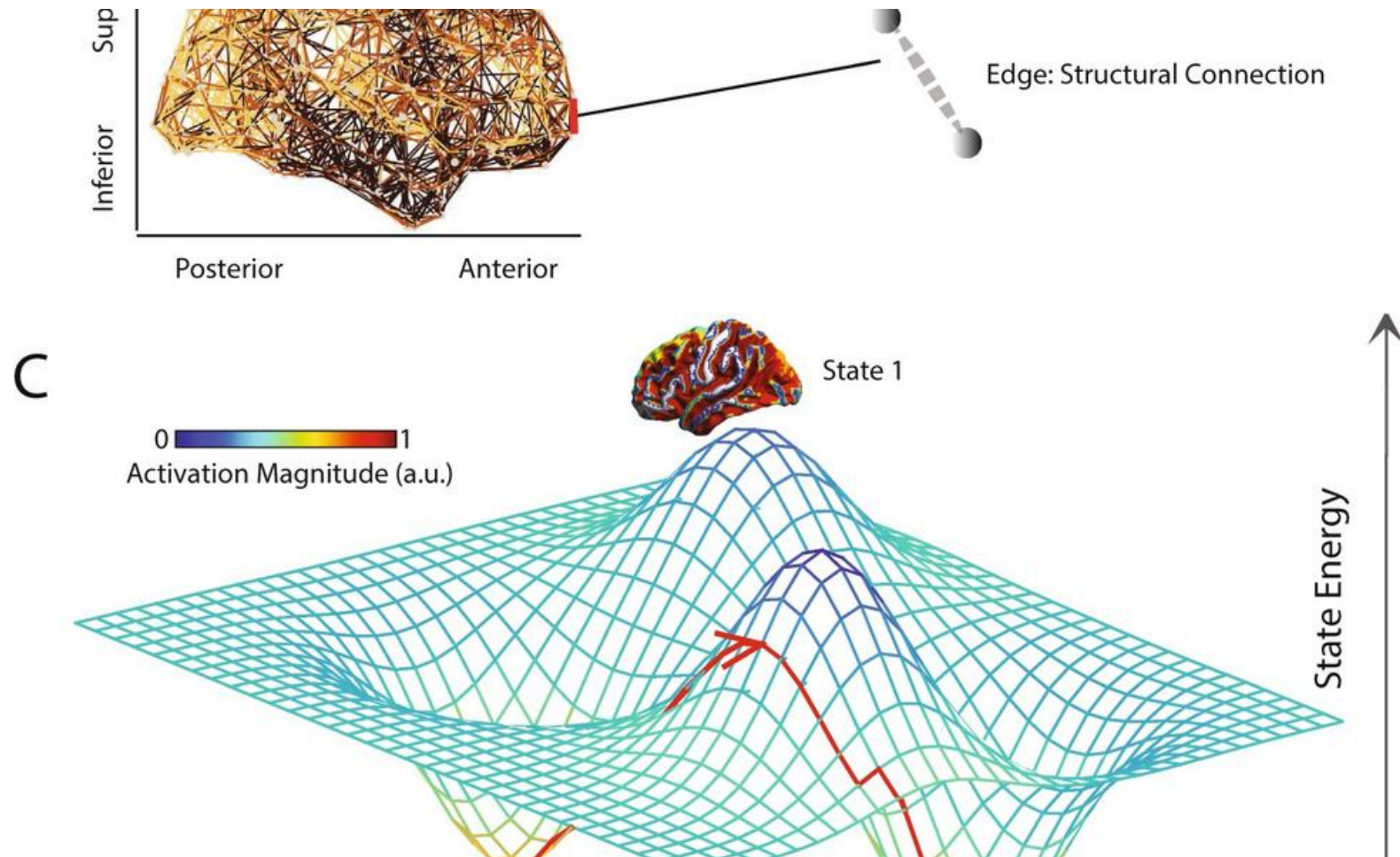
- Temporarily destabilizes rigid patterns
- Increases flexibility and plasticity
- Permits emergence of new configurations



Key Insight: Healing may require temporary destabilization before higher-order integration can emerge.

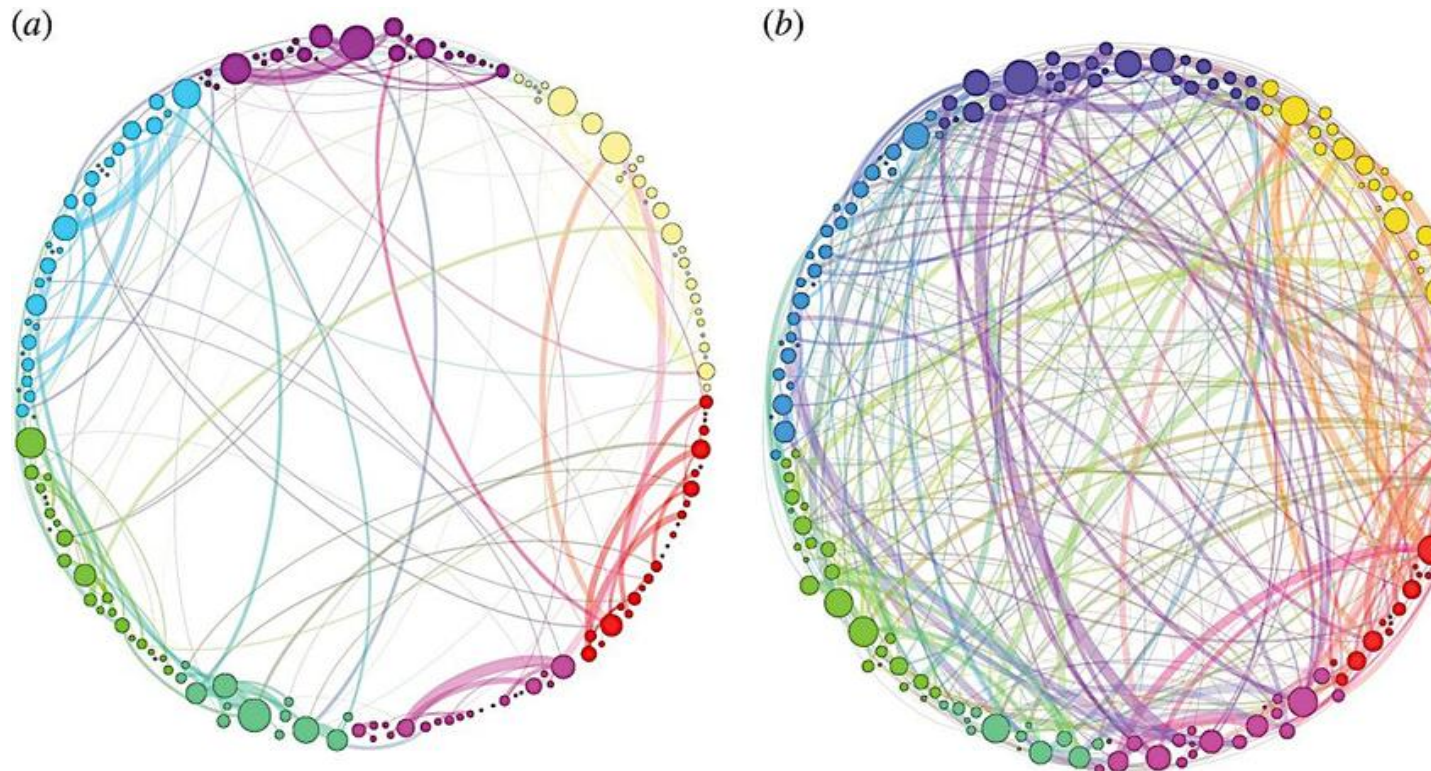
Daws, R. E., et al. *Nature Medicine*, 2022. 28(4), 844–851

Complexity and the Brain



Gu, S., et al. *Science Reports* 8, 2018.

Network Connectivity Between Hubs



Petri G, *J R Soc Interface* 2014; 11(101):20140873.

Neuroplasticity: The ability to change

Gul Dolen: psychedelics reopen critical periods of development: Windows of heightened learning and change

Learning: accelerated
Environment: outsized impact
Relational experience shapes growth

Ketamine: 48 hours

Psilocybin: 2 weeks

LSD: 3 weeks

Ibogaine: months?



Nardou R,... GL, Dölen *Nature*. 2023 Jun;618(7966):790-798.

Dölen G, *Annu Rev Neurosci*. 2026 Apr 16.

Experience Drives = research must adapt

If psychedelics create increased sensitivity to meaning, relationship and context: removal of expectancy becomes a misguided task

New Model Must Include:

Context sensitivity

Non-linear change

Relational learning

Participatory causation

Psychological reorganization



Psychedelics

SUPPORT AN INWARD JOURNEY OF DISCOVERY



Ketamine/PM is NOT a complete Mental health care system

No avenue for prevention

Not appropriate for many conditions

Not an educational format

Not acceptable to many populations

Ignores lifestyle and self-care tools

Highly intensive and expensive for mild presentations



The Necessary Marriage

Integrative Medicine

- Regulation and Prevention
- Whole-person assessment
- Chronic illness care and lifestyle medicine

Psychedelic Medicine

- Perturbation and neuroplasticity
- Rapid perspective shift and transformation
- Existential healing

Together:

- Stabilization → Perturbation → Reintegration → Coherence

The future of mental health may integrate regulation, transformation, and meaning into a unified model of healing.



Psychedelic Medicine

A NEW MODEL USING OLD TOOLS



Definitions

- Classical psychedelics:

LSD, Mescaline (peyote, San Pedro), DMT
(ayahuasca and toad), Psilocybin mushrooms

- Empathogens:

MDA, MDMA, 3-MMC, Methyone

- Other psychedelics:

Ibogaine, 2CB

- Dissociative Agents

Ketamine, NO2, DXM



What if we could enhance psychotherapy with meds?

Enhanced engagement

Profound excitement and anticipation

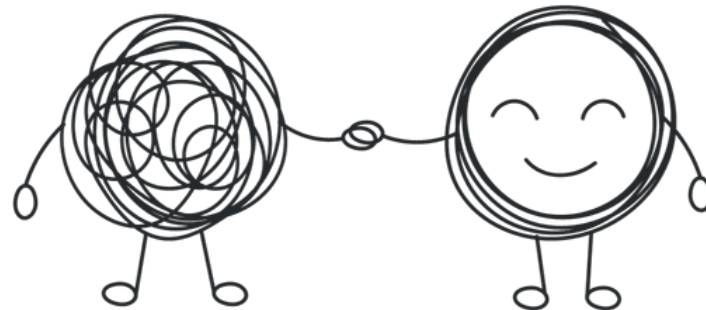
Enhanced access to trauma and new perspectives

Increased awareness of conflicts and challenges

Increased motivation to change

Less defensiveness and fear

Enhanced neuroplasticity = more change



New medicines for an old model?

JUNE 17, 1944

NARCO-ANALYSIS WITH NITROUS OXIDE

BRITISH
MEDICAL JOURNAL 811

that direct spread from bed-pans was the cause of the epidemic, as pathogenic organisms were not recovered from any in use.

Summary

An outbreak of haemolytic streptococcal infection among puerperal women is described. All the 7 cases were infected with the same type of streptococcus. It is suggested that the infection was spread, directly or indirectly, from a lavatory seat in the receiving ward.

NARCO-ANALYSIS WITH NITROUS OXIDE

BY

C. H. ROGERSON, M.D., M.R.C.P., D.P.M.

Medical Director, Cassel Hospital

Since anaesthetics were first used in surgery it has been common knowledge that during the periods of induction and recovery the tongue of the patient tends to be loosened and expressions are uttered which would ordinarily be repressed. This observation merely bears witness to the truth of the saying, *In vino veritas*. During recent years psychiatrists have made use of this phase of lowered self-criticism and self-control for various purposes. The anaesthetic agents that have been chiefly employed in psychiatry have been the barbiturate group of basal narcotics.

Narco-analysis in the Twilight State

I first became interested in the possible utilization of the twilight state produced by these agents, in suitable dosage, by the accidental observation at Guy's Hospital that it was exceptionally easy to convey suggestion to patients who were recovering from avertin anaesthesia. The matter was there

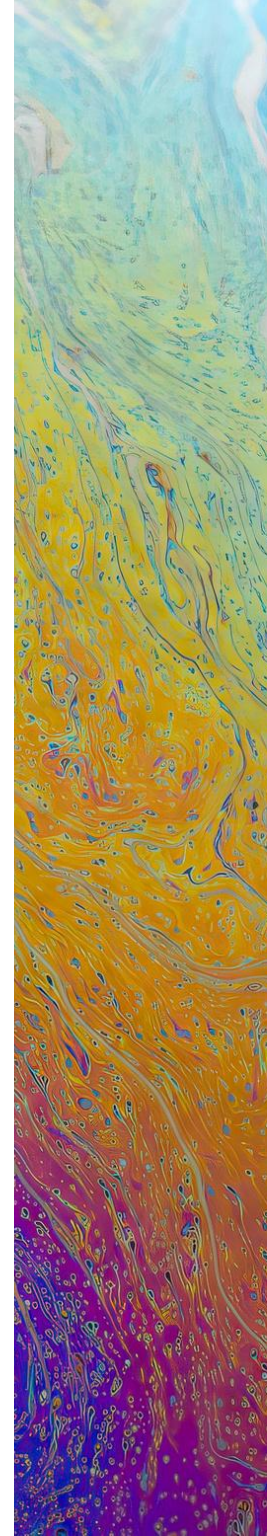
—namely, that the method is not as time-saving as one would like. In order to carry it out with adequate safeguards for the patient an assistant is necessary; the patient must be prepared as if for a short general anaesthetic, and resuscitation materials must be at hand. This preparation must be repeated for each injection, although in some cases the progress made at a single session may be very limited.

The Nitrous Oxide Method

During the past 12 months a way has been found of overcoming these objections by the substitution of inhaled nitrous oxide for intravenous barbiturates as the anaesthetic agent. Experiments with nitrous oxide were begun because many patients and normal individuals spoke of the remarkable feeling of release, of freedom, and of power which they experienced under gas. Such feelings generally point to just that reduction of the normal critical faculties which it is the aim of narco-analysis to achieve.

It was found that a slow induction of analgesia, using a mixture of gas and air, gave the best results, and for this purpose the Minnitt obstetrical gas-air-analgesia apparatus proved ideal. This has a number of advantages over the ordinary gas-anaesthesia apparatus. First, the flow of gas is regulated by the patient's breathing, so that there is no waste. Secondly, the patient himself controls his intake of gas and can stop at any moment; fear is thus almost entirely eliminated. Lastly, the apparatus is simple and requires almost no manipulation by the psychiatrist.

The proportion of gas to air delivered by the machine in normal usage is about 45%. This is enough for many patients, but can be increased if necessary by closing one or two of the



The Psychedelic Framework

CONTAINER, CATALYST AND CARRIER



The Psychedelic Framework

THREE CORE ELEMENTS:

1

Relationship, safety,
setting, trust
= Container



2

Agent to alter
consciousness-ketamine,
MDMA, breath, DMT, etc.
= Catalyst



3

Supports to enhance the
inner focus and free
awareness-music, eye
shades = Carrier



MDMA

A NEW USE FOR AN OLD AGENT



MDMA:

Pharmacology

Increases release of:

serotonin (5-HT)

norepinephrine (NE)

dopamine (DA)

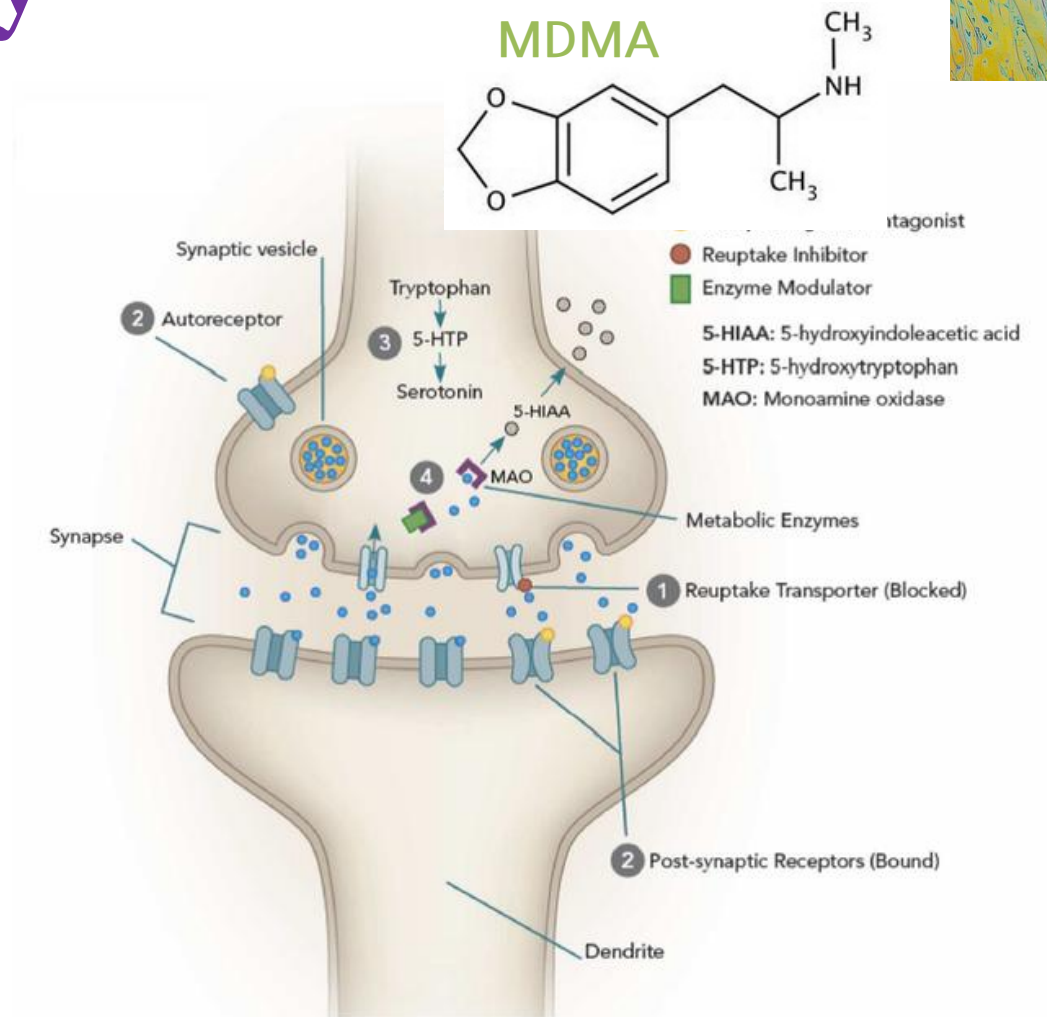
Enhances release of hormones:

oxytocin

prolactin

vasopressin

cortisol



[nature](#) > [nature medicine](#) > [articles](#) > [article](#)

Article | [Open access](#) | [Published: 14 September 2023](#)

MDMA-assisted therapy for moderate to severe PTSD: a randomized, placebo-controlled phase 3 trial

[Jennifer M. Mitchell](#) , [Marcela Ot'alara G.](#), [Bessel van der Kolk](#), [Scott Shannon](#), [Michael Bogenschutz](#), [Yevgeniy Gelfand](#), [Casey Paleos](#), [Christopher R. Nicholas](#), [Sylvestre Quevedo](#), [Brooke Balliett](#), [Scott Hamilton](#), [Michael Mithoefer](#), [Sarah Kleiman](#), [Kelly Parker-Guilbert](#), [Keren Tzarfaty](#), [Charlotte Harrison](#), [Alberdina de Boer](#), [Rick Doblin](#), [Berra Yazar-Klosinski](#) & [MAPP2 Study Collaborator Group](#)

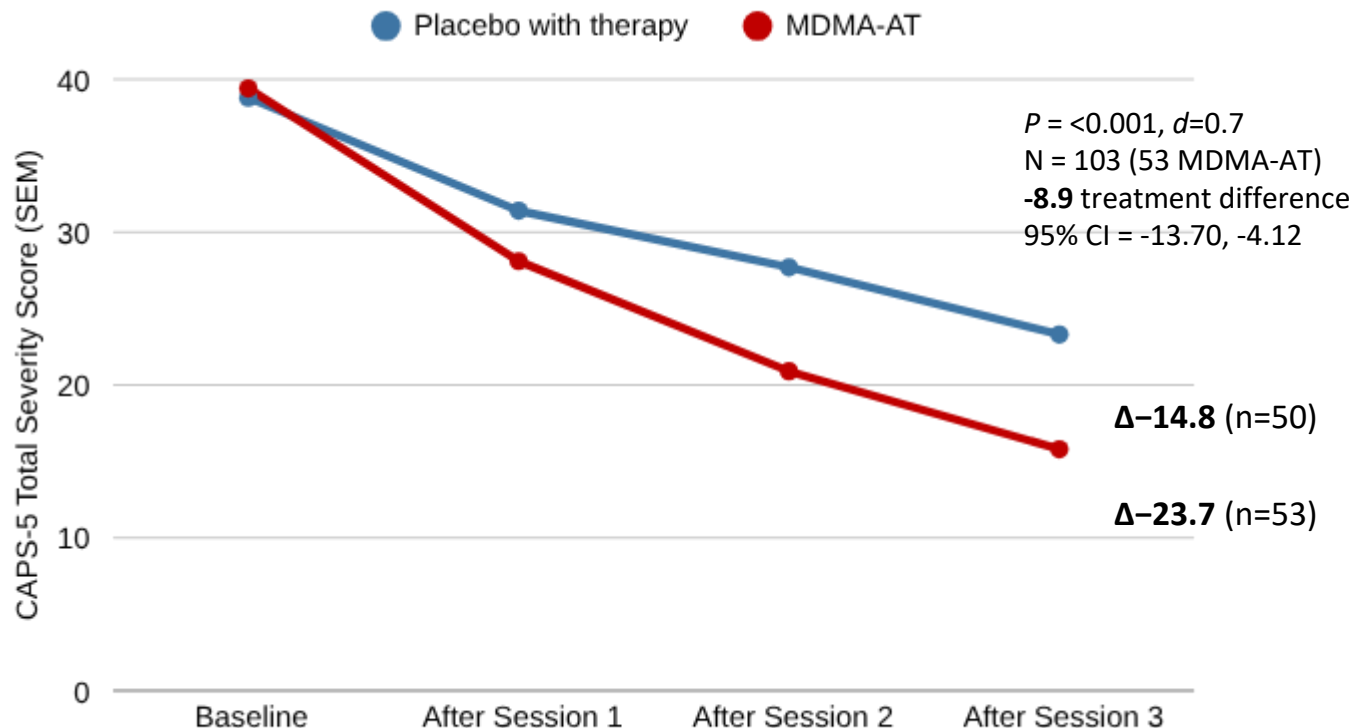
Nature Medicine **29**. 2473–2480 (2023) | [Cite this article](#)



MAPP2: Primary endpoint:

CHANGE IN PTSD SYMPTOMS, MEASURED BY CAPS-5 TOTAL SEVERITY

Least squares mean change in CAPS-5 Severity Scores by group from baseline to 18 weeks

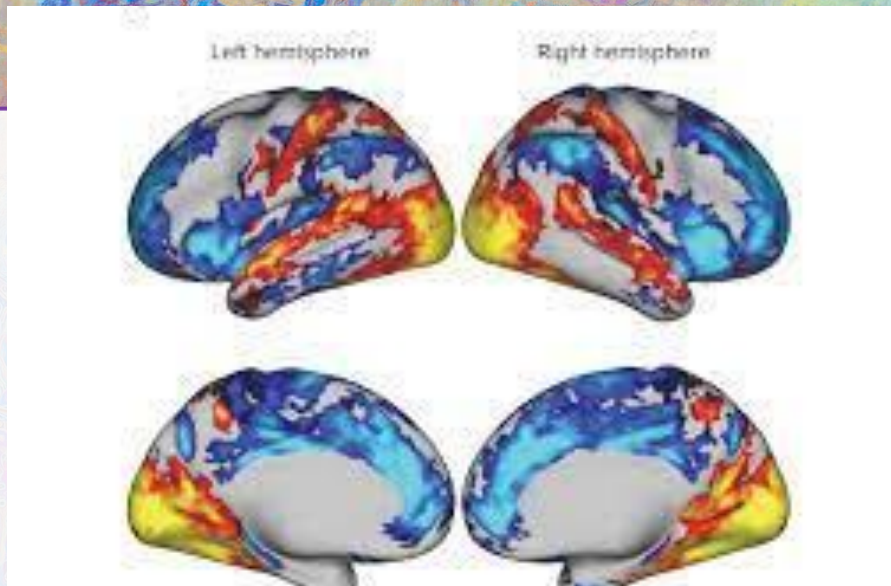


A 10-point decrease in CAPS-5 was defined as "clinically significant"¹

Primary analysis was completed using least square means from a mixed model repeated measure (MMRM) model.

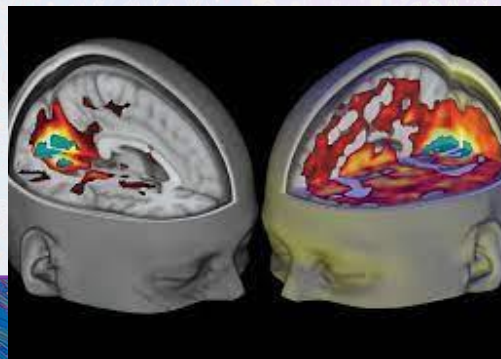
CAPS-5, Clinician-Administered PTSD Scale for DSM-5; CI, 95% confidence interval; MDMA-AT, 3,4-methylenedioxymethamphetamine-assisted therapy; SDS, Sheehan Disability Scale

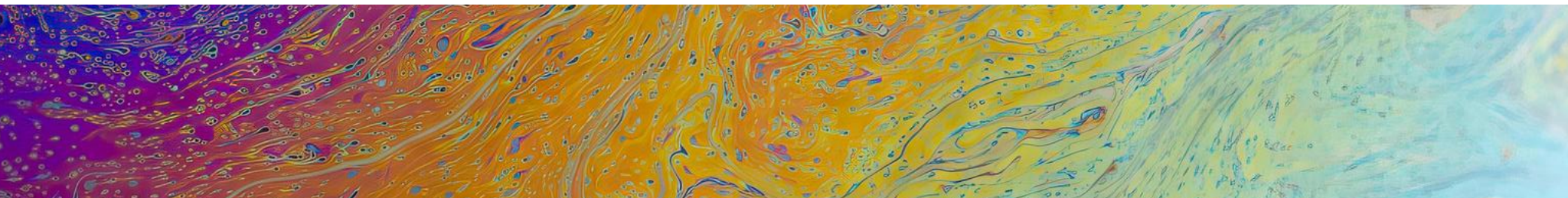
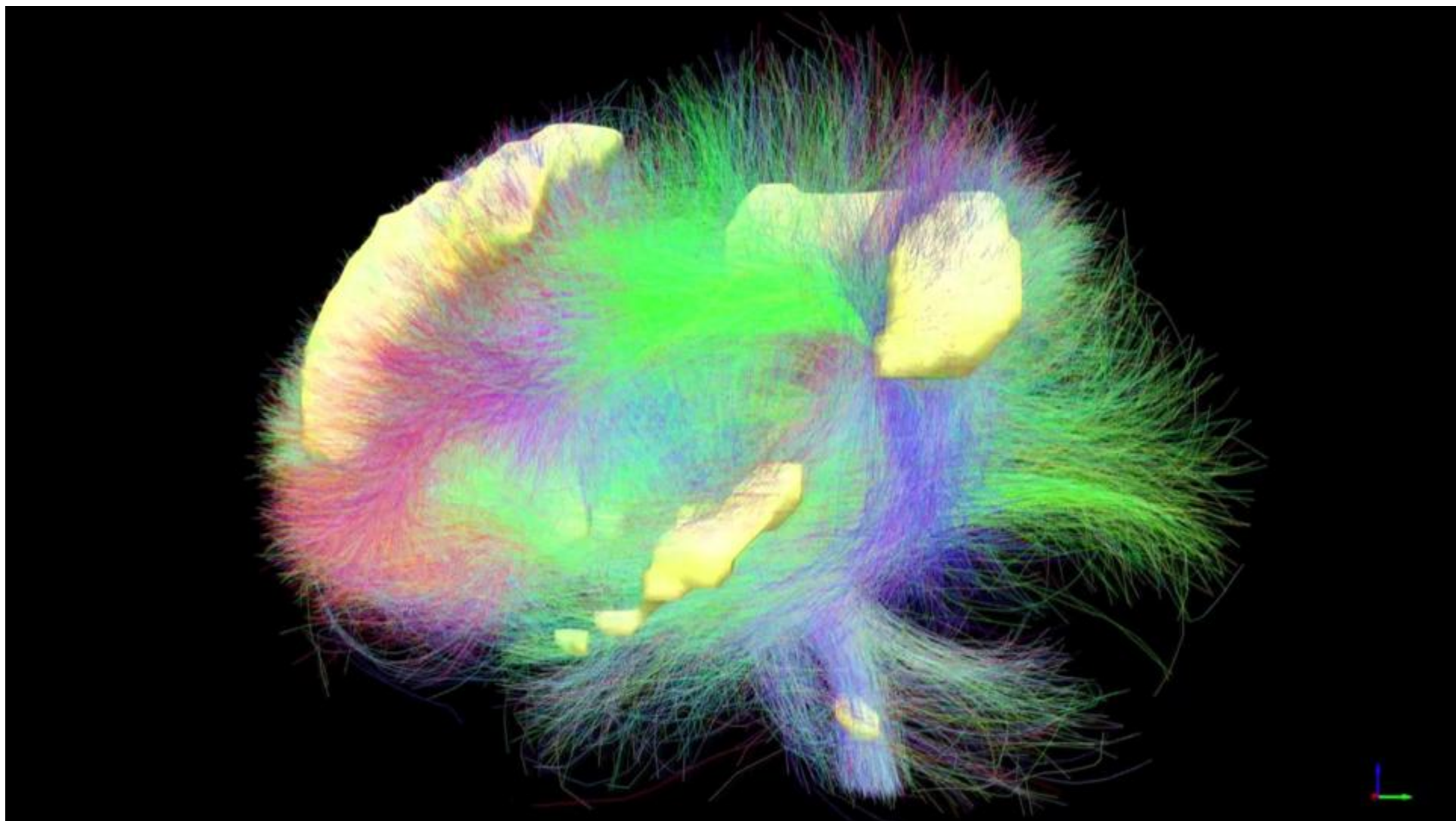
Mitchell JM et al. Nat Med. [Published online ahead of print Sept 14 2023] DOI:10.1038/s41591-023-02565-4.



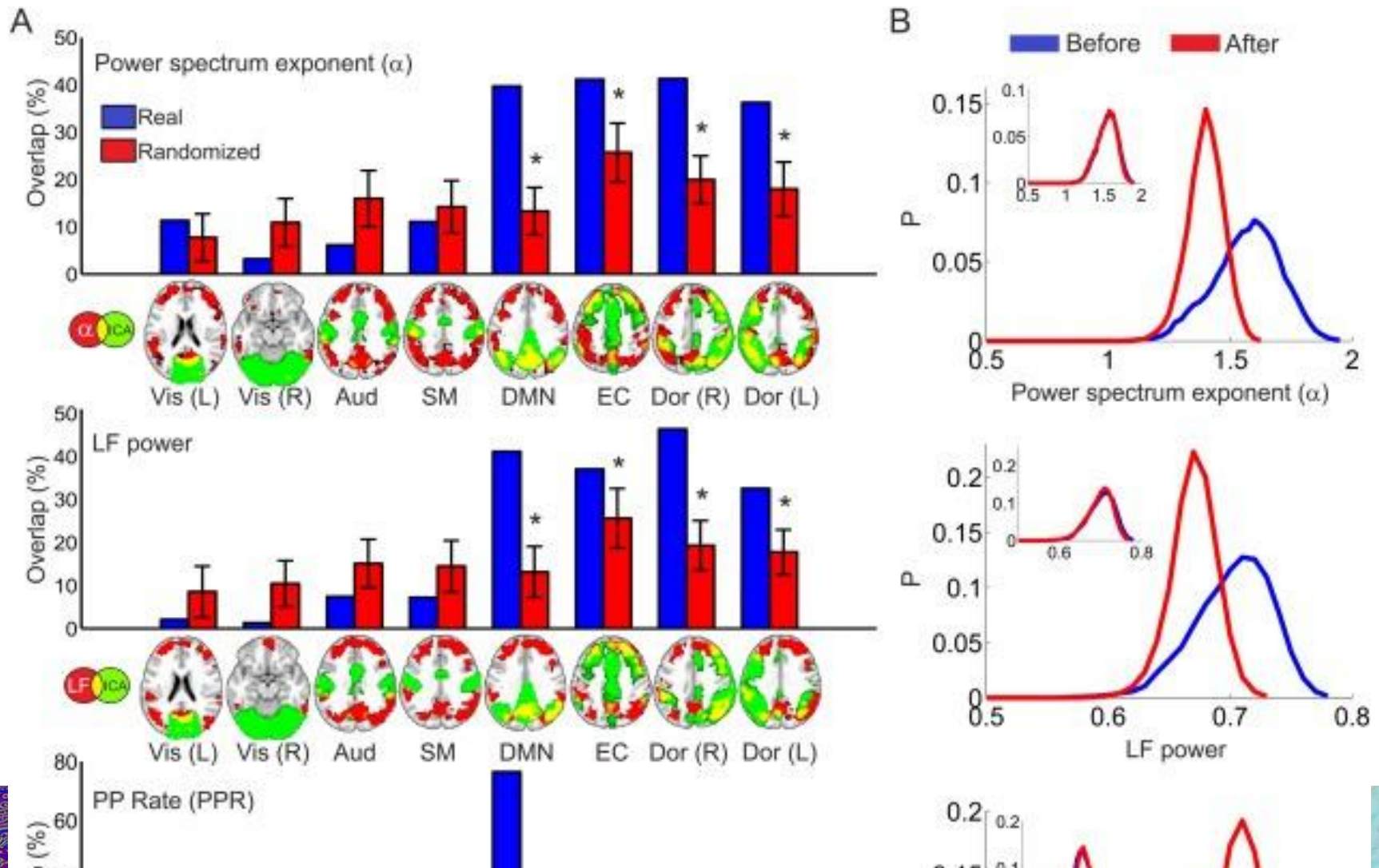
Psychedelics and the Brain

WHAT DOES THIS TELL US ABOUT WHO WE ARE?

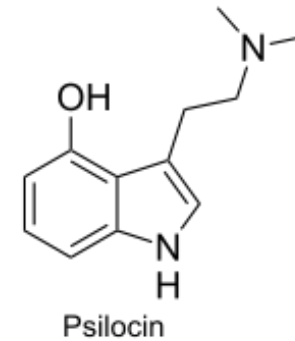




DMN responds to Psilocybin



Psilocybin



- Potent agonist at

- 5-HT1A
- 5-HT2C
- 5-HT2A

- Psychedelic effects blocked by **ketanserin** (selective 5-HT2A antagonist)



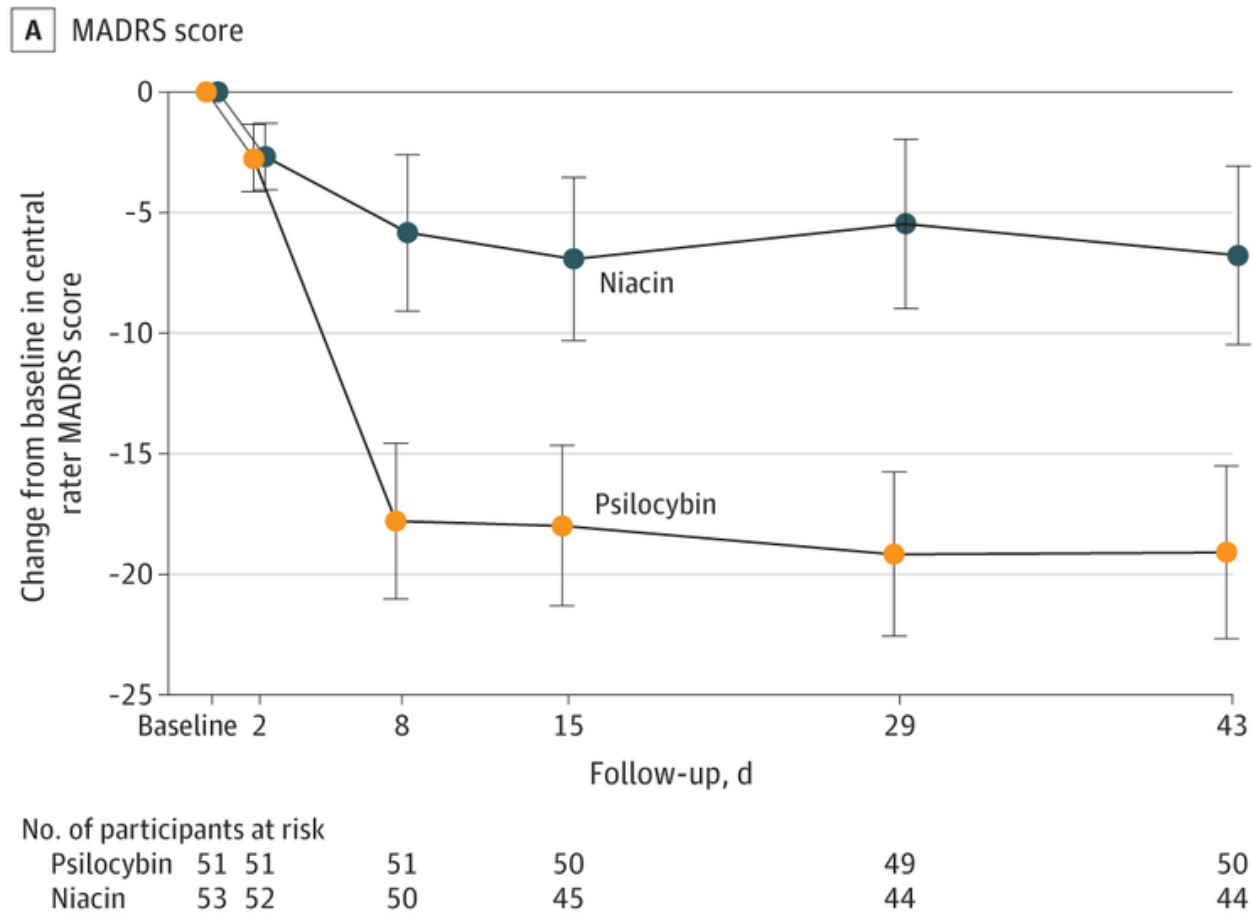
MDD: Just One Dose

- RCT of 104 adults; Placebo controlled (Niacin)
- 25 mg of psilocybin with psychological support
- Primary outcome: MADRS via central rater
- Rapid and sustained anti-depressant effect
- No serious treatment-emergent adverse events.

Raison, C. *JAMA*. 2023;330(9):843-853. doi:10.1001/jama.2023.14530

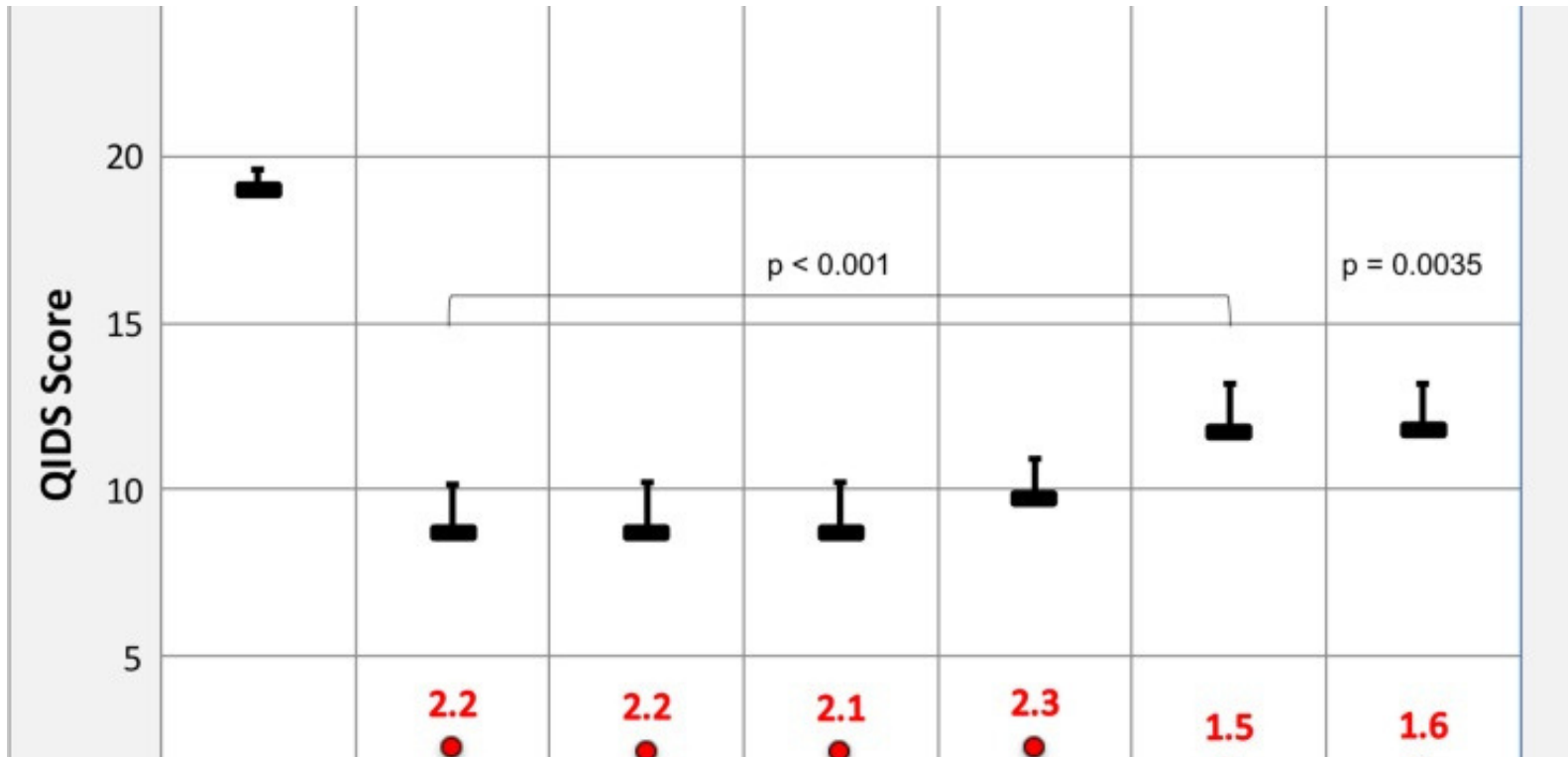


Psilocybin for Major Depressive Disorder



Raison, C. *JAMA*. 2023;330(9):843-853. doi:10.1001/jama.2023.14530

Only two doses, yet results last



Carhart-Harris, R *Psychopharmacology* (Berl) 2018; 235(2): 399–408.

SI: Just one dose

- Open label study of 25mg of psilocybin in 20 adults
- Chronic treatment resistant SI and MDD
- Structured preparation and integration (6 sessions total)

Psilocybin: effective reduction in SI at 1, 3 and 12 weeks.

12 weeks: $d = 1.46$

van der Vaart A, et al. *J Clin Psychiatry*, 2026. May 13; 87(2):26



The Ultimate Unblinding: Time

- Original RCT: 24 participants with MDD, off antidepressants.
- Enrolled 2017-2019: 2 doses of psilocybin (20mg/70kg and 30mg/70kg)
- 5 years later: 21 of 24 enrolled; 18 completed
- For those missing-original baseline scores used.
- 67% remained in remission.
- Relapses were brief and short lived
- Improvements noted in a wide range of functional measures

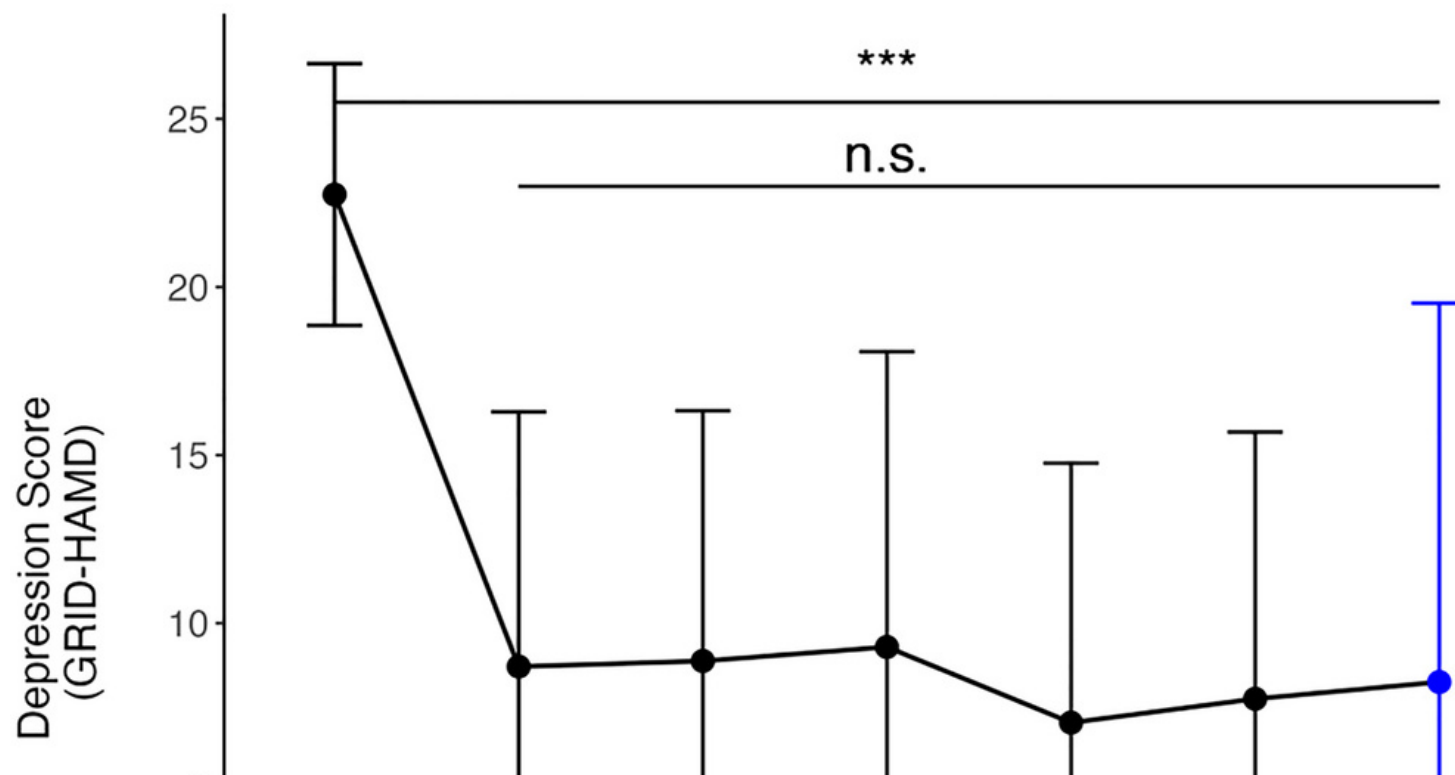


Davis AK, et al. *JAMA Psychiatry*. 2021;78(5):481–489. doi:10.1001

Davis AK, et al. *Journal of Psychedelic Studies*. Published online September 04, 2025. doi:10.1556

Response? Remission? Cure?

Longitudinal GRID-HAMD Depression Scores

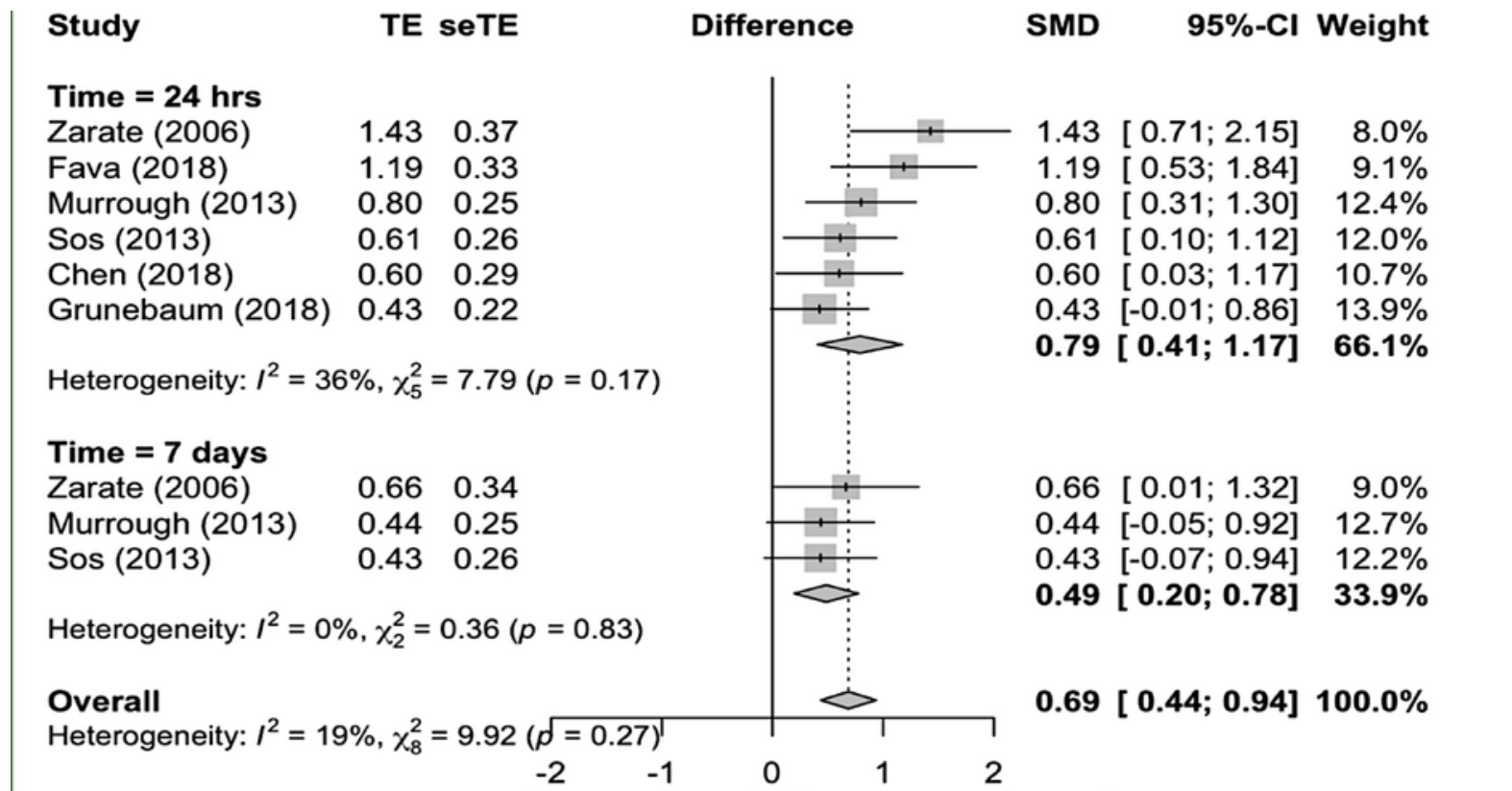


Ketamine

$C_{13}H_{16}ClNO$



Robust: IV Ketamine for Depression



The New Order?

New Online

Views **50**

Citations **0**

Altmetric **2**

Viewpoint

ONLINE FIRST

October 25, 2023

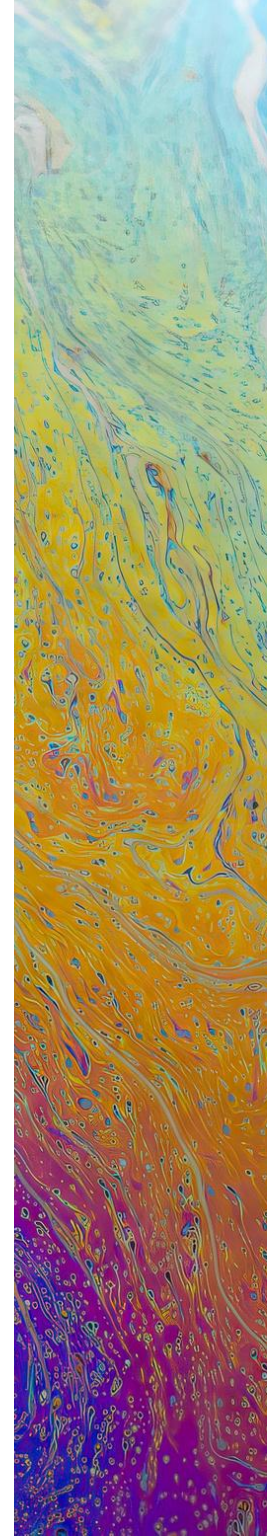
Choosing Between Ketamine and Electroconvulsive Therapy for Outpatients With Treatment-Resistant Depression—Advantage Ketamine?

Sanjay J. Mathew, MD^{1,2}; Manish K. Jha, MBBS^{3,4}; Amit Anand, MD⁵

» [Author Affiliations](#)

JAMA Psychiatry. Published online October 25, 2023. doi:10.1001/jamapsychiatry.2023.3979

This Viewpoint examines key issues stemming from several recent reports of electroconvulsive therapy (ECT) vs ketamine infusion for improving depressive symptoms in treatment-resistant depression (TRD). These studies include 2 large noninferiority trials—one with inpatients¹ and another with a predominantly outpatient sample²—



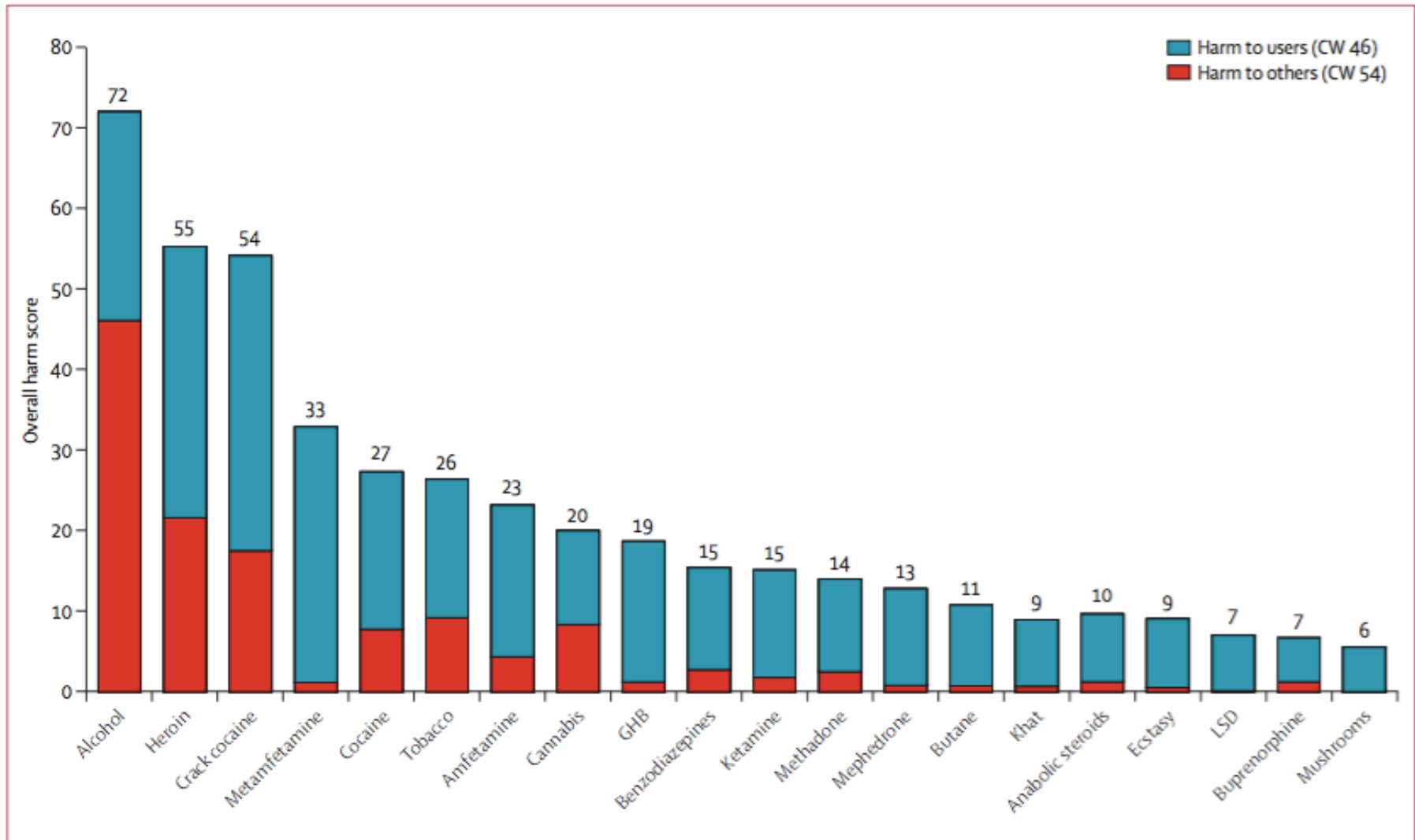


Safety and Risk

PREFERENCE FOR TIE DYE?

Drug Harm Scale

NUTT, DAVID LANCET 2010, 376



Generally well tolerated

JAMA[®]

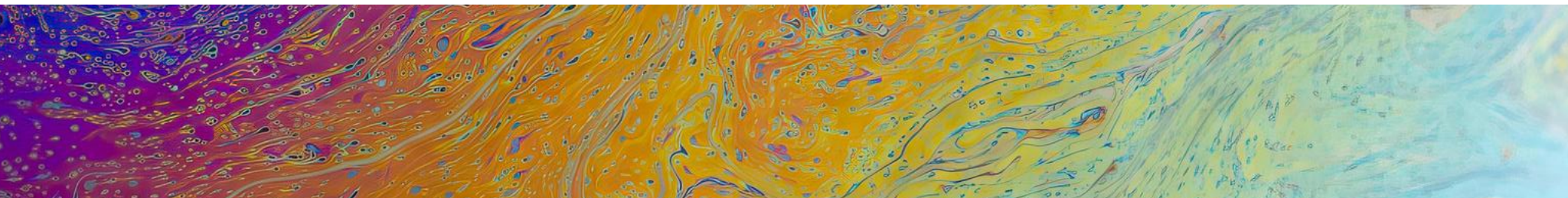
“In this systematic review and meta-analysis, classic psychedelics were generally well tolerated in clinical or research settings according to the existing literature, although SAEs did occur. These results provide estimates of common AE frequencies and indicate that certain catastrophic events reported in recreational or nonclinical contexts have yet to be reported in contemporary trial participants.”

— **Jared T. Hinkle, MD, PhD¹**, *et al.*, Center for Psychedelic and Consciousness Research, Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland and other institutions

[Adverse Events in Studies of Classic Psychedelics: A Systematic Review and Meta-Analysis.](#)

JAMA Psychiatry. November 30, 2024.

No completed suicides, no persistent psychotic disorder and no HPPD noted in trials





The Mystical Experience

IS IT GOD OR A HALLUCINATION?

Elements of Mystical Experience



Unity (core element)



Ineffability



Sacredness



Transcendence of
time



Noetic Quality-
ultimate reality



Durability



Mystical Experience: Drives healing

An ever-increasing number of research reports indicates that the gain observed in psychedelic treatment derives from the mystical experience and not psychedelic intensity.

“...a greater number of mystical experiences and personal insights correlated with higher mental health outcomes. **The degree of mystical experience also correlated with those reporting complete or almost complete improvement.**”

SARRIS, J ET AL. *J AFFECTIVE DISORDERS REPORTS*, 2021 (4): 100098



Psychedelics alter our core beliefs

- 2374 subjects rated before/after a powerful psychedelic experience
- Factor analysis of 45 statements yielded 4 positive factors
- Dualism, Spirituality, Non-mammalian Consciousness and Mammalian Consciousness all showed large effect sizes (0.72-0.90).
- Belief in greater power/god/ultimate reality increased from 29% to 59%
- **The mystical quality of the experience drove results**
- Superstition decreased



Nayak, S et al *J Psychopharmacology* 2023 Jan;37(1):80-92.

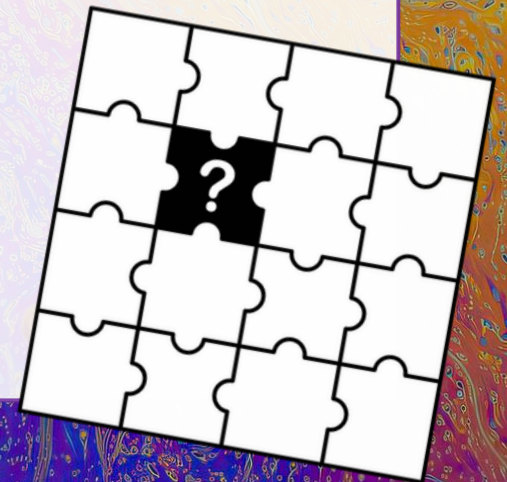
Psychedelics alter our core beliefs

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 - **The mystical quality of the experience drove results**
 - Superstition decreased
- "Belief changes assessed after the experience (an average 8.4 years) remained largely unchanged at the time of survey"**

Nayak, S et al *J Psychopharmacology* 2023 Jan;37(1):80-92.

WHAT IS MISSING?

WHAT ELSE DO WE NEED RIGHT NOW?



What does mental and emotional health look like?

WHAT IS OUR GOAL?



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

R. R. Griffiths · W. A. Richards · U. McCann · R. Jesse

Received: 20 January 2006 / Accepted: 27 May 2006 / Published online: 7 July 2006
© Springer-Verlag 2006

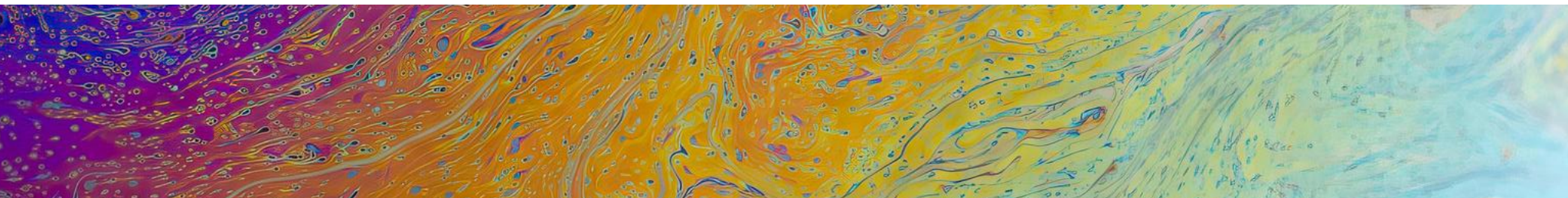
Abstract

Rationale Although psilocybin has been used for centuries for religious purposes, little is known scientifically about its acute and persisting effects.

Objectives This double-blind study evaluated the acute and longer-term psychological effects of a high dose of psilocybin relative to a comparison compound administered under comfortable, supportive conditions.

Materials and methods The participants were hallucinogen-naïve adults reporting regular participation in religious or

obscure the study design, six additional volunteers received methylphenidate in the first two sessions and unblinded psilocybin in a third session. The 8-h sessions were conducted individually. Volunteers were encouraged to close their eyes and direct their attention inward. Study monitors rated volunteers' behavior during sessions. Volunteers completed questionnaires assessing drug effects and mystical experience immediately after and 2 months after sessions. Community observers rated changes in the volunteer's attitudes and behavior.



It has power

ONE MONTH LATER

- 83%: “This was a top five event in my life”
- 89% : “It created behavioral change”
- Intensity of psilocybin experience not predictive
- **Intensity of mystical experience is predictive**
- Effects sustain for 14 months (self rated & outside validation)

Griffiths, *Psychopharmacology* 2006, (187): 268.



Observed Effects



Love of Others



Decreased Hatred



Increased
Gratitude for Life



Increased Reverence



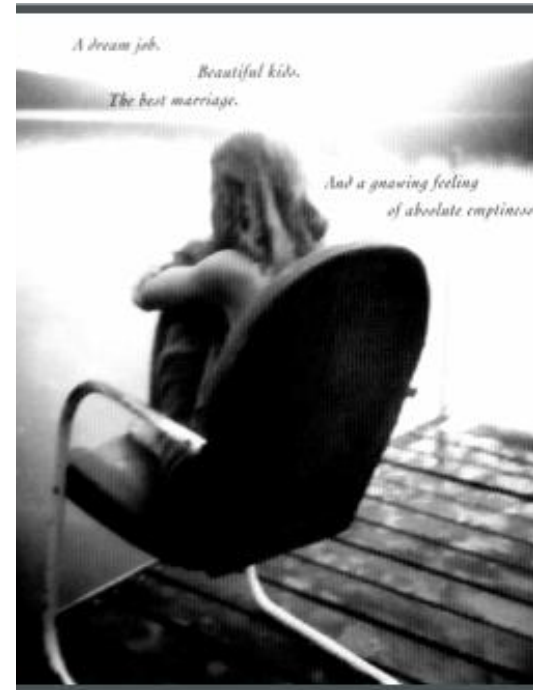
Increased Altruism

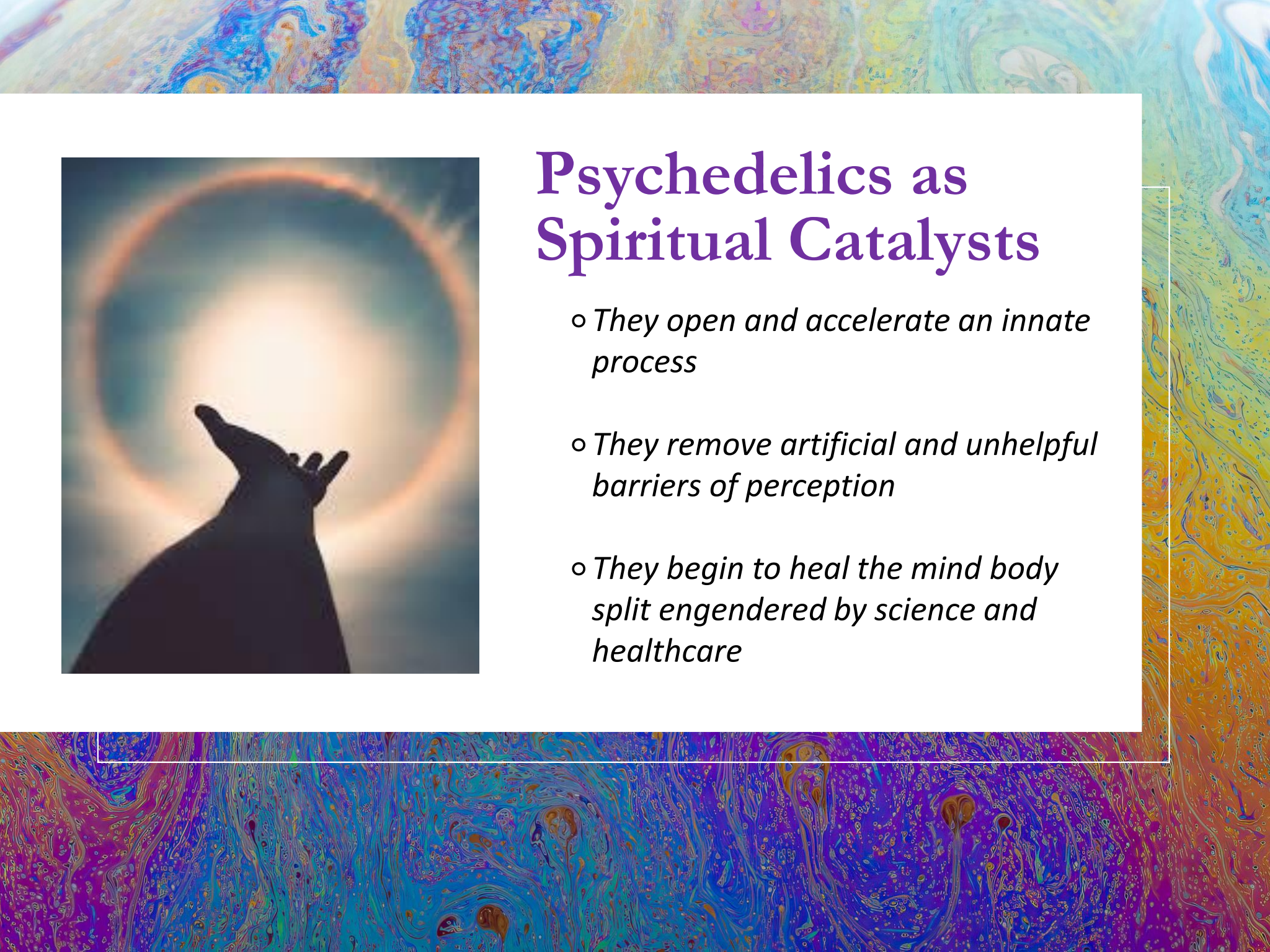
GRIFFITHS, *PSYCHOPHARMACOLOGY* 2006, (187): 268.



Components of Spiritual Distress

- Suffering
- Lack of meaning and purpose
- Fear and dread
- Hopelessness
- Isolation
- Stress and conflict
- Suicidal thoughts





Psychedelics as Spiritual Catalysts

- *They open and accelerate an innate process*
- *They remove artificial and unhelpful barriers of perception*
- *They begin to heal the mind body split engendered by science and healthcare*

We are part of something greater

- Mystery is omnipresent
- There is no “other”
- Awe is reasonable
- Hope is a given

Ecology = love



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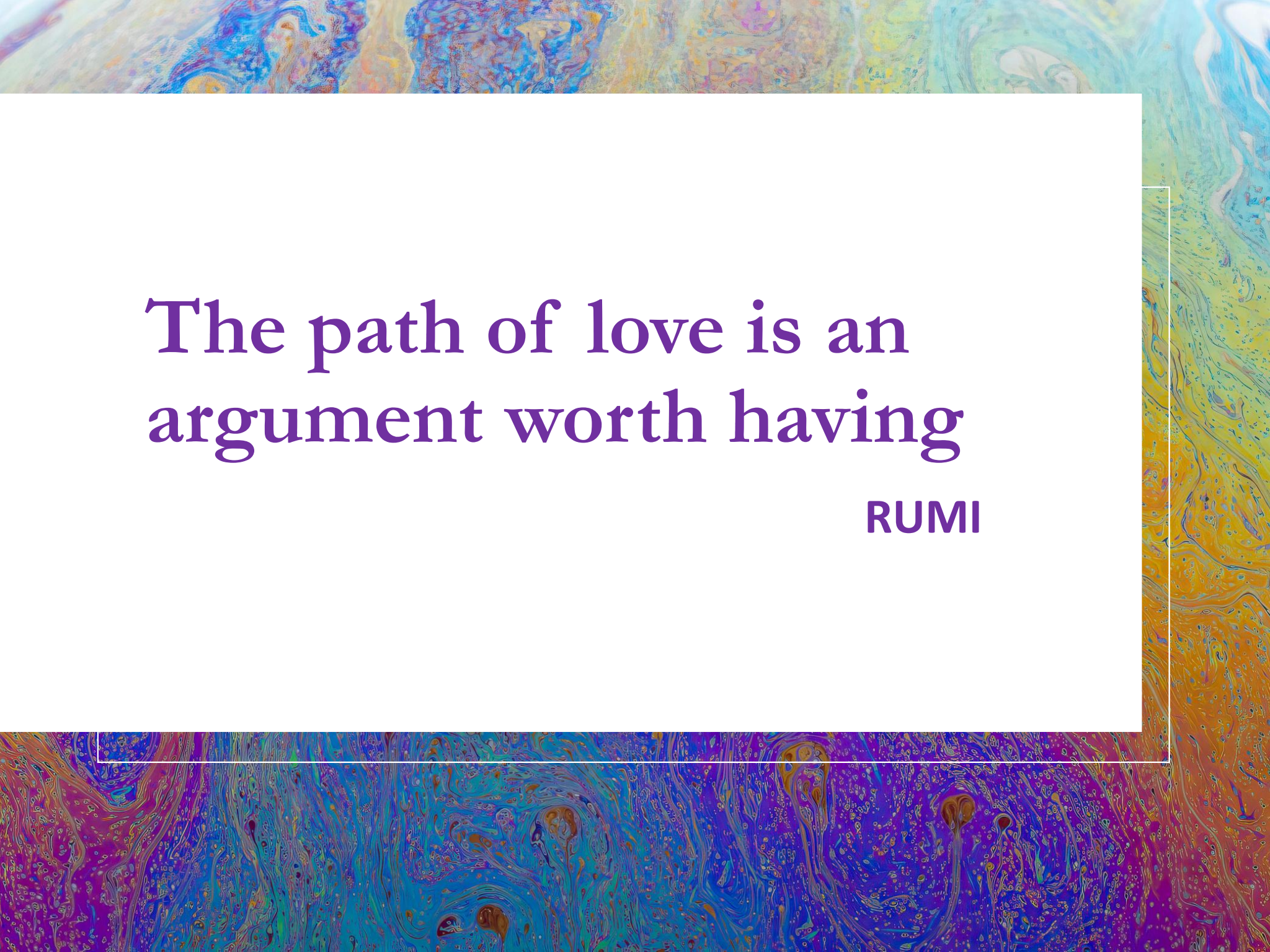
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The path of love is an
argument worth having

RUMI

Resources

- Holland, Julie. (2001) *Ecstasy: The Complete Guide* Rochester, VT: Park Street Press.
- Lawlor, Sean. (2024) *Psychedelic Revival*. Boulder, CO: Sounds True
- MAPS protocol, etc: www.MAPS.org
- Nuwer, Rachel. (2023) *I Feel Love: MDMA and the Quest for Connection in a Fractured World*. New York: Bloomsbury Publishing
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