

BEACON 2026



Psychedelics and Neural Plasticity

How Psychedelics Help the Brain Adapt, Reorganize, and Heal



A PRESENTATION BY
LORENZO PASQUINI, PHD

Psychedelics and Neural Plasticity

Lorenzo Pasquini, PhD

Lorenzo.Pasquini@ucsf.edu

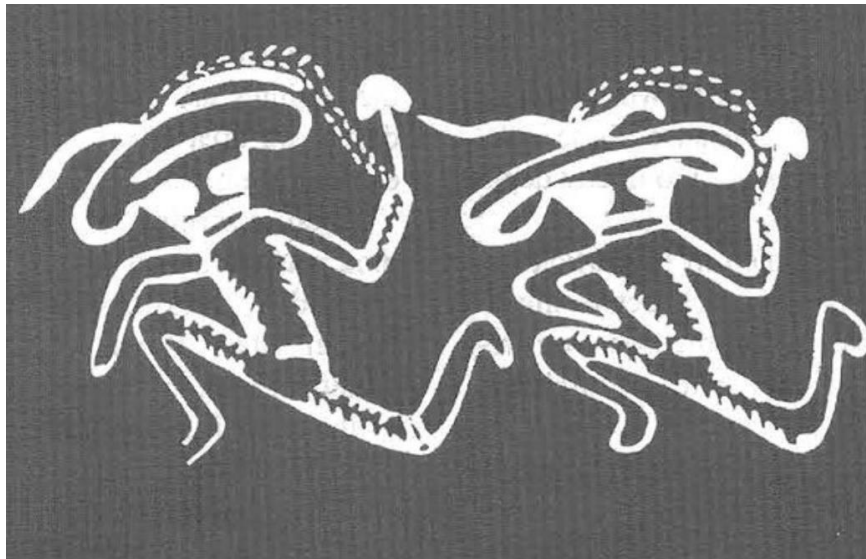
UCSF Department of Neurology

Beacon Conference March 21st 2026

1. What are psychedelics and why should we care?

Psychedelic substances

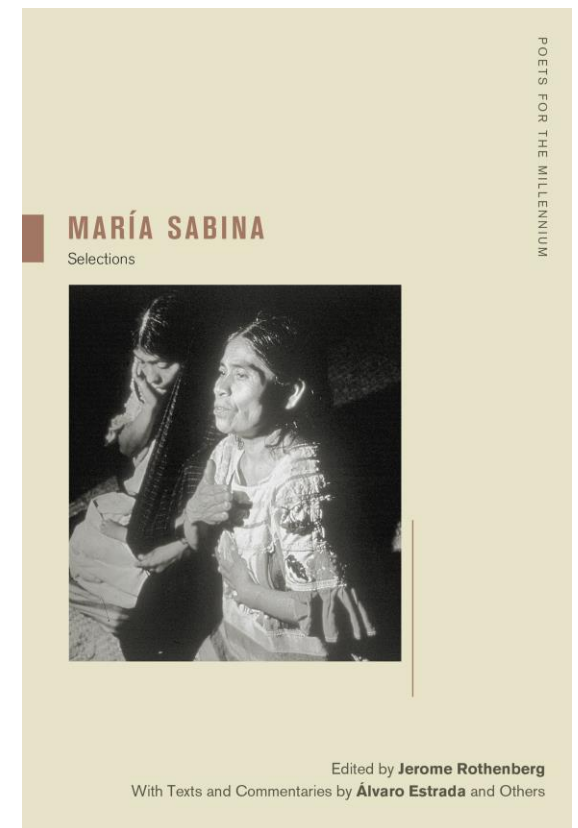
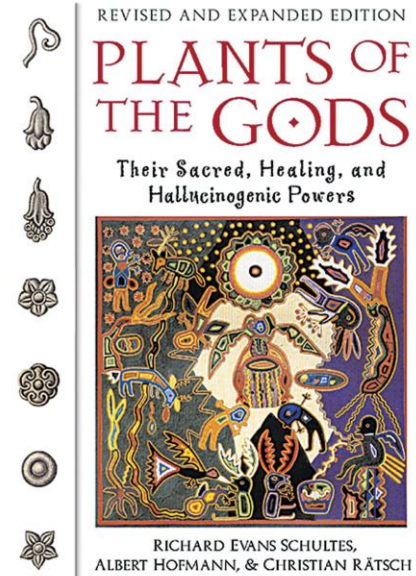
- Naturally occurring substances used since time immemorial for cultural and medicinal uses



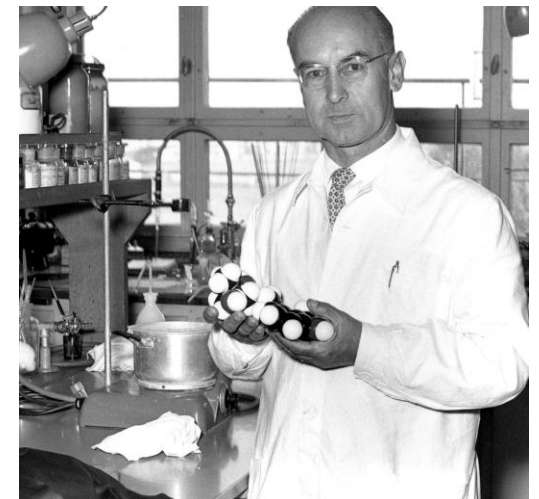
Samorini 2001: Tin Tazariff, Tassili, Algeria, 9,000 years B.P.



Cultural and medicinal uses of Psilocybe mushrooms. Modified from Borhegyi, 1961; Wasson, 1980.



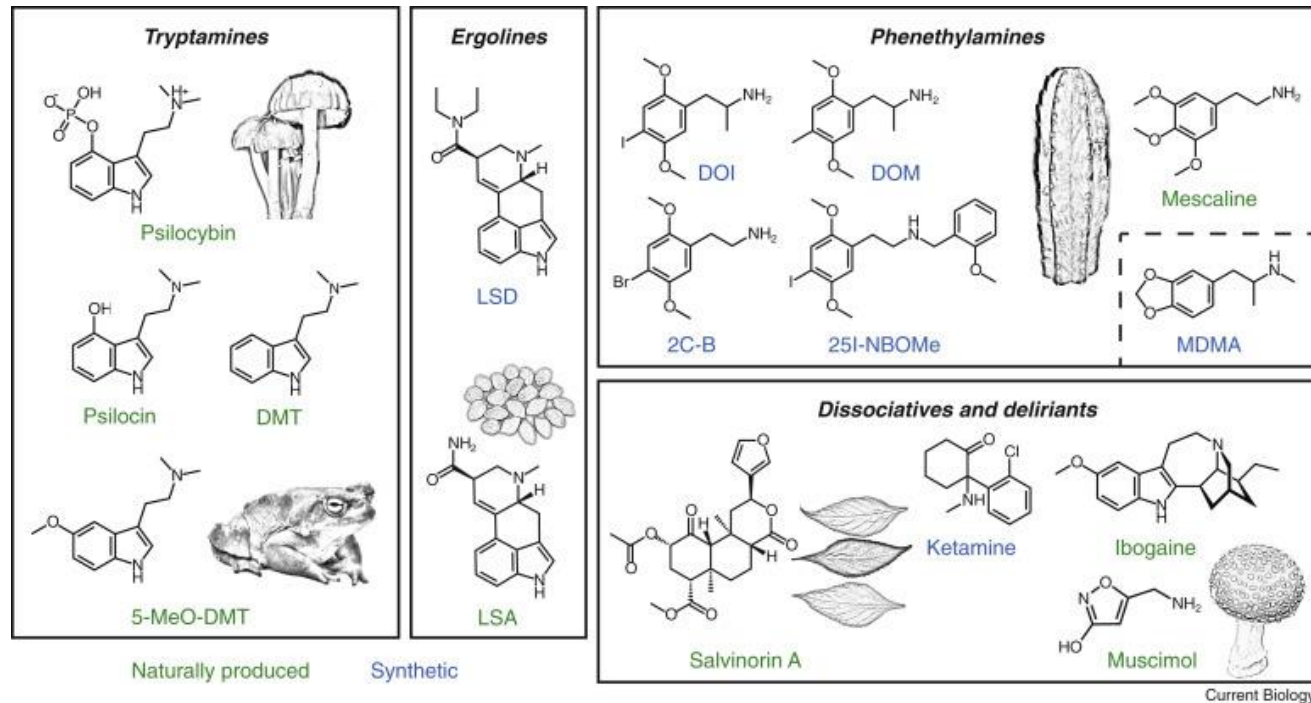
Jay 2013: Albert Hofmann



Psychedelic substances

- Naturally occurring substances used since time immemorial for cultural and medicinal uses

- Psilocybin, LSD, DMT**

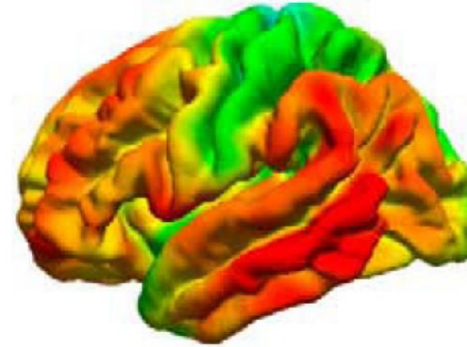


Kelmendi et al., 2022

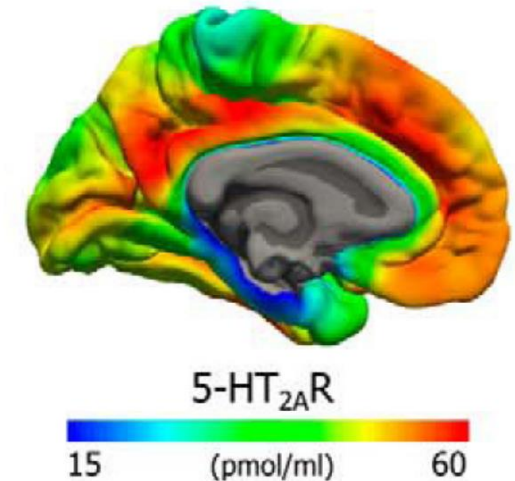
Current Biology

Psychedelic substances

- Naturally occurring substances used since time immemorial for cultural and medicinal uses
- Psilocybin, LSD, DMT
- **High affinity to the serotonergic 5HT_{2A} receptor**

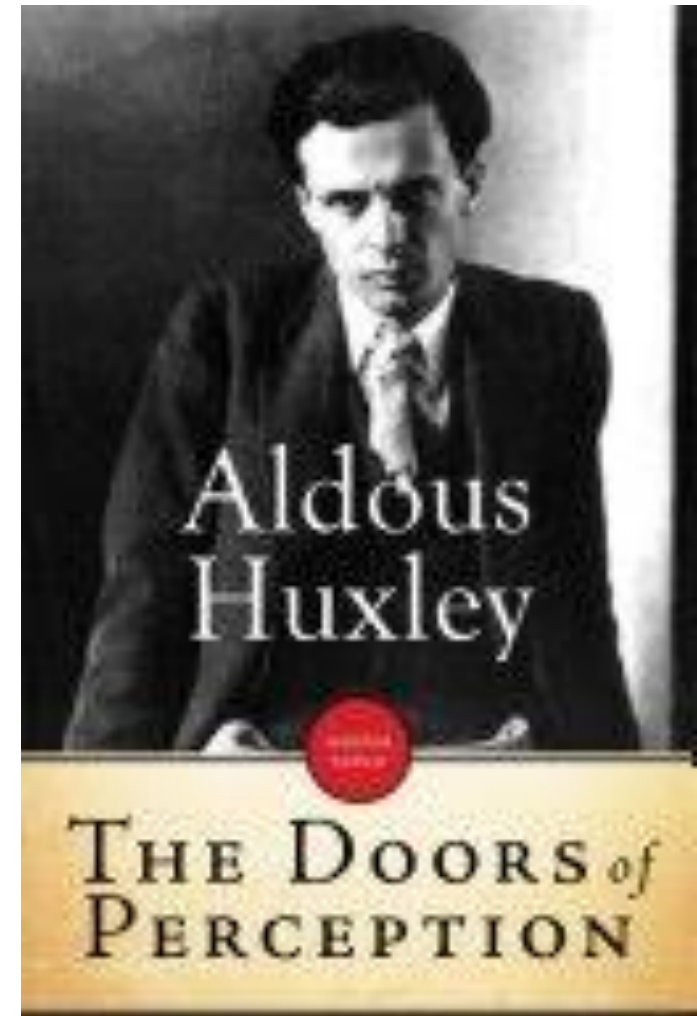


Beliveau et al. 2017



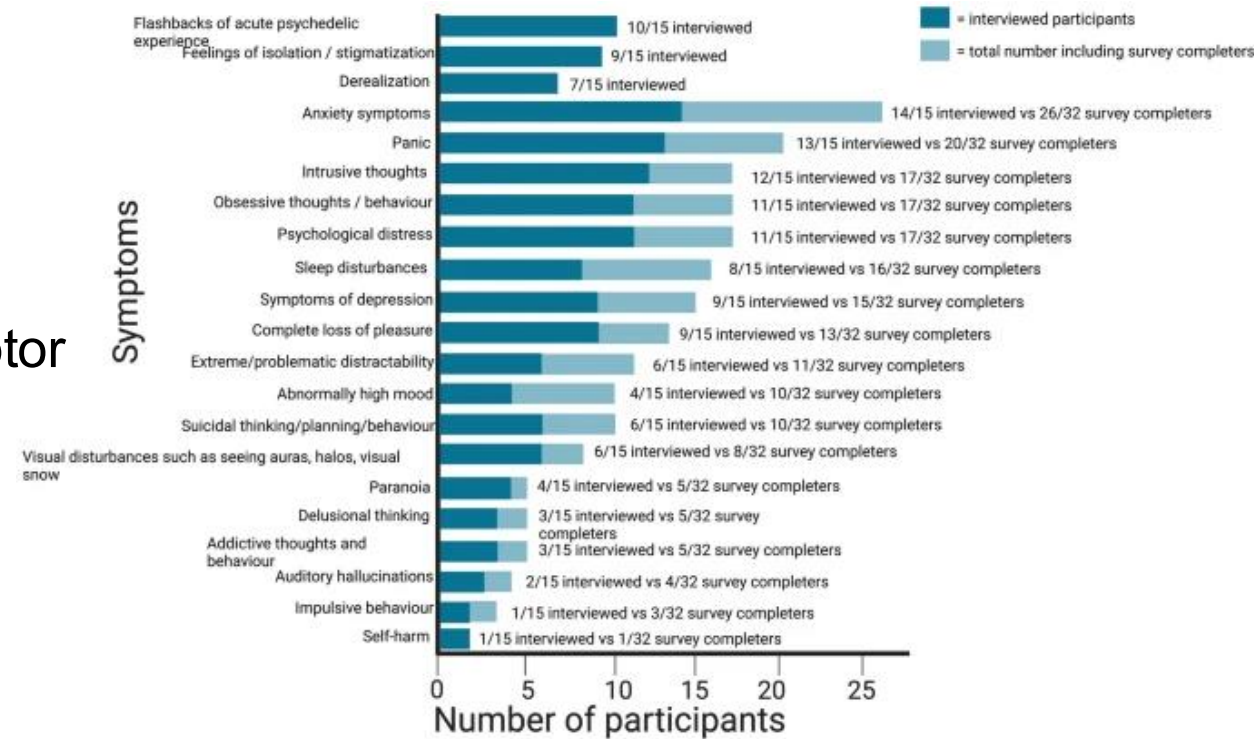
Psychedelic substances

- Naturally occurring substances used since time immemorial for cultural and medicinal uses
- Psilocybin, LSD, DMT
- High affinity to the serotonergic 5HT_{2A} receptor
- **Induce altered states of consciousness**

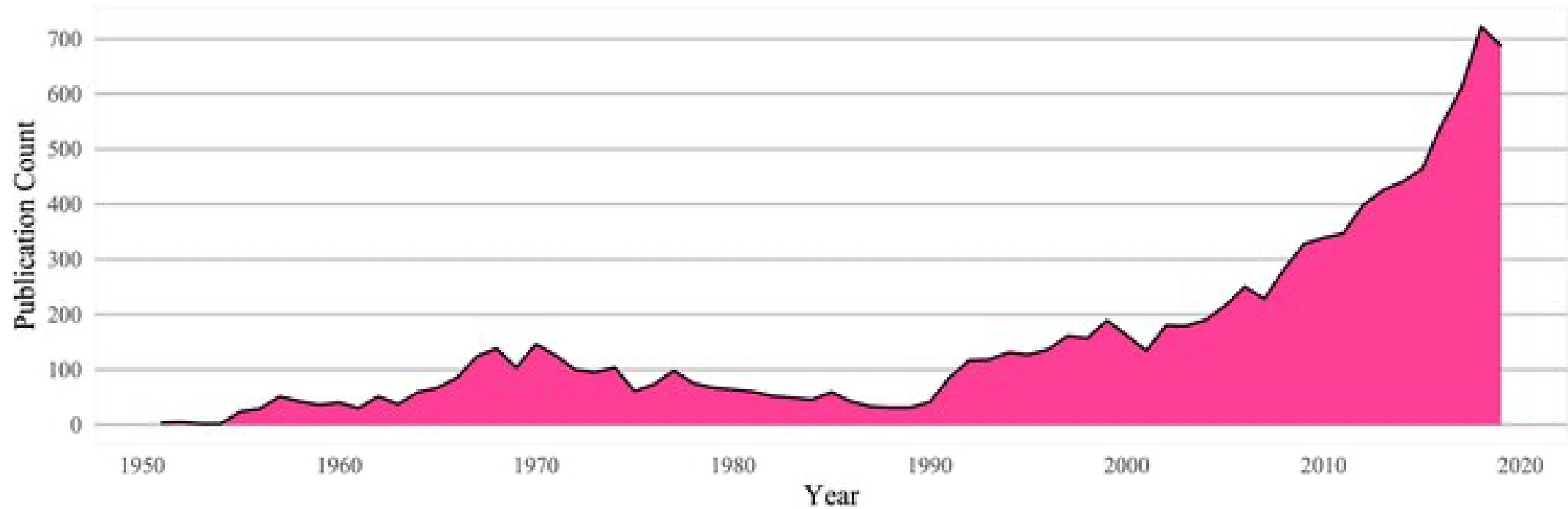


Psychedelic substances

- Naturally occurring substances used since time immemorial for cultural and medicinal uses
- Psilocybin, LSD, DMT
- High affinity to the serotonergic 5HT2A receptor
- Induce altered states of consciousness
- **Risk factors**



Psychedelic substances and research



Petranker et al., 2020

Psychedelic substances and mental health

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

Roland R Griffiths, Matthew W Johnson, Michael A Carducci, more...

[Show all authors](#) ▾

First Published November 30, 2016 | Research Article | [Find in PubMed](#) |

 Check for updates

<https://doi.org/10.1177/0269881116675513>

[Article information](#) ▾



Psychedelic substances and mental health

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

Roland R Griffiths, Matthew W Johnson, Michael A Carducci, more...

[Show all authors](#) ▾

First I THE LANCET
https: Psychiatry

Submit Article

Article



ARTICLES | [VOLUME 3, ISSUE 7, P619-627, JULY 01, 2016](#)

PD

Psilocybin with psychological support for treatment-resistant depression: an open-label feasibility study

Dr Robin L Carhart-Harris, PhD • [Mark Bolstridge, MD](#) • [James Rucker, MD](#) [†] • [Camilla M J Day, MD](#) [†] •

[David Erritzoe, MD](#) • [Mendel Kaelen, BSc](#) • et al. [Show all authors](#) • [Show footnotes](#)

[Open Access](#) • Published: May 17, 2016 • DOI: [https://doi.org/10.1016/S2215-0366\(16\)30065-7](https://doi.org/10.1016/S2215-0366(16)30065-7) •

Check for updates

Psychedelic substances and mental health

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

Roland R Griffiths, Matthew W Johnson, Michael A Carducci, more...

[Show all authors](#) ▾

First published in THE LANCET Psychiatry
[https://doi.org/10.1016/S2215-0169\(16\)00127-0](https://doi.org/10.1016/S2215-0169(16)00127-0)

Submit Article

Article



ARTICLES | [VOLUME 3, ISSUE 7, P619-627, JULY 01, 2016](#)

Psilocybin with psychological support for treatment-resistant depression: an open-label feasibility study

[Dr Robin L Carhart-Harris, PhD](#) • [Mark Bolstridge, MD](#) • [James Rucker, MD](#) • [David Erritzoe, MD](#) • [Mendel Kaelen, BSc](#) • et al. [Show all authors](#) • [Show footnotes](#)

[Open Access](#) • Published: May 17, 2016 • DOI: [https://doi.org/10.1016/S2215-0169\(16\)00127-0](https://doi.org/10.1016/S2215-0169(16)00127-0)

Check for updates

Rapid antidepressant effects of the psychedelic ayahuasca in treatment-resistant depression: a randomized placebo-controlled trial

Published online by Cambridge University Press: **15 June 2018**

[Fernanda Palhano-Fontes](#), [Dayanna Barreto](#), [Heloisa Onias](#), [Katia C. Andrade](#), [Morgana M. Novaes](#), [Jessica A. Pessoa](#), [Sergio A. Mota-Rolim](#), [Flávia L. Osório](#), [Rafael Sanches](#) and [Rafael G. dos Santos](#)

[Show all authors](#) ▾

Psychedelic substances and mental health

Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: a randomised, double-blind trial

Roland R Griffiths, Matthew W Johnson, Michael A Carducci, more...

First published in THE LANCET Psychiatry
[https://doi.org/10.1016/S2215-0366\(18\)30135-4](https://doi.org/10.1016/S2215-0366(18)30135-4)

Article

ARTICLES | VOLUME 3, ISSUE 7, P619-627, JULY 01, 2016

Psilocybin with psychological support for treatment of major depressive disorder: an open-label feasibility study

Dr Robin L Carhart-Harris, PhD • Mark Bolstridge, MD • James Rucker, MD • David Erritzoe, MD • Mendel Kaelen, BSc • et al. [Show all authors](#) • [Show footnotes](#)

Open Access • Published: May 17, 2016 • DOI: [https://doi.org/10.1016/S2215-0366\(16\)30069-0](https://doi.org/10.1016/S2215-0366(16)30069-0)

 Check for updates


Decreases in depression and anxiety in patients with life-threatening cancer: a randomised, double-blind trial
THE LANCET Psychiatry

Submit Article

ARTICLES | VOLUME 5, ISSUE 6, P486-497, JUNE 01, 2018

3,4-methylenedioxymethamphetamine (MDMA)-assisted psychotherapy for post-traumatic stress disorder in military veterans, firefighters, and police officers: a randomised, double-blind, dose-response, phase 2 clinical trial

Michael C Mithoefer, MD • Ann T Mithoefer, BSN • Allison A Feduccia, PhD • Lisa Jerome, PhD • Prof Mark Wagner, PhD • Joy Wymer, PhD • et al. [Show all authors](#)

Published: May 01, 2018 • DOI: [https://doi.org/10.1016/S2215-0366\(18\)30135-4](https://doi.org/10.1016/S2215-0366(18)30135-4) •  Check for updates

Published online by Cambridge University Press: 15 June 2018

Fernanda Palhano-Fontes, Dayanna Barreto, Heloisa Onias, Katia C. Andrade, Morgana M. Novaes, Jessica A. Pessoa, Sergio A. Mota-Rolim, Flávia L. Osório, Rafael Sanches and Rafael G. dos Santos

[Show all authors](#)

Psychedelic substances and mental health

Psilocybin produces substantial and sustained decreases in depression and anxiety in patients: a randomised, double-blind trial
nature medicine

Roland R Griffiths, Matthew

First I THE LANCET
https:// Psychiatry

Article

Explore content ▾ About the journal ▾ Publish with us ▾

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

Article | [Open Access](#) | [Published: 10 May 2021](#)

MDMA-assisted therapy for severe PTSD: a randomized, double-blind, placebo-controlled phase 3 study

[Jennifer M. Mitchell](#)  [Michael Bogenschutz](#), ... [Rick Doblin](#) [+ Show authors](#)

ARTICLES | VOLU

Psilocybin
an open-l

Dr Robin L Carhart-Harris, PhD   [Mark Bolstridge, MD](#) • [James Rucker, M](#)

[David Erritzoe, MD](#) • [Mendel Kaelen, BSc](#) • et al. [Show all authors](#) • [Show foot](#)

[Open Access](#) • Published: May 17, 2016 • DOI: <https://doi.org/10.1016/S2215-0>

 [Check for updates](#)


THE LANCET

Submit Article

97, JUNE 01, 2018

methamphetamine (MDMA)-assisted psychotherapy
ress disorder in military veterans, firefighters, and
omised, double-blind, dose-response, phase 2

[ithoefer, BSN](#) • [Allison A Feduccia, PhD](#)   • [Lisa Jerome, PhD](#) •
[er, PhD](#) • et al. [Show all authors](#)

[https://doi.org/10.1016/S2215-0366\(18\)30135-4](https://doi.org/10.1016/S2215-0366(18)30135-4) •  [Check for updates](#)

Published online by Cambridge University Press: **15 June 2018**

[Fernanda Palhano-Fontes](#), [Dayanna Barreto](#), [Heloisa Onias](#), [Katia C. Andrade](#), [Morgana M. Novaes](#),
[Jessica A. Pessoa](#), [Sergio A. Mota-Rolim](#), [Flávia L. Osório](#), [Rafael Sanches](#) and [Rafael G. dos Santos](#)

[Show all authors](#)

Psychedelic substances and mental health

Psilocybin produces substantial and sustained decreases in depression and anxiety in patients: a double-blind trial
nature medicine

Roland R Griffiths, Matthew

First in THE LANCET Psychiatry
<https://www.thelancet.com>

Article

Explore content

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

Article | [Open Access](#)

MDMA-assisted psychotherapy vs placebo in the treatment of adult patients with alcohol use disorder: a randomized clinical trial

[Jennifer M. Mitchell](#)

ARTICLES | VOLUME

Psilocybin-assisted therapy for major depression: an open-label, phase 2b trial

Dr Robin L Carhart-Harris, PhD

David Erritzoe, MD • Mendel Kaalen, MD

Open Access • Published: May 17, 2022

Check for updates

Original Investigation

August 24, 2022

Percentage of Heavy Drinking Days Following Psilocybin-Assisted Psychotherapy vs Placebo in the Treatment of Adult Patients With Alcohol Use Disorder

A Randomized Clinical Trial

Michael P. Bogenschutz, MD¹; Stephen Ross, MD¹; Snehal Bhatt, MD²; et al

[Author Affiliations](#) | [Article Information](#)

JAMA Psychiatry. 2022;79(10):953-962. doi:10.1001/jamapsychiatry.2022.2096

Submit Article



psychotherapy
nd

Psychedelic substances and mental health

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trial of Psilocybin versus Escitalopram for Depression

Robin Carhart-Harris, Ph.D., Bruna Giribaldi, B.Sc., Rosalind Watts, D.Clin.Psy., Michelle Baker-Jones, B.A., Ashleigh Murphy-Beiner, M.Sc., Roberta Murphy, M.D., Jonny Martell, M.D., Allan Blemings, M.Sc., David Erritzoe, M.D., and David J. Nutt, M.D.

ABSTRACT

Michael P. Bogenschutz, MD¹; Stephen Ross, MD¹; Snehal Bhatt, MD²; et al

» [Author Affiliations](#) | [Article Information](#)

JAMA Psychiatry. 2022;79(10):953-962. doi:10.1001/jamapsychiatry.2022.2096

Psilocybin produces
and anxiety in patients
double-blind trial

Roland R Griffiths, Matthew

First in THE LANCET
https:// Psychiatry

Article

ARTICLES | VOLU

Psilocybin
an open-l

Dr Robin L Carhart-Harris, PhD
David Erritzoe, MD • Mendel Kaelen

Open Access • Published: May 17, 20

Check for updates

Submit Article



ys Following
oy vs Placebo in the
Alcohol Use

erapy
and
2

Psychedelic substances and mental health

Psilocybin p
and anxiety
double-blind

Roland R Griffiths

First I THE LAI
https: Psychiatry

Articl



ESTABLISHED IN 1812

NOVEMBER 3, 2022

VOL. 387 NO. 18

Single-Dose Psilocybin for a Treatment-Resistant Episode of Major Depression

G.M. Goodwin, S.T. Aaronson, O. Alvarez, P.C. Arden, A. Baker, J.C. Bennett, C. Bird, R.E. Blom, C. Brennan, D. Bruschi, L. Burke, K. Campbell-Coker, R. Carhart-Harris, J. Cattell, A. Daniel, C. DeBattista, B.W. Dunlop, K. Eisen, D. Feifel, M.K. Forbes, H.M. Haumann, D.J. Hellerstein, A.I. Hoppe, M.I. Husain, L.A. Jelen, J. Kamphuis, J. Kawasaki, J.R. Kelly, R.E. Key, R. Kishon, S. Knatz Peck, G. Knight, M.H.B. Koolen, M. Lean, R.W. Licht, J.L. Maples-Keller, J. Mars, L. Marwood, M.C. McElhiney, T.L. Miller, A. Mirow, S. Mistry, T. Mletzko-Crowe, L.N. Modlin, R.E. Nielsen, E.M. Nielson, S.R. Offerhaus, V. O'Keane, T. Páleníček, D. Printz, M.C. Rademaker, A. van Reemst, F. Reinholdt, D. Repantis, J. Rucker, S. Rudow, S. Ruffell, A.J. Rush, R.A. Schoevers, M. Seynaeve, S. Shao, J.C. Soares, M. Somers, S.C. Stansfield, D. Sterling, A. Strockis, J. Tsai, L. Visser, M. Wahba, S. Williams, A.H. Young, P. Ywema, S. Zisook, and E. Malievskaia

ABSTRACT

Check for updates

Submit Article

01, 2018

f MEDICINE

.E

Escitalopram

on

, Rosalind Watts, D.Clin.Psy.,
rphy-Beiner, M.Sc.,
Allan Blemings, M.Sc.,
. Nutt, M.D.

psychotherapy
refighters, and
se, phase 2

me, PhD

ck for updates

es,
DS

ABSTRACT

Psychedelic substances and mental health

Psilocybin Original Investigation

and anxiety
double-blind
August 31, 2023

Roland R Gr

Single-Dose Psilocybin Treatment for Major

First I THE
https: Psyc

Depressive Disorder

Article

A Randomized Clinical Trial

Charles L. Raison, MD¹; Gerard Sanacora, MD, PhD²; Joshua Woolley, MD, PhD^{3,4}; et al

» Author Affiliations | Article Information

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

A. Strockis, J. Tsai, L. Visser, M. Wahba, S. Williams, A.H. Young, P. Ywema, S. Zisook, and E. Malievskaia

ABSTRACT

Check for updates

ABSTRACT

Submit Article

IE

psychotherapy
refighters, and
se, phase 2

me, PhD

lopram

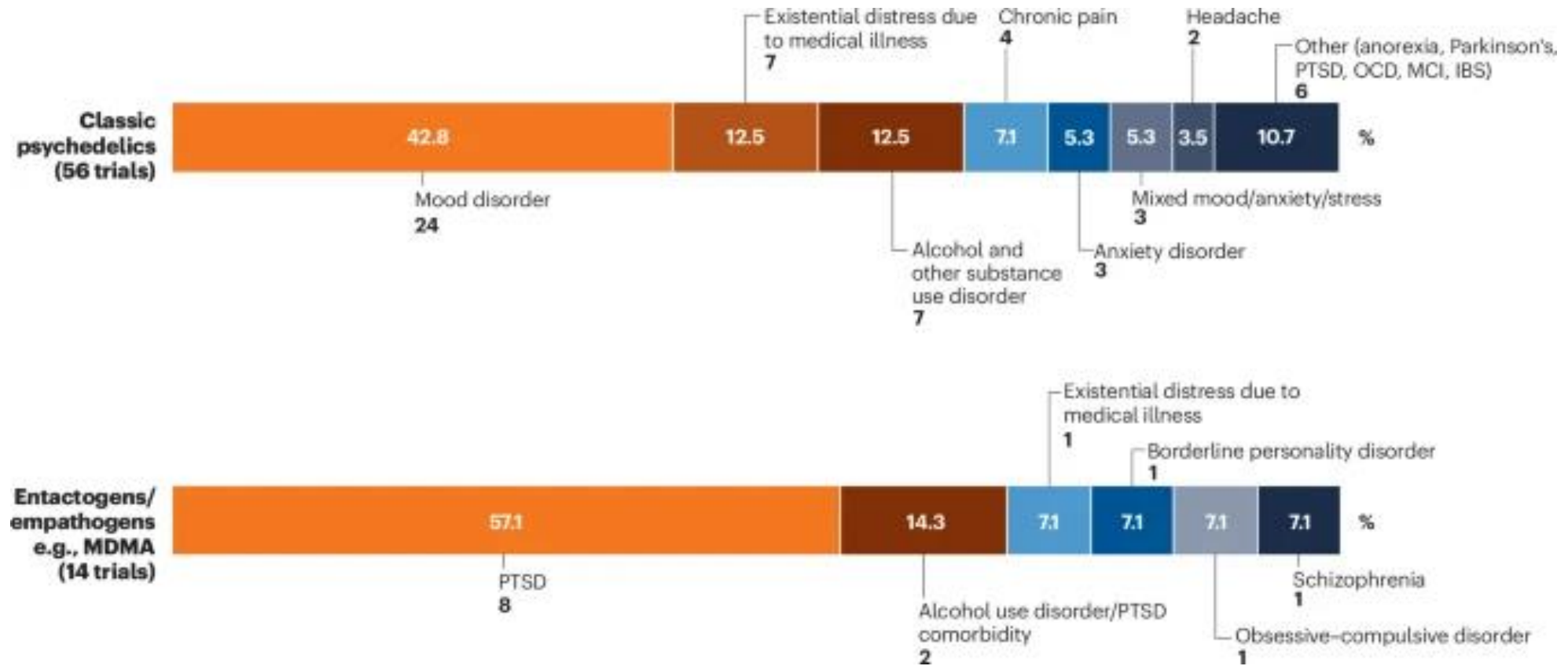
ck for updates

Matts, D.Clin.Psy.,
; M.Sc.,

Allan Blemings, M.Sc.,
. Nutt, M.D.

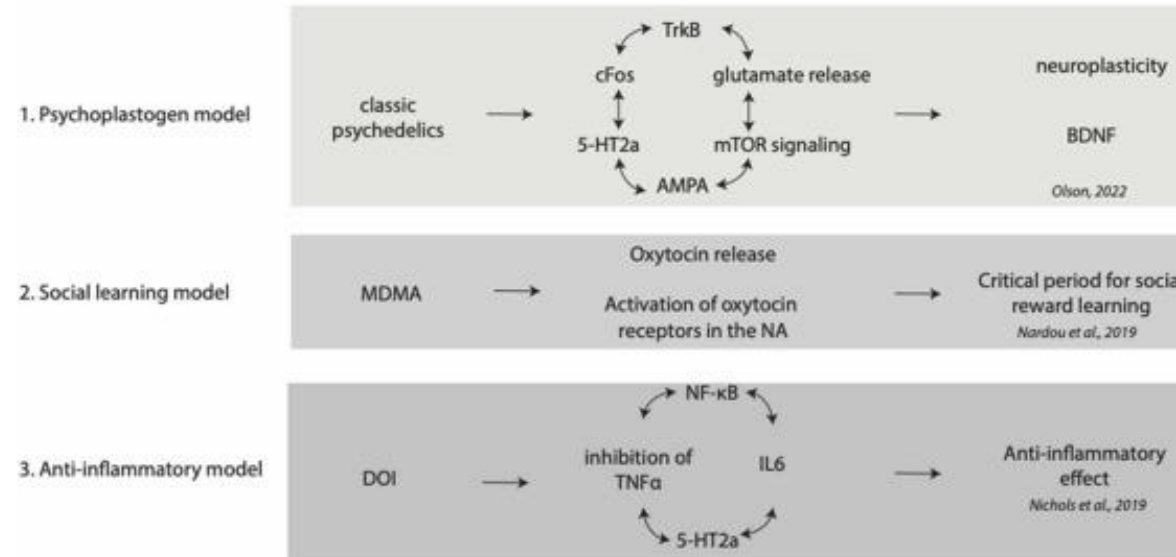
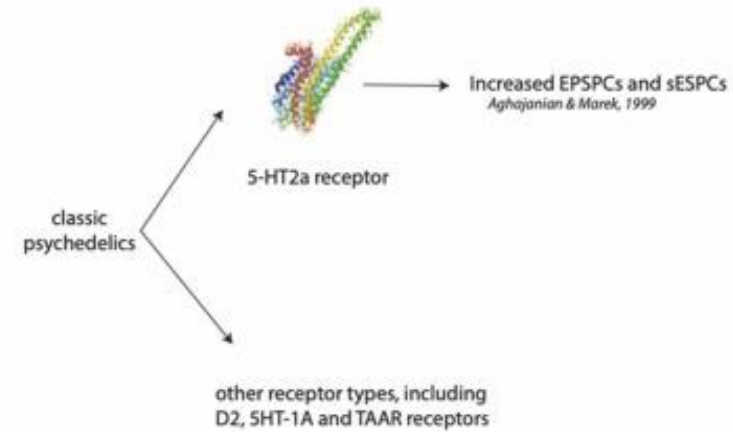
es,
DS

Active phase 2/3 clinical trials

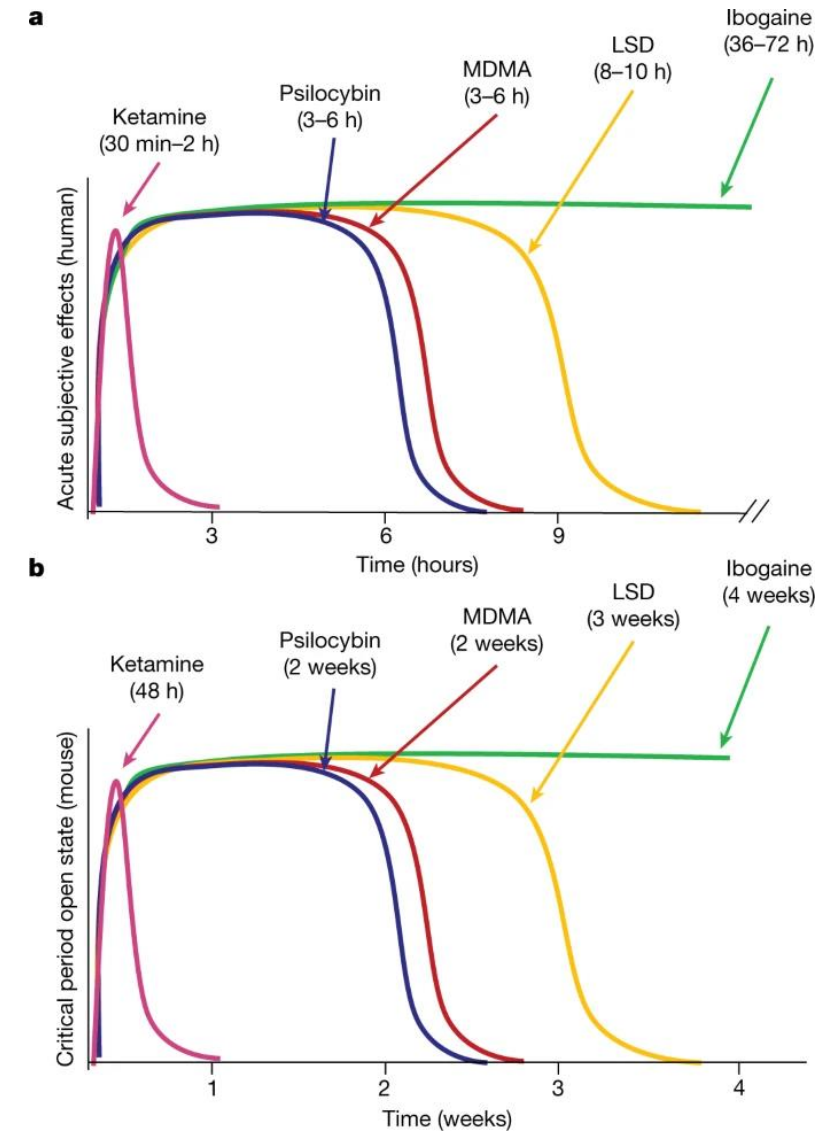
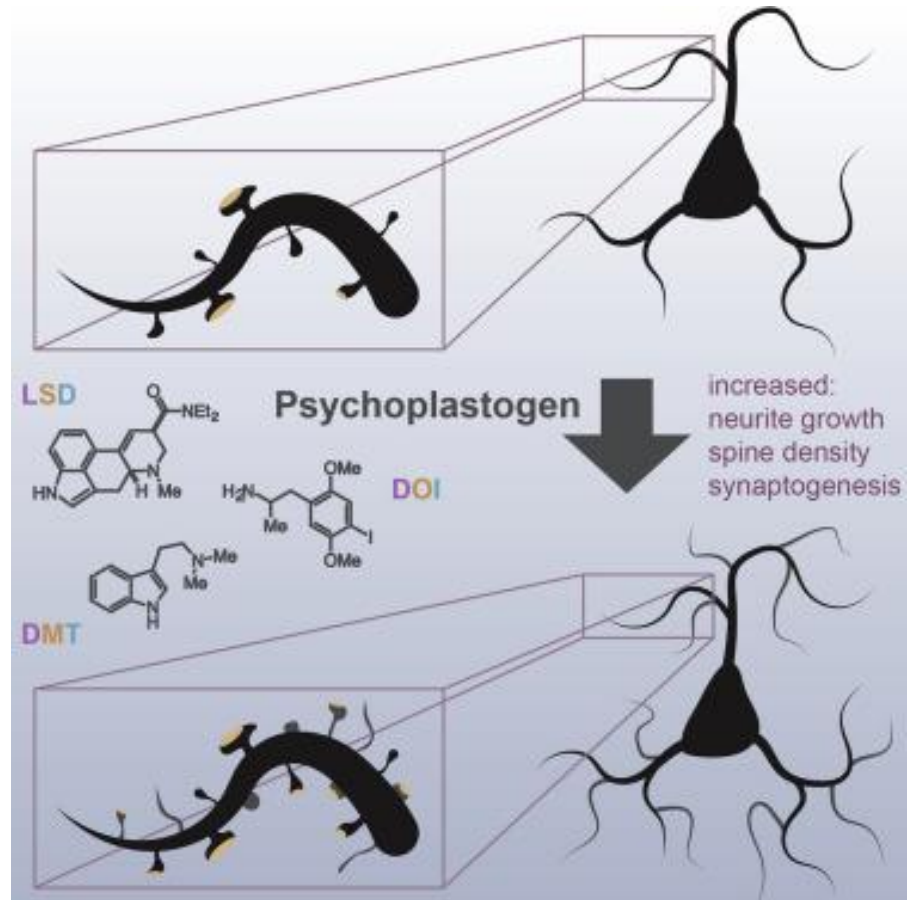


Psychedelic substances: potential mechanisms of action

- Neuroplasticity
 - Social learning
 - Anti-inflammation
-
- Updating beliefs



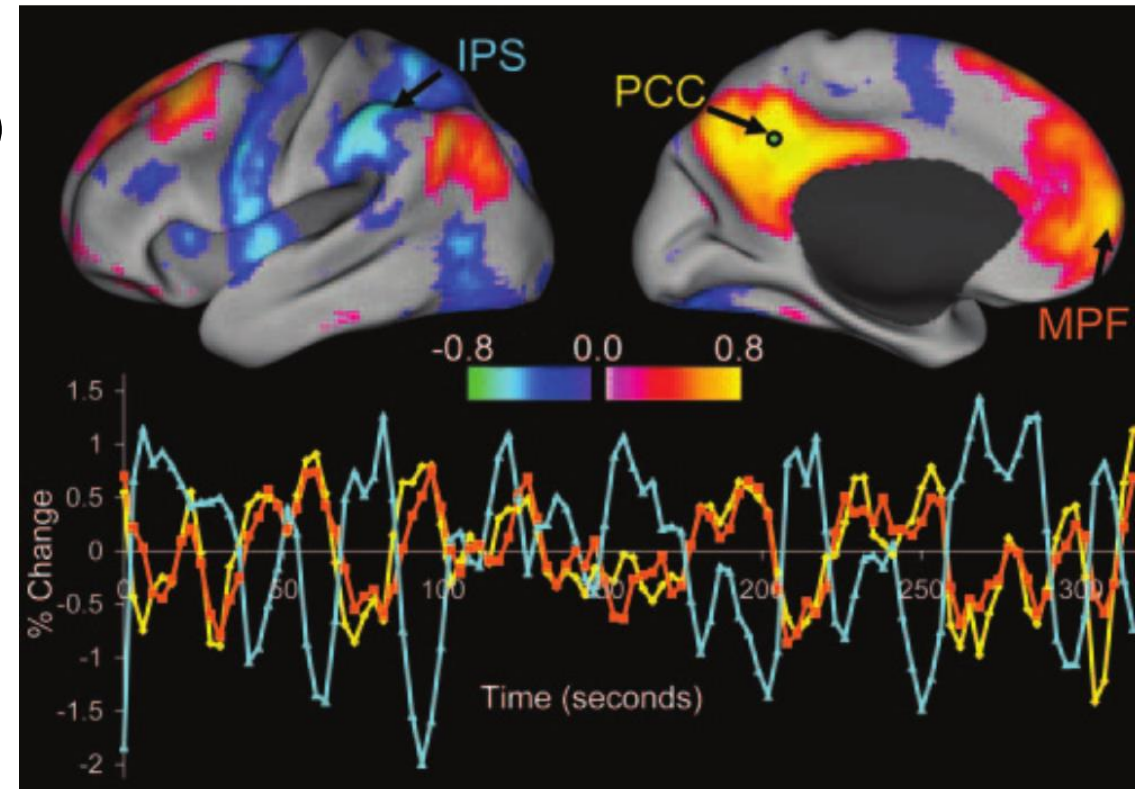
Psychedelics reopen the social reward learning critical period



2. Can we map these plasticity-related changes in the human brain?

Intrinsic functional connectivity

- **Coherent fluctuations** in the BOLD signal (<0.1 Hz) among distant gray matter regions
- Used to map large-scale **brain networks**



Fox et al. 2005

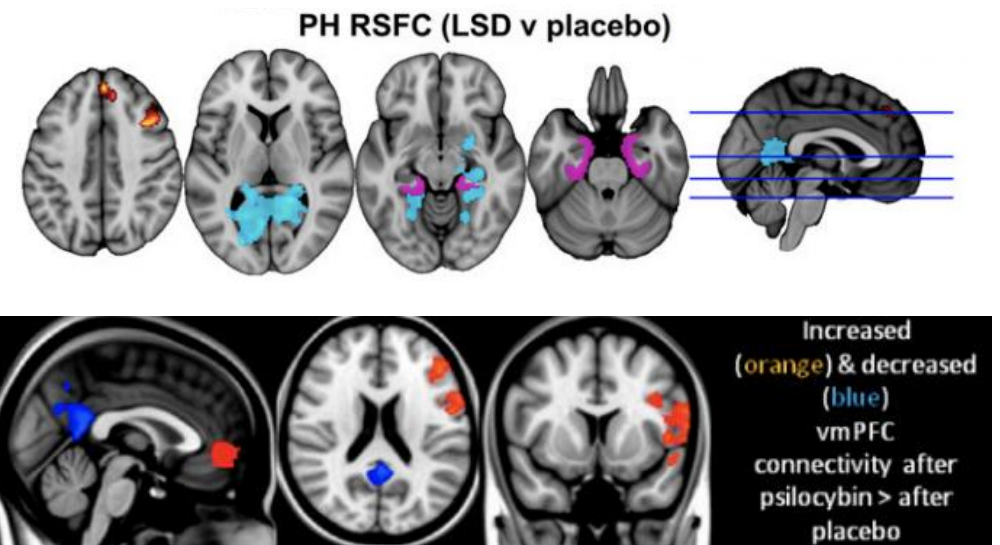
Neural correlates of acute psychedelic effects

- **LSD:** reduced connectivity between parahippocampal cortices and posterior cingulate cortex
- **Psilocybin:** reduced connectivity between posterior cingulate cortex and vmPFC

Psilocybin desynchronizes the human brain

[Joshua S. Siegel](#) , [Subha Subramanian](#), [Demetrius Perry](#), [Benjamin P. Kay](#), [Evan M. Gordon](#), [Timothy O. Laumann](#), [T. Rick Reneau](#), [Nicholas V. Metcalf](#), [Ravi V. Chacko](#), [Caterina Gratton](#), [Christine Horan](#), [Samuel R. Krimmel](#), [Joshua S. Shimony](#), [Julie A. Schweiger](#), [Dean F. Wong](#), [David A. Bender](#), [Kristen M. Scheidter](#), [Forrest I. Whiting](#), [Jonah A. Padawer-Curry](#), [Russell T. Shinohara](#), [Yong Chen](#), [Julia Moser](#), [Essa Yacoub](#), [Steven M. Nelson](#), ... [Nico U. F. Dosenbach](#) [+ Show authors](#)

[Nature](#) **632**, 131–138 (2024) | [Cite this article](#)



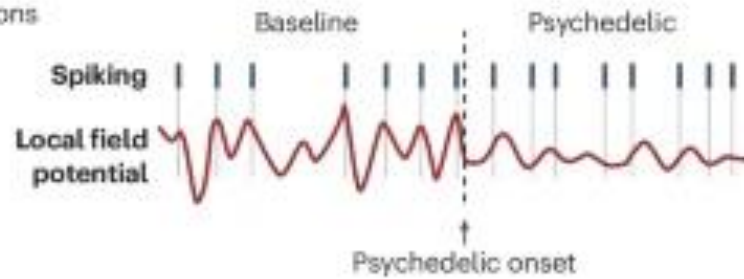
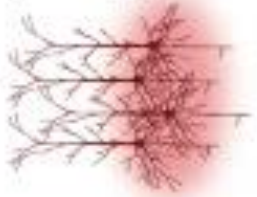
Carhart-Harris et al. 2012, 2016

Psilocybin desynchronizes the human brain

a Microscale

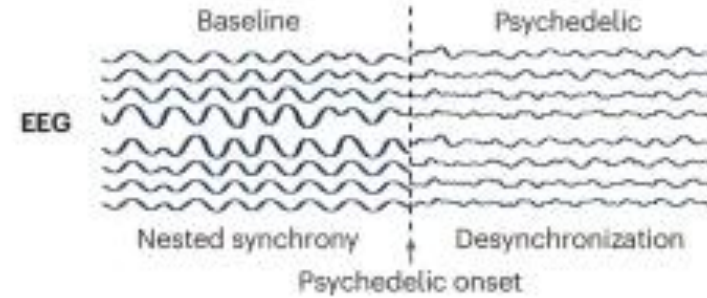
Divergence of single-unit spiking from the LFP

5-HT_{2A}-expressing pyramidal neurons



b Large scale

↓ synchrony : ↑ spatial complexity (entropy)

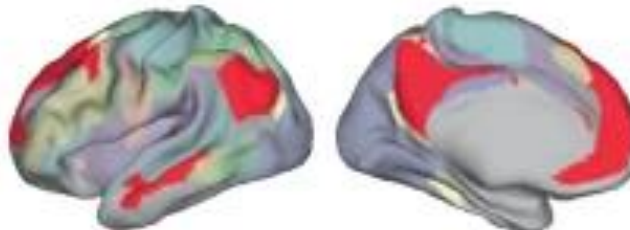


5-HT_{2A} receptor density



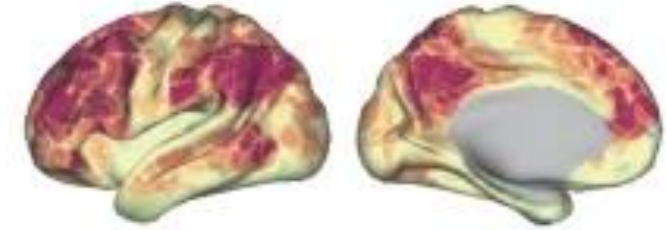
¹¹C-Cimbi-36
15 60
(pmol ml⁻¹)

Default mode network



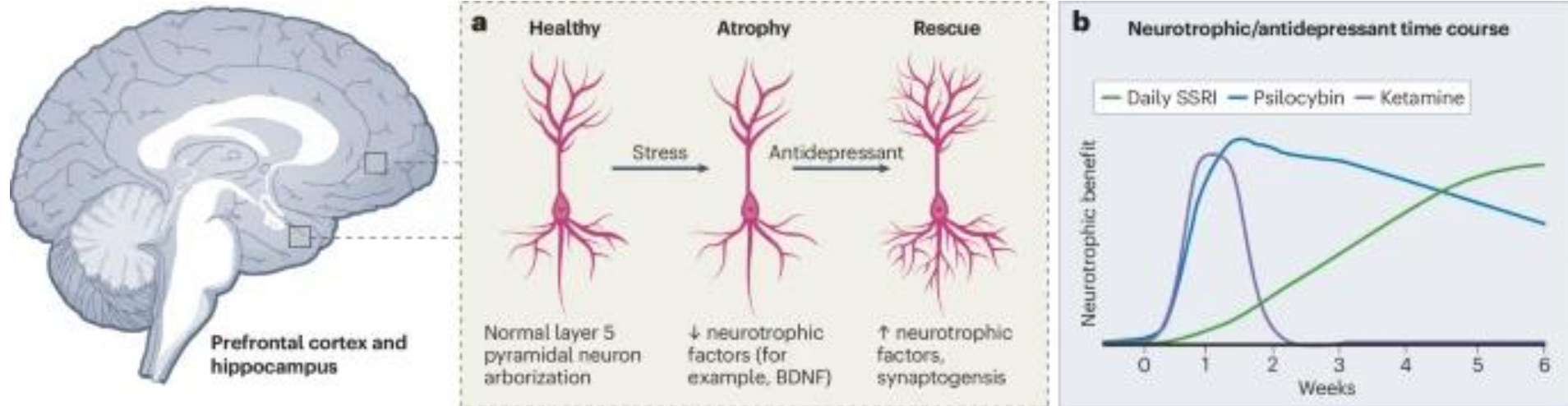
- Sense of self
- Introspection

Desynchronization

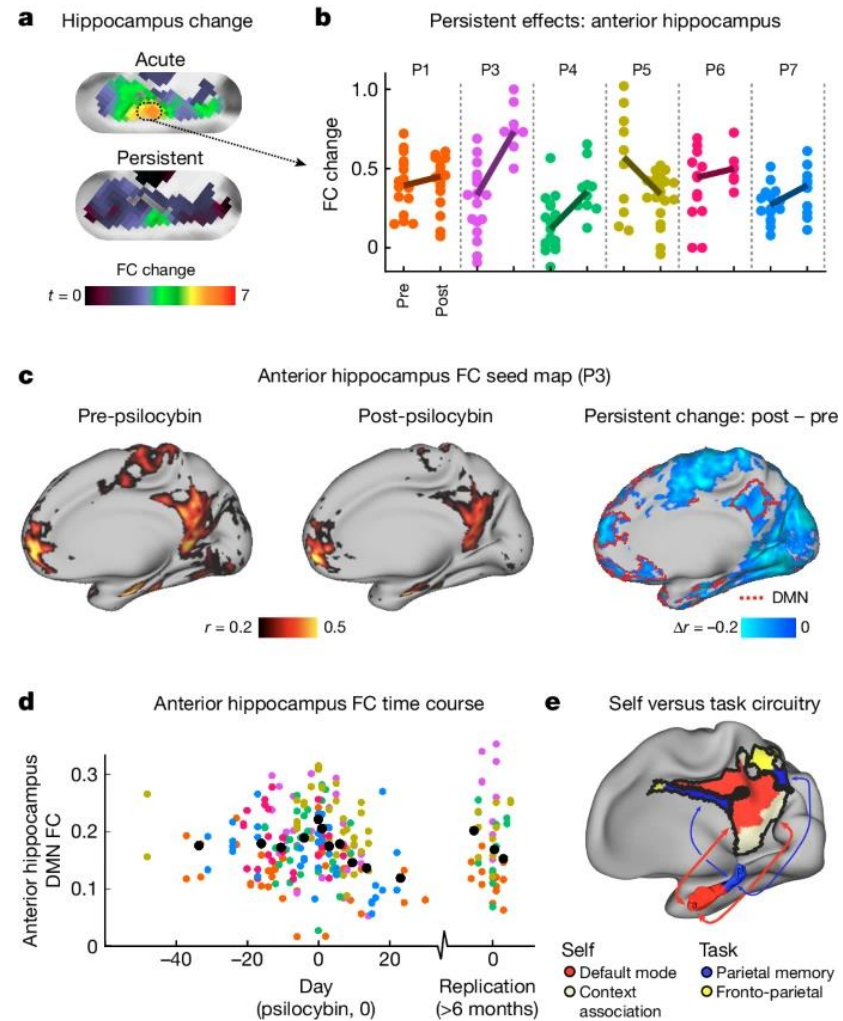


-0.05 0.05
ΔLocal NGSC

Psilocybin's neurotrophic and therapeutic effects

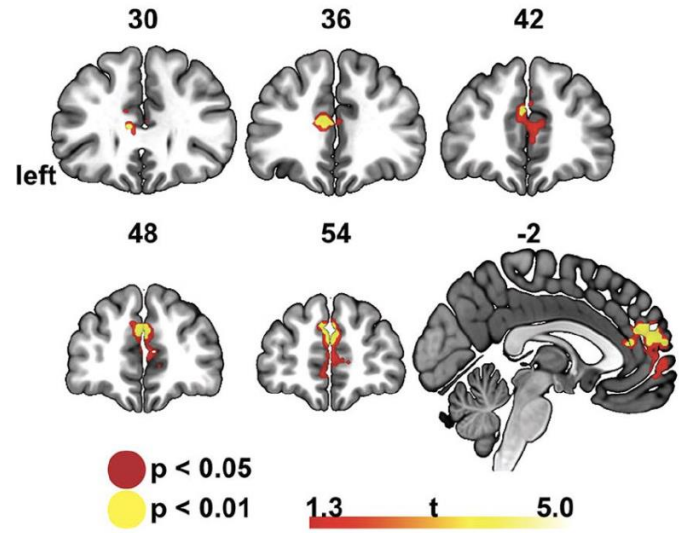


Persisting effects: hippocampal connectivity

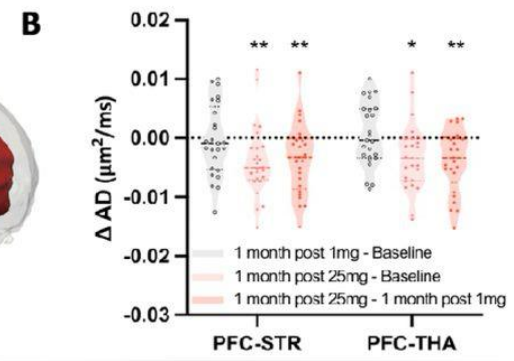
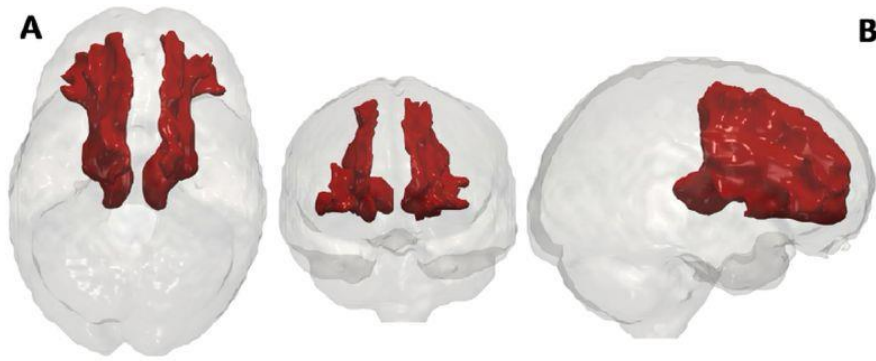
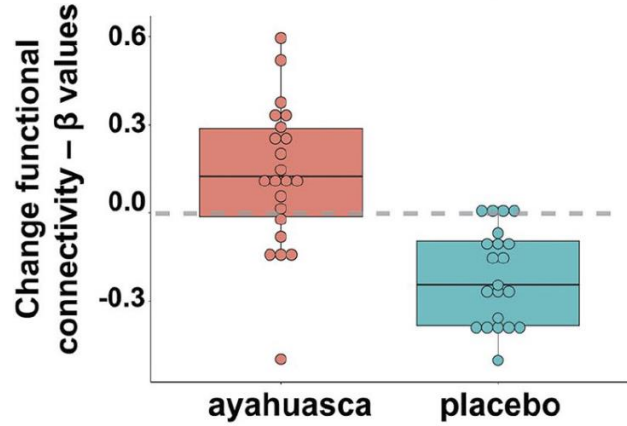


Persisting effects: prefrontal cortex

(a) **Saliience network**
Change ayahuasca > change placebo



(b) **Saliience network**




3. Frontiers: psychedelics for older adult

Psychedelic and older adults: Parkinson's disease

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

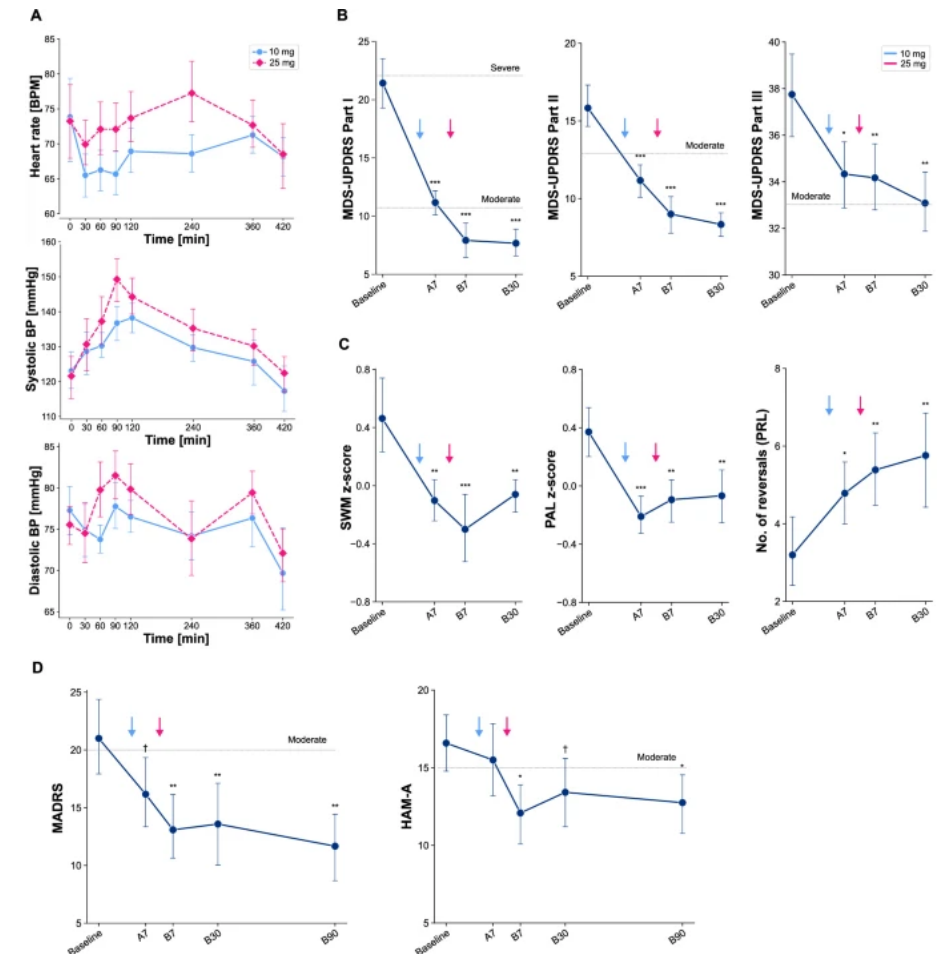
Article | [Open access](#) | Published: 09 April 2025

Psilocybin therapy for mood dysfunction in Parkinson's disease: an open-label pilot trial

[Ellen R. Bradley](#) , [Kimberly Sakai](#), [Gisele Fernandes-Osterhold](#), [Balázs Szigeti](#), [Connie Ludwig](#), [Jill L. Ostrem](#), [Caroline M. Tanner](#), [Meredith A. Bock](#), [Katiah Llerena](#), [Patrick R. Finley](#), [Aoife O'Donovan](#), [Jose Rafael P. Zuzuarregui](#), [Zachary Busby](#), [Amber McKernan](#), [Andrew D. Penn](#), [Aliss C. C. Wang](#), [Raymond C. Rosen](#) & [Joshua D. Woolley](#)

[Neuropsychopharmacology](#) **50**, 1200–1209 (2025) | [Cite this article](#)

36k Accesses | 14 Citations | 242 Altmetric | [Metrics](#)



Psychedelic and older adults: Alzheimer's disease



Center for Psychedelic & Consciousness Research

[About](#) [Enroll in a Study](#) [Media](#) [Resources](#) [Employment](#) [Contact](#) [Donate](#)



Psilocybin is Being Studied as a Potential Aid for Depression in Early Alzheimer's Disease

Have you recently been diagnosed with Alzheimer's Disease? Are you feeling depressed? Sign up to participate in a research study examining a unique approach to depression in people with Mild Cognitive Impairment (MCI) or early Alzheimer's Disease (AD).

Researchers at Johns Hopkins University are studying psilocybin – a psychoactive substance found in certain kinds of mushrooms – to see whether it can help people with depression and Alzheimer's Disease when administered in a safe and supportive setting. Volunteers will additionally receive free counseling.

To find out more about this study, call 410-550-5466.

Principal Investigators: Albert Garcia-Romeu, Ph.D. & Paul B. Rosenberg, M.D.

Protocol: IRB00175915



Psychedelic and older adults







The American Journal of Geriatric Psychiatry

Volume 32, Issue 9, September 2024, Pages 1047-1059



Regular Research Article

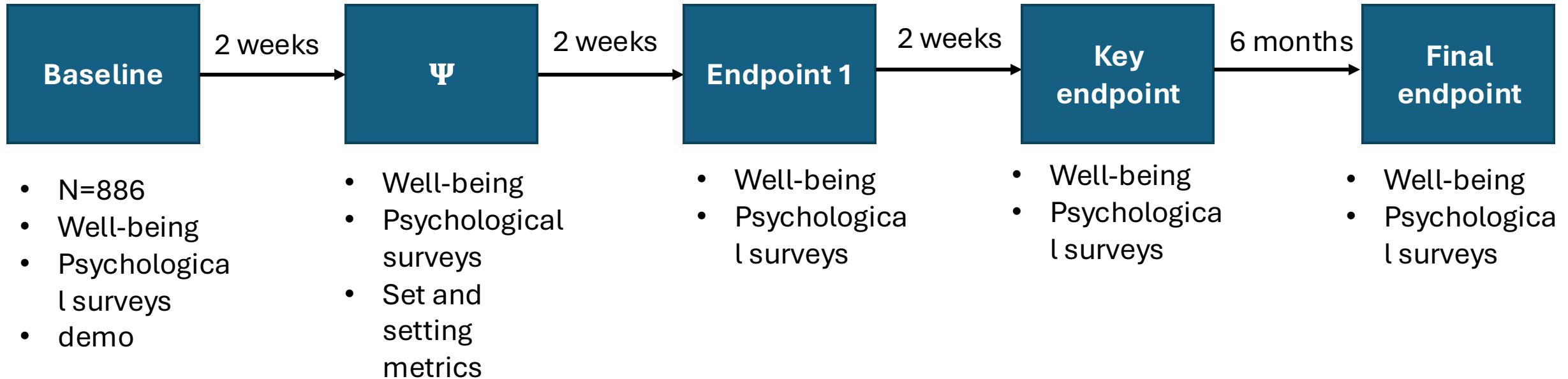
Effects of Psychedelics in Older Adults: A Prospective Cohort Study

Hannes Kettner M.Sc. ^{a b}  , Leor Roseman Ph.D. ^{b c}, Adam Gazzaley M.D., Ph.D. ^{a d},
Robin L. Carhart-Harris Ph.D. ^{a b d}, Lorenzo Pasquini Ph.D. ^a  

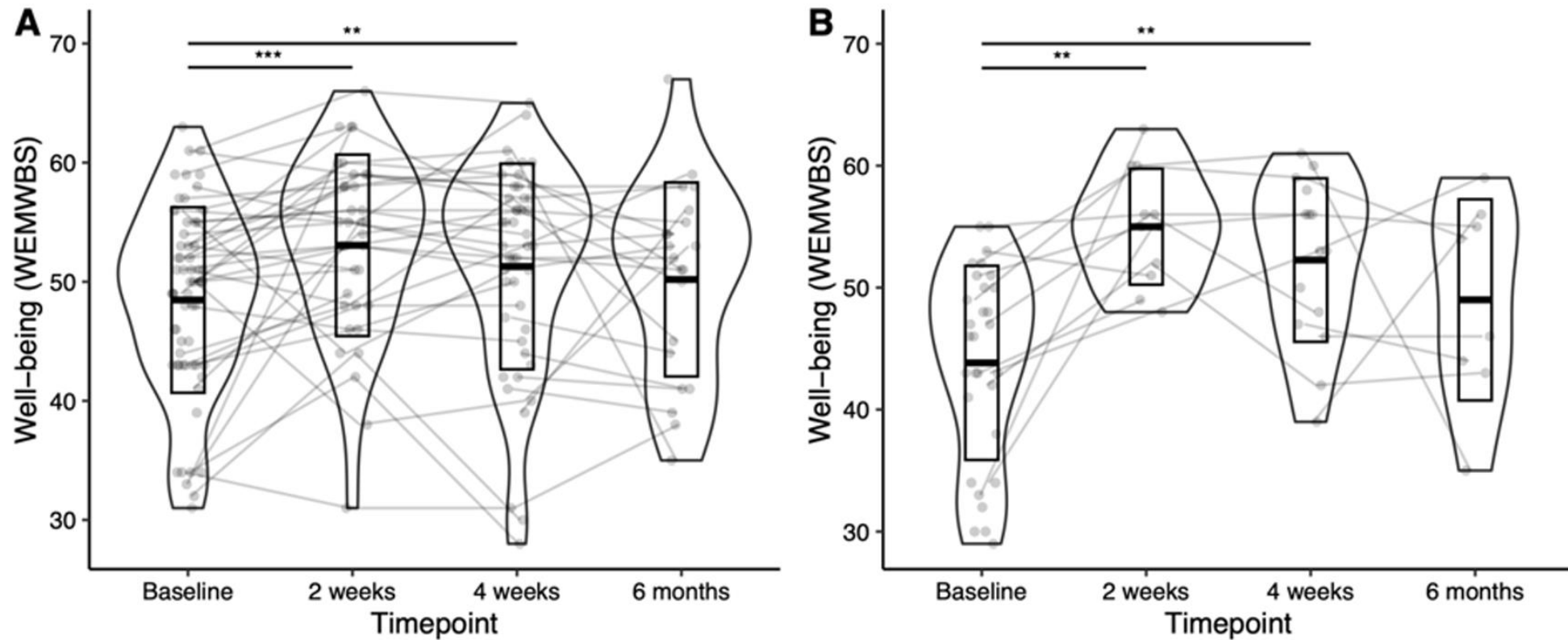
Questions

- How is well-being changing in older adults attending guided psychedelic sessions?
- Are there any predictors of well-being change?

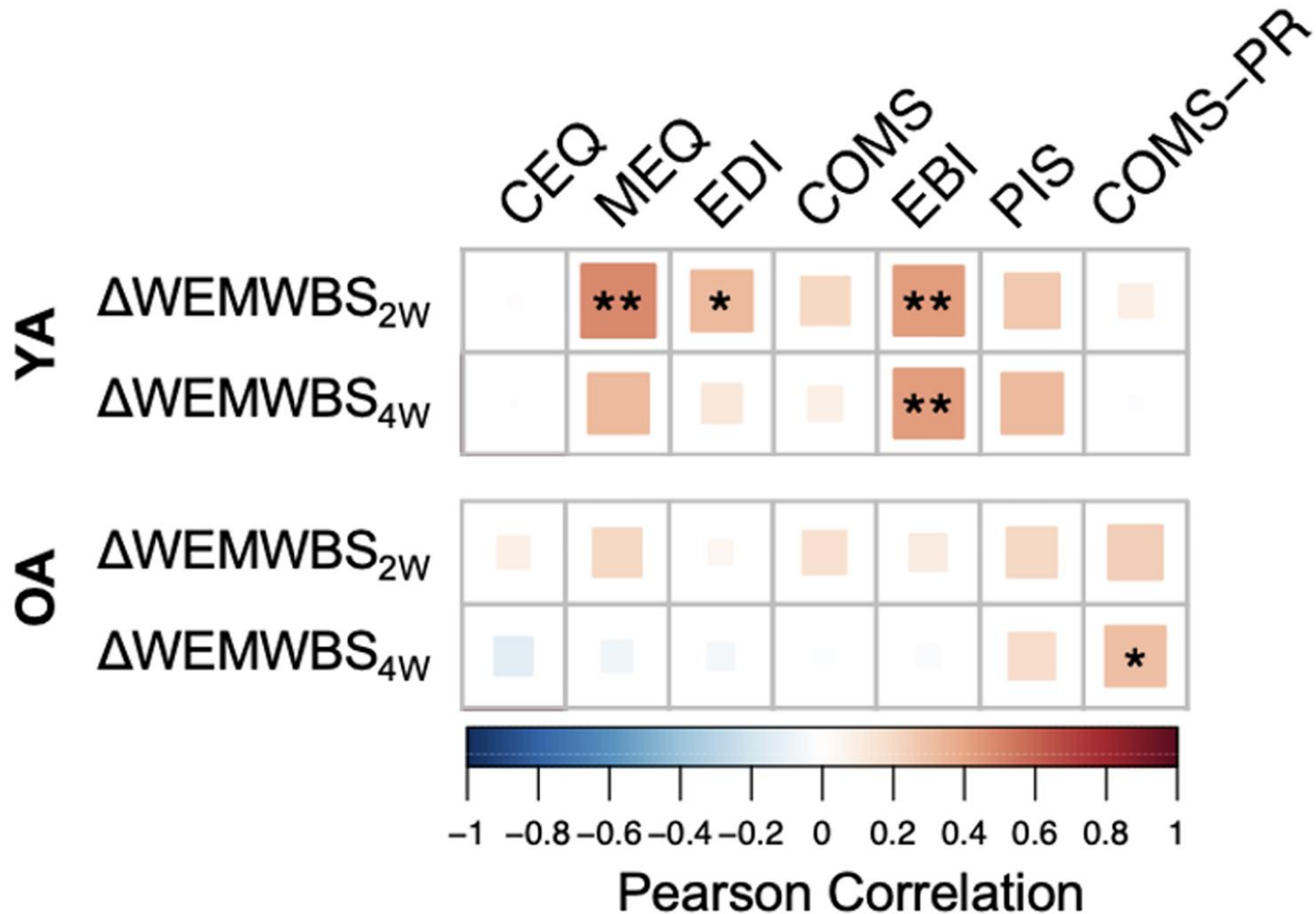
Study design



Well-being improves in older adults following psychedelic sessions

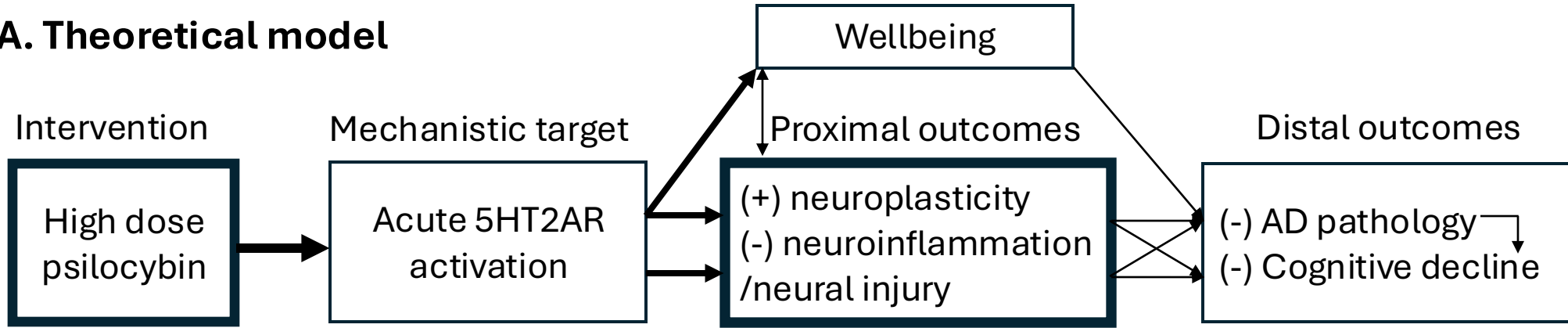


Experiential predictors of well-being change in older adults compared to younger adults

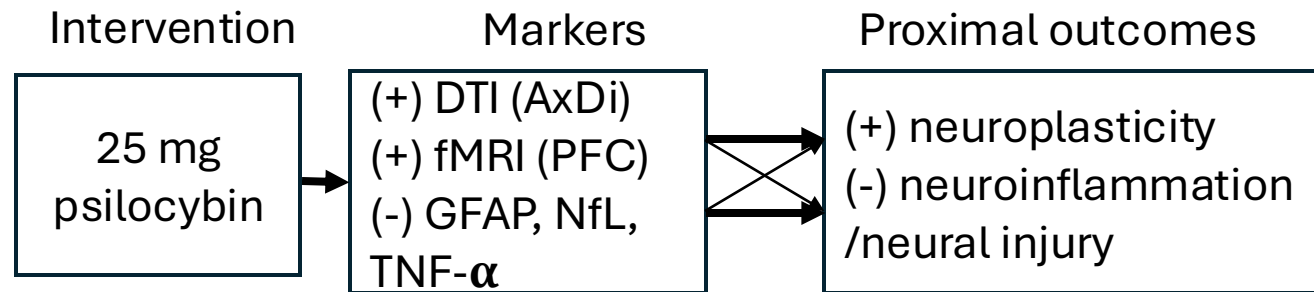


Conceptual model

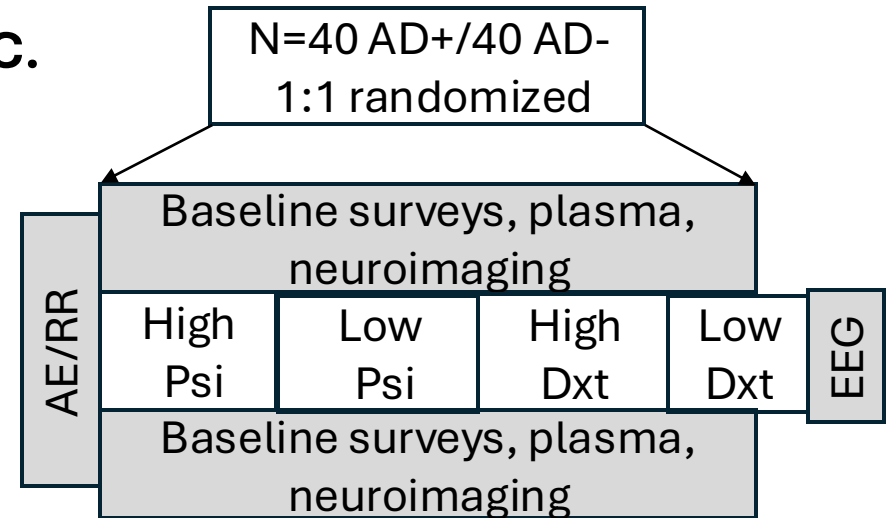
A. Theoretical model



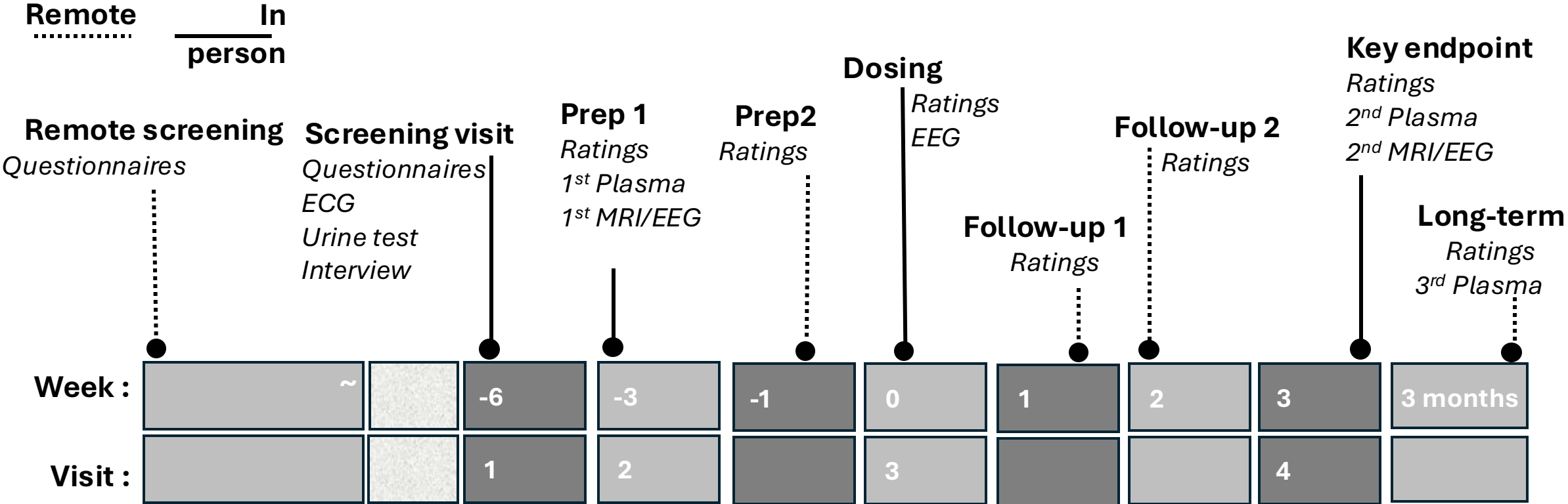
B. Conceptual model



C.



Trial design



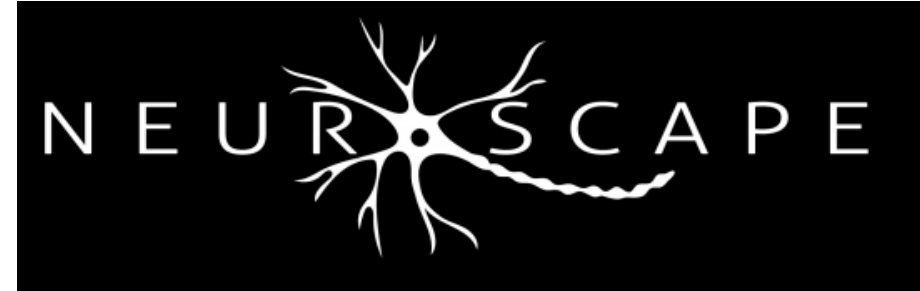
Conclusions

- **Psychedelic substances are serotonergic 5HT_{2A} receptor agonist increasingly explored for their fast and sustained effects on clinical symptoms**
- **Mechanisms of action may include increased neuroplasticity, anti-inflammatory properties, as well as opening a window for social reward**
- **Acutely, psychedelics desynchronize the brain; longitudinally psychedelics may affect the hippocampus and prefrontal cortex**
- **Psychedelics interventions are being investigated for older adults**

Acknowledgements

Adam Gazzaley
Robin Carhart-Harris
Jennifer Mitchell
Andrea Rosati
Dawn Weinstein
Hannes Kettner
Manesh Girn
Patrick McConnell
Avery Ostrand
Kate Allison
Maya Desai
Gabriella Mace
Leor Roseman
Study participants

Gustavo Deco
Jakub Vohryzek
Anira Eschrich
Yonatan Sanz Pearl



UCSF Weill Institute for
Neurosciences

Imperial College
London





BEACON 2026

THANK YOU

UCSF

Memory and
Aging Center
Department of Neurology