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State of Psychedelic Research in 2025

David B. Yaden, PhD

Griffiths Professor of Psychedelic Research

Department of Psychiatry and Behavioral Sciences

Johns Hopkins University School of Medicine



Disclosures

If you have disclosures, state:

My spouse/partner and I have the following relevant financial relationship with a commercial interest to disclose:

- Personal Lecturing fees from Integrative Psychiatry Institute
 - Personal Consulting Fee from Soneira
- Research funds for a study from Gracias Family Foundation



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- Alzheimer's Disease
- Smoking Cessation
- Major Depressive Disorder (MDD)/Alcohol Use Disorder (AUD)
- EEG
- Obsessive Compulsive Disorder (OCD)
- Cannabis Use Disorder (CUD)
- Opioid Use Disorder (OUD)
- Post Traumatic Stress Disorder (PTSD)
- Anorexia Nervosa
- Chronic Low Back Pain and Depression (CLBP+D)
- Post-Traumatic Stress Disorder (PTSD)



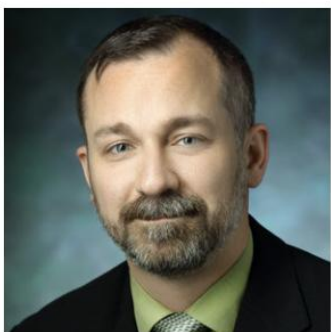
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Bit Yaden, MD

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Clinical Director



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Instructor



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Research Associate



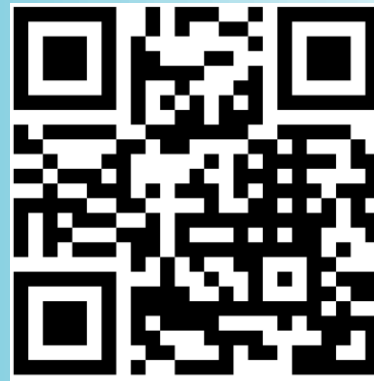
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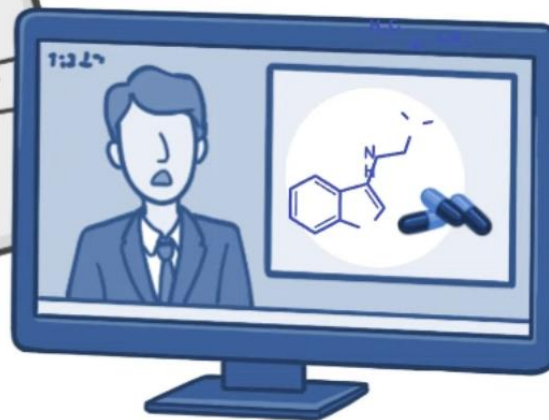
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* **PSYCHEDELICS** may have some therapeutic potential. However, there are some cautions to keep in mind.

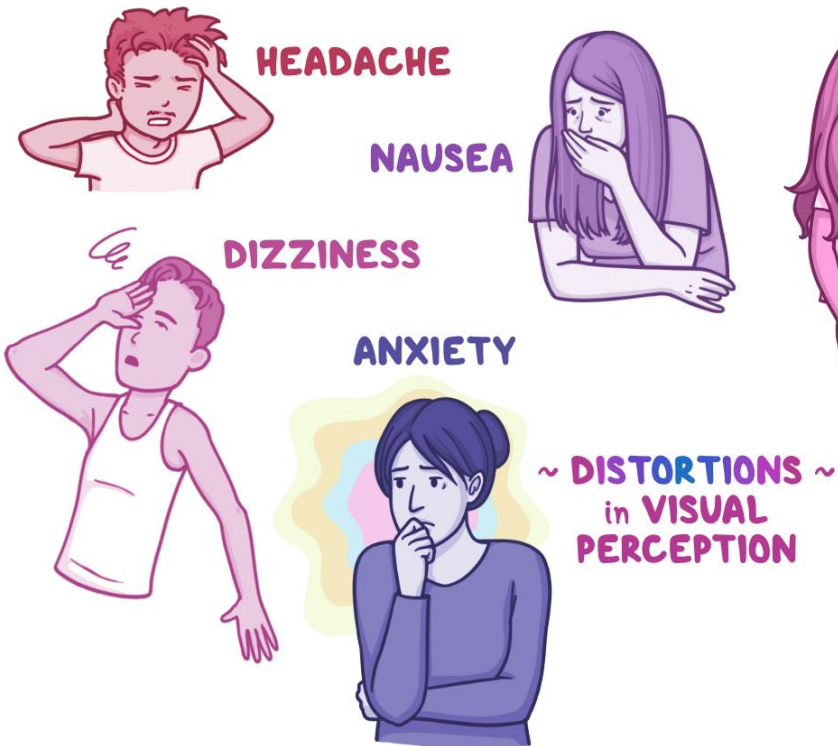




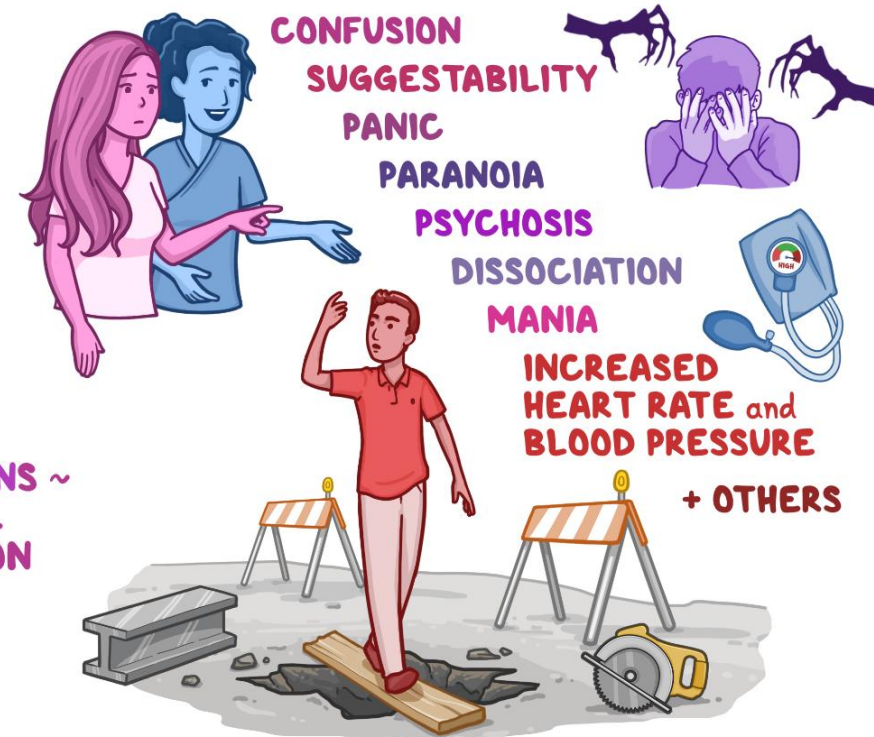
Research is
STILL ONGOING.
There is a lot that
we still have to learn!



MINOR ADVERSE EVENTS:



MAJOR ADVERSE EVENTS:





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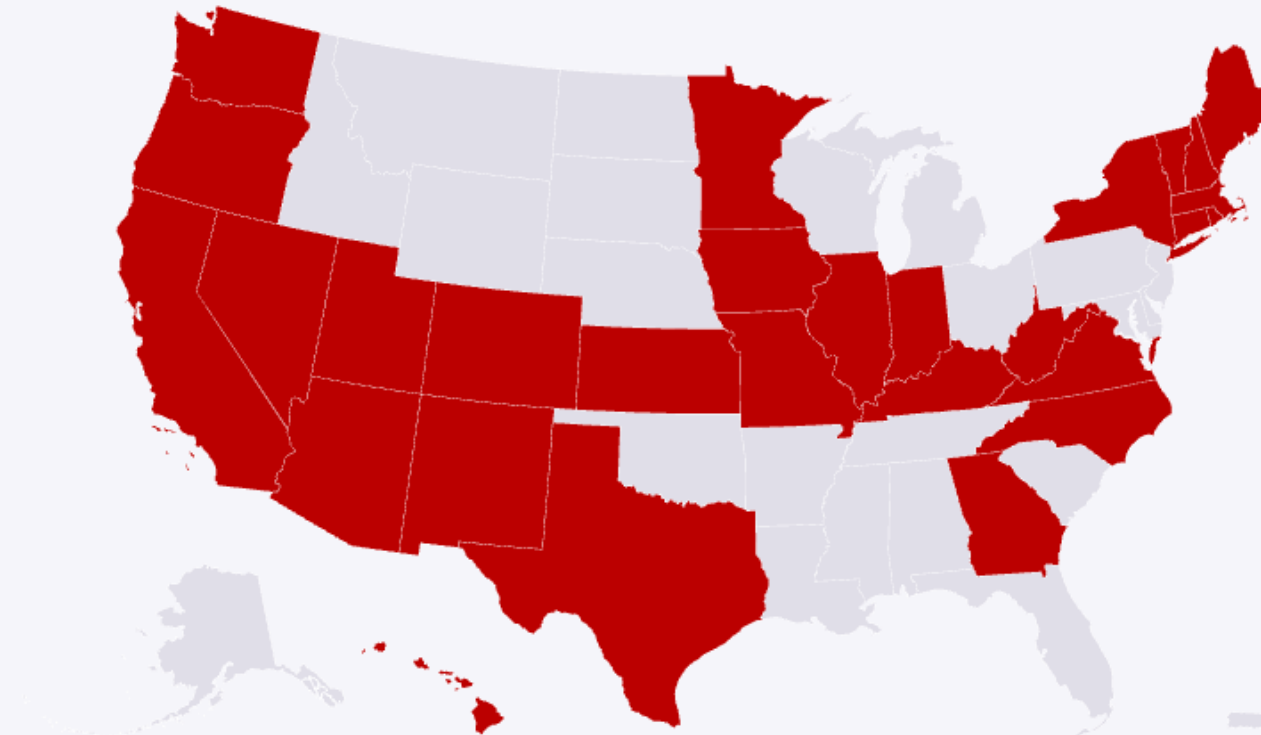
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State of Psychedelic Research in 2025



Psychedelics-Related Bills Introduced in 2025

States where lawmakers have introduced psychedelics-related bills so far in the current legislative session.



Via Psychedelic Alpha • Data as of April 2, 2025



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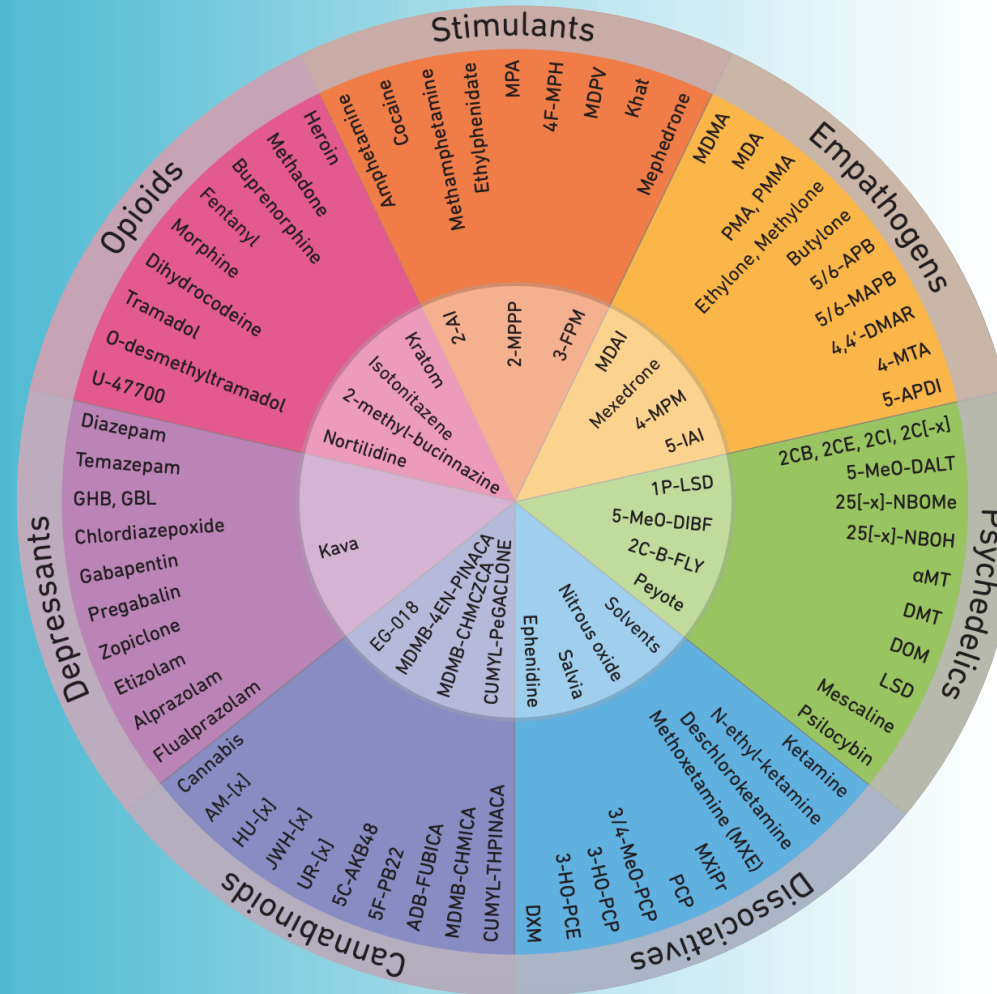
- Terminology
- Hype Cycle
- Substances
- Measures
- Outcomes
- Issues

'Psychedelics' – Both Broad and Narrow



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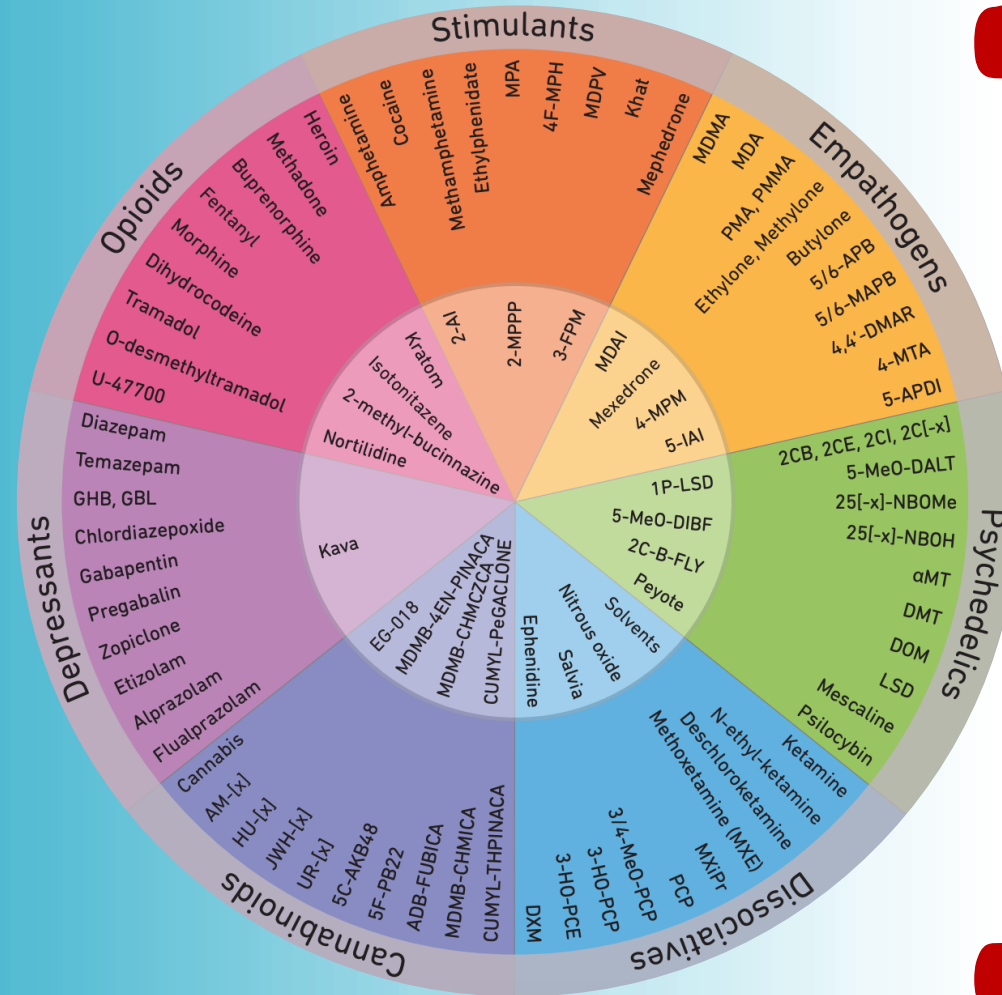
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'Psychedelics' – Both Broad and Narrow



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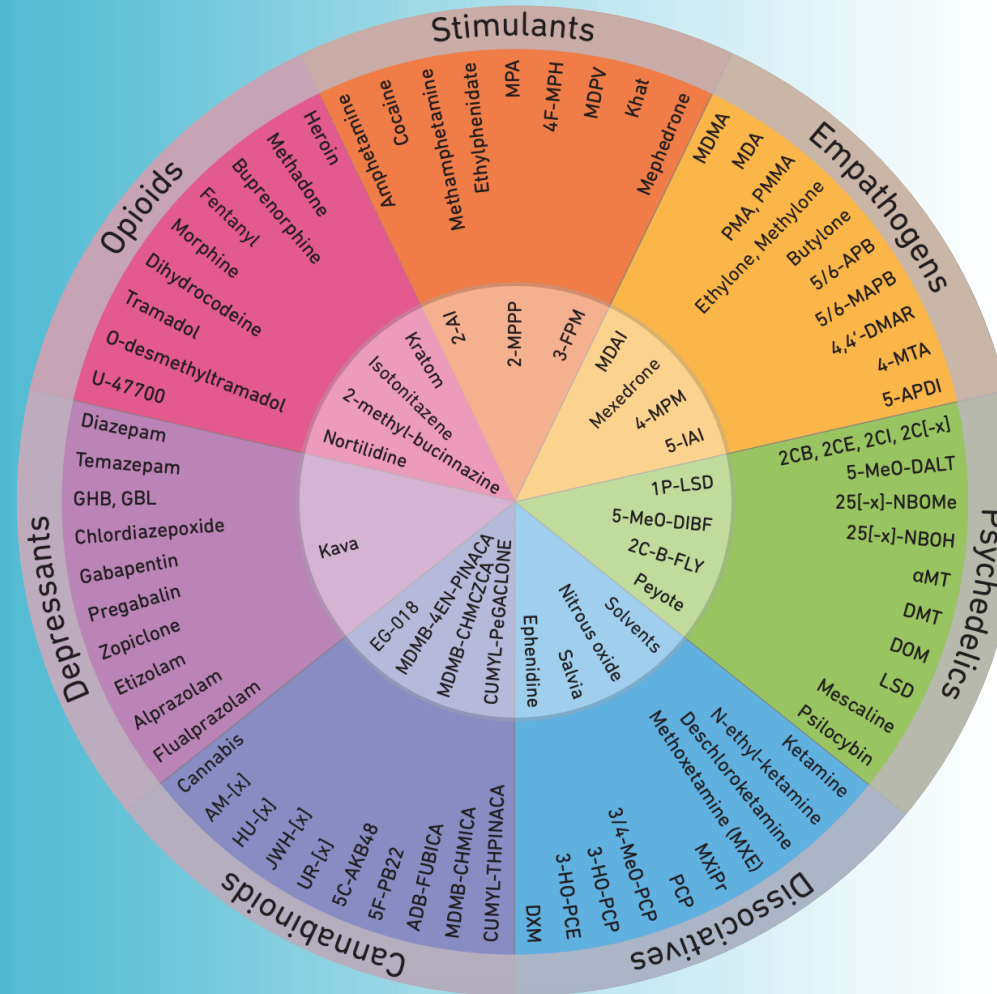
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'Psychedelics' – Both Broad and Narrow



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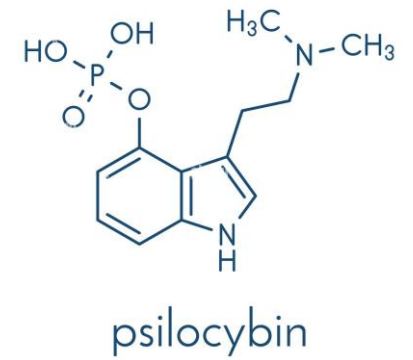
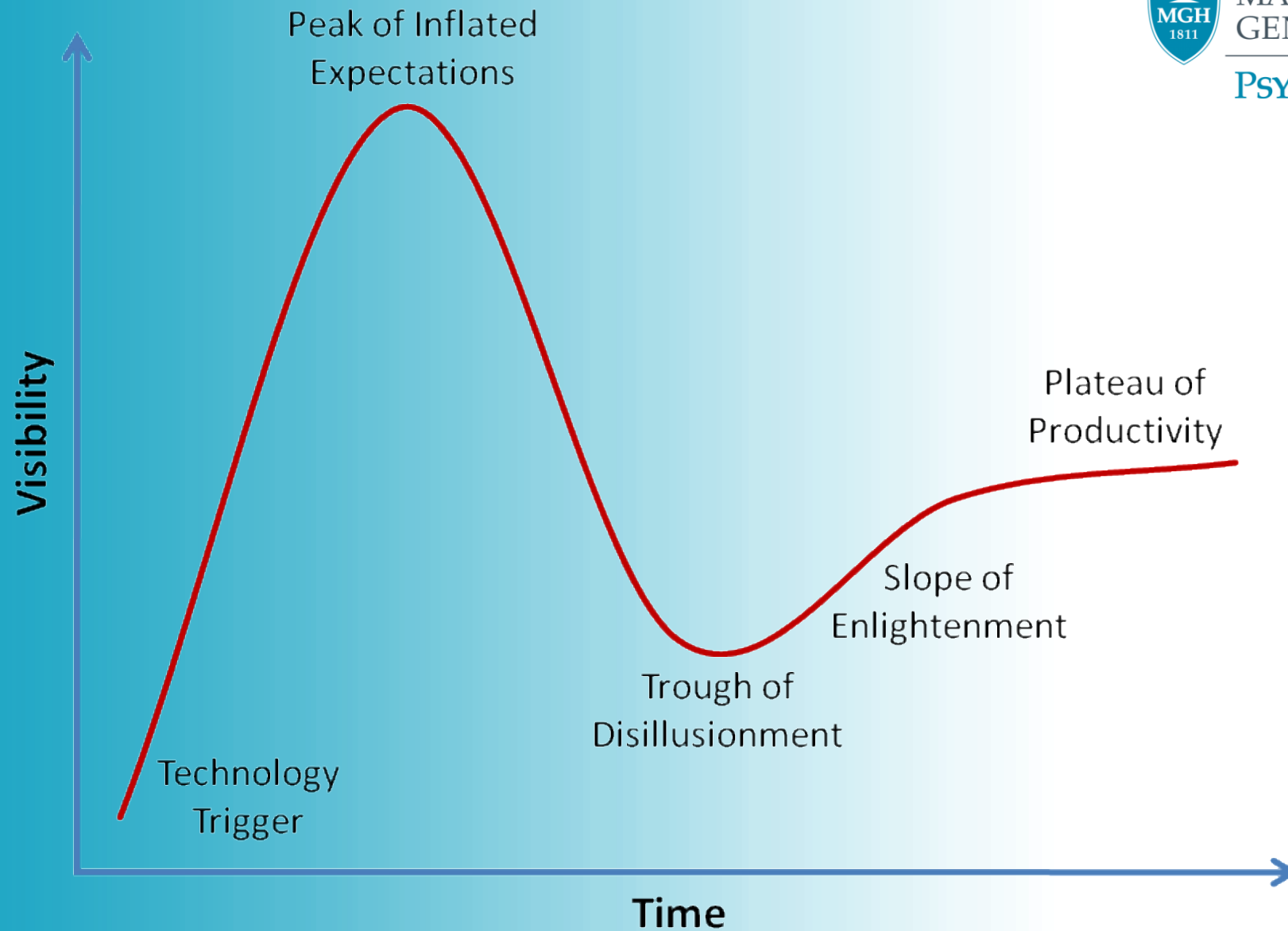
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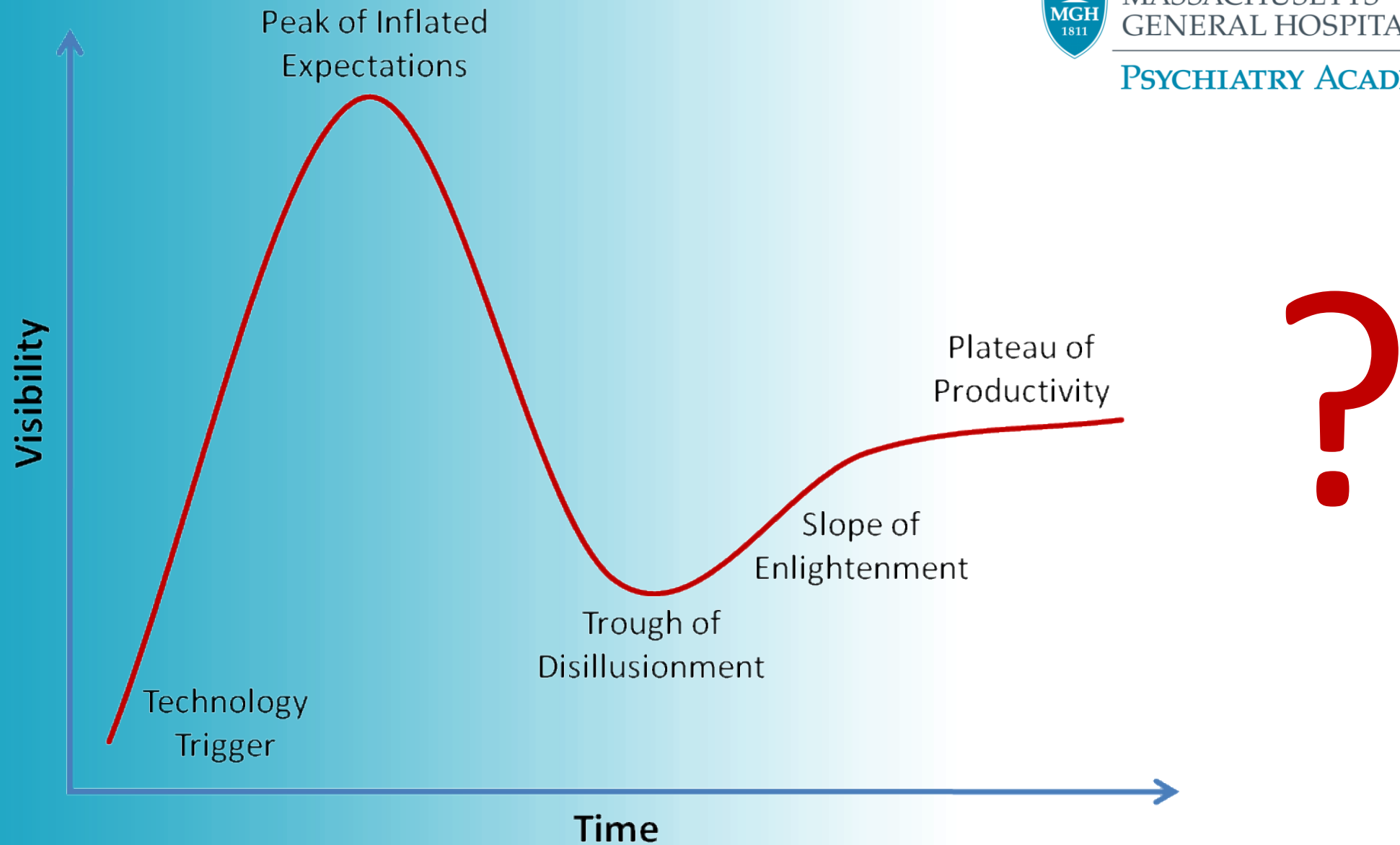


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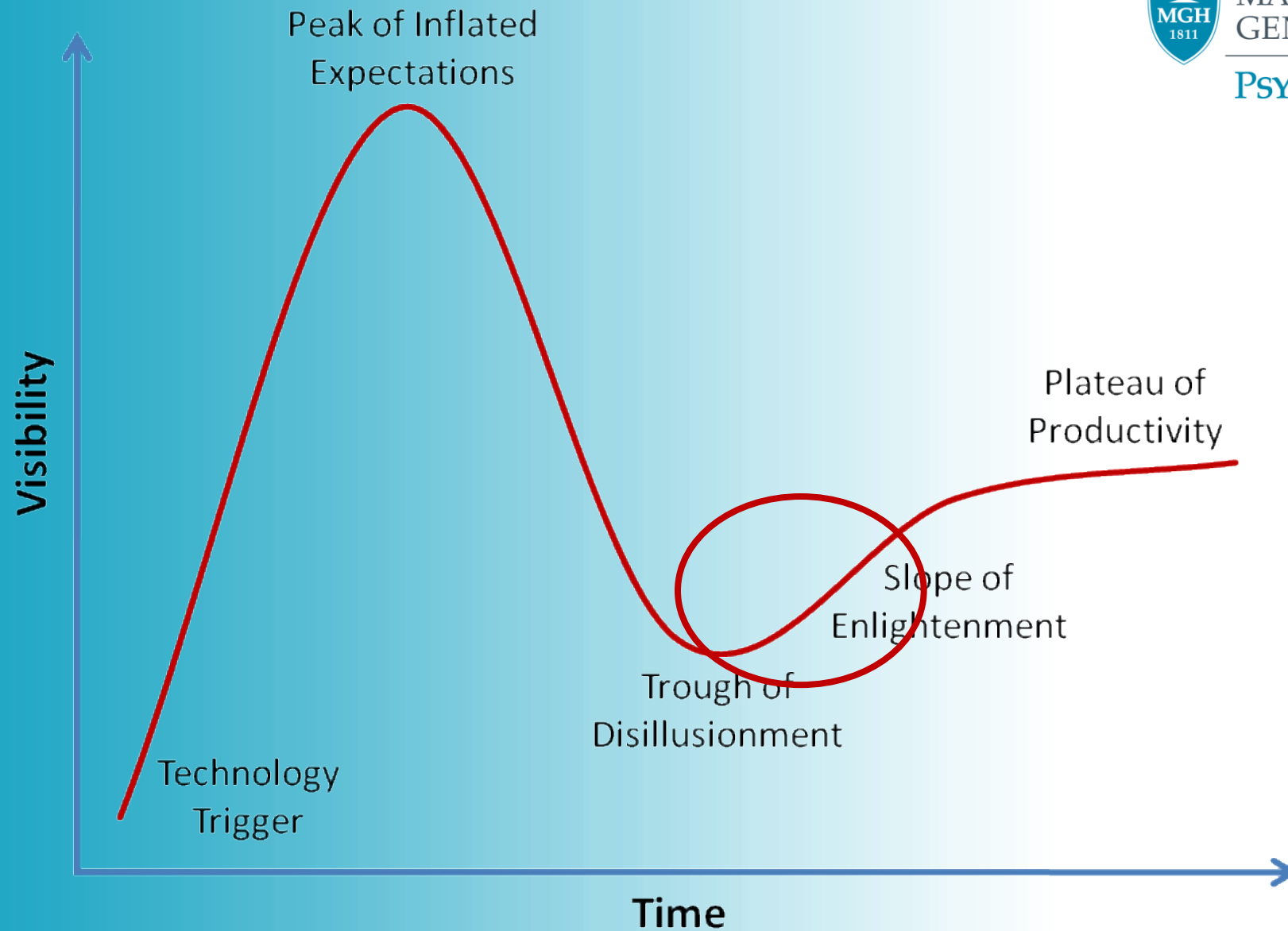


- Terminology
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- Issues





Yaden, Potash, & Griffiths, JAMA Psychiatry, 2022



Yaden, Potash, & Griffiths, JAMA Psychiatry, 2022



“The word *renaissance* comes from the French word for rebirth; however, this may be somewhat of a misnomer as it has been more than 2 decades since clinical psychedelic research resumed in the US. We believe this new era of psychedelic research is no longer being reborn but rather coming into maturity.”

Yaden, Yaden, & Griffiths, *JAMA Psychiatry*, 2021



“The word *renaissance* comes from the French word for rebirth; however, this may be somewhat of a misnomer as it has been more than 2 decades since clinical psychedelic research resumed in the US. We believe this new era of psychedelic research is no longer being reborn but rather **[should be]** coming into maturity.”

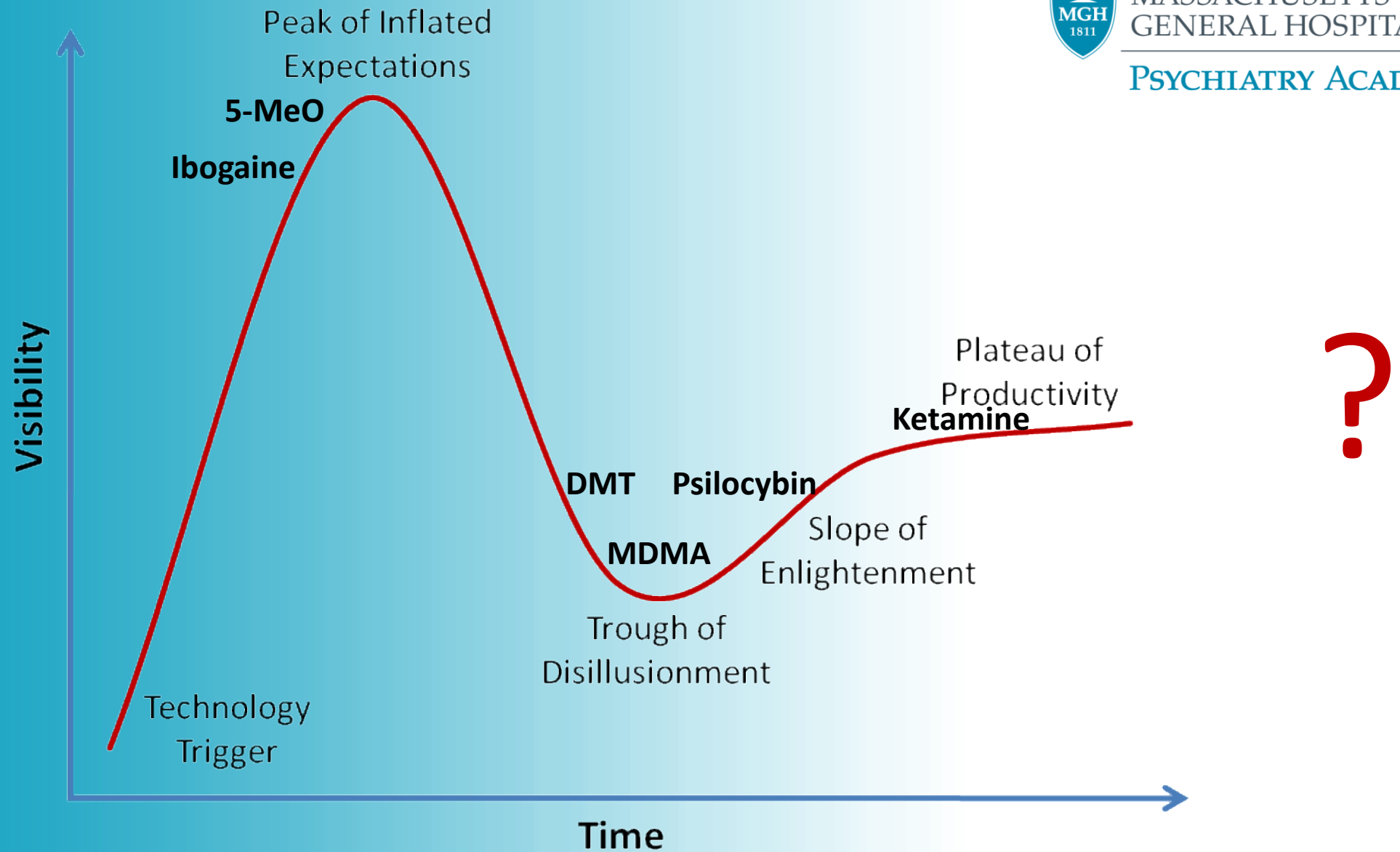
Yaden, Yaden, & Griffiths, *JAMA Psychiatry*, 2021



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Yaden, Potash, & Griffiths, JAMA Psychiatry, 2022



- Terminology
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Explanatory Level

Pharmacological Level



Neural Level



Psychological Level



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



Review article

Pharmacological, neural, and psychological mechanisms underlying psychedelics: A critical review

Michiel van Elk^{a,*}, David Bryce Yaden^b




^a Institute of Psychology, Leiden University, Wassenaarseweg 52, 2333 AK Leiden, the Netherlands

^b The Center for Psychedelic and Consciousness Research, Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, USA



Level of Analysis



Explanatory Level	Mechanism of Action
Pharmacological Level	 <p>Activation of 5HT_{2a}, Dopamine & TAAR-receptors (Nichols, 2004) Psychoplastogen model (Ly et al., 2018) Critical period for social reward learning (Nardou et al., 2019) Anti-inflammatory model (Nichols et al., 2017)</p>
Neural Level	 <p>CSCT model: Reduced thalamo-cortical filtering of internal and external information (Vollenweider & Geyer, 2001) REBUS model: Loosening of priors and increased bottom-up prediction error signaling (Carhart-Harris & Friston, 2019) CCC model: Disruption of the claustrum-cortical circuit resulting in network instability (Barrett et al., 2020)</p>
Psychological Level	 <p>Altered and Affective states: - Mystical Experience (Griffiths et al., 2006) - Feeling of Awe (Hendricks, 2018) - Ego Dissolution (Nour et al, 2016) - Enhanced perception of Emotions (Hartogsohn, 2018) Cognition: - Psychological Flexibility (Davis et al., 2020) - Cognitive Flexibility (Doss et al., 2020) - Creativity / Problem solving (Mason et al., 2021) - Mindfulness (Madsen et al., 2020) Beliefs: - Supernatural attributions & beliefs (Griffiths et al., 2019) - Metaphysical beliefs (Timmermanns, 2021) - Meaning (Hartogsohn, 2018) - Suggestibility (Carhart-Harris et al., 2015) Social: - Connectedness (Carhart-Harris et al., 2018) - Communitas (Kettner et al., 2021) - Empathy (Davis et al., 2020) Behavior: - Habit and behavior change (Teixeira et al., 2022)</p>

Explanatory Level	
Pharmacological Level 	
Neural Level 	
Psychological Level 	



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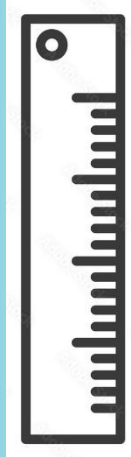
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Psychometric Measures



Clinically relevant acute subjective effects of psychedelics beyond mystical experience

David B. Yaden¹✉, Sean P. Goldy¹, Brandon Weiss¹ & Roland R. Griffiths^{1,2}

Yaden, Goldy, Weiss, & Griffiths, 2024, Nature Rev Psych

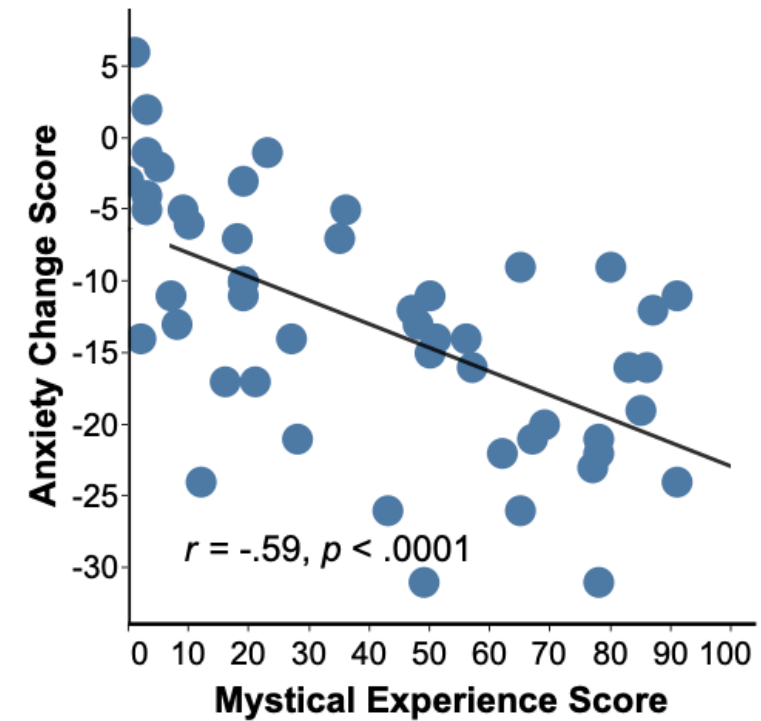
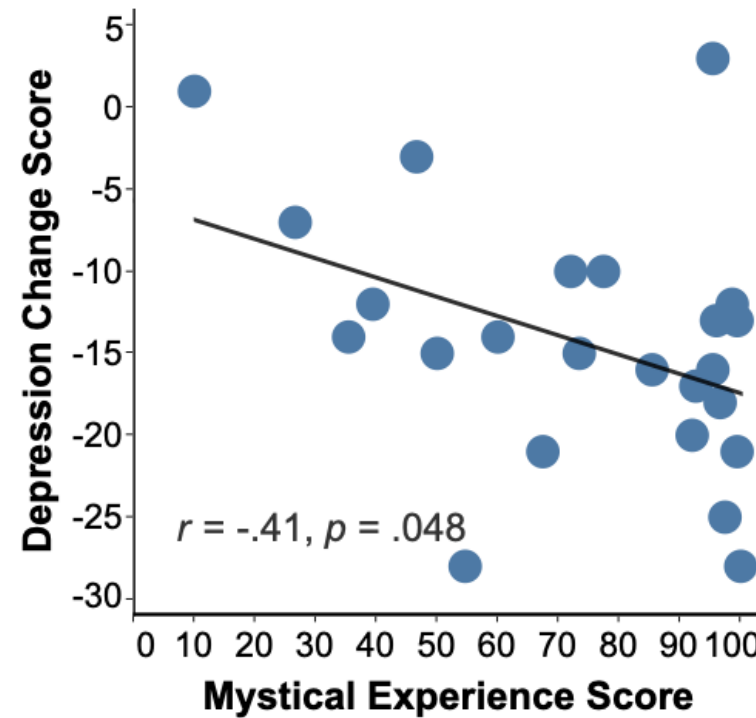
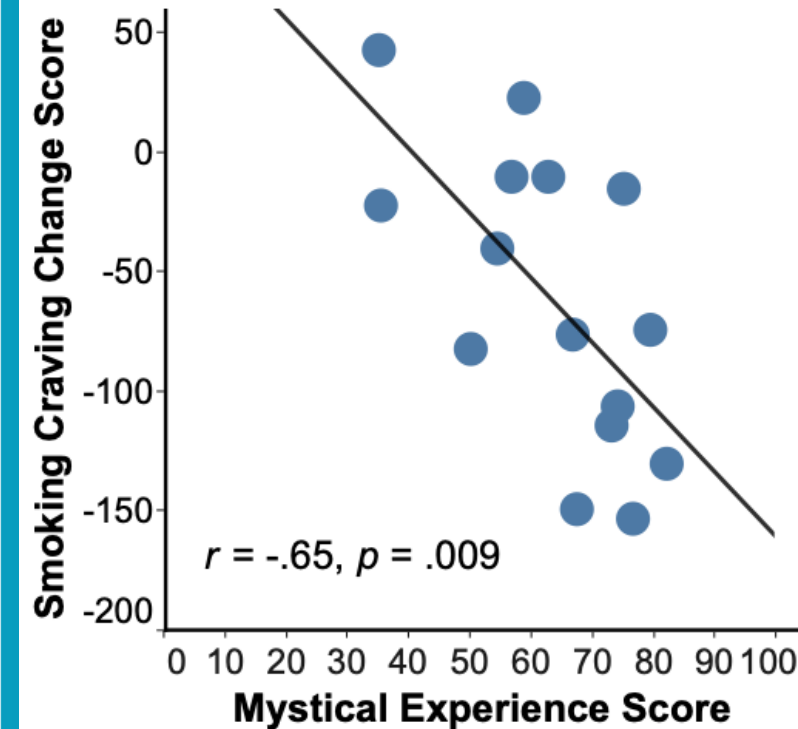
- Mystical Experience Questionnaire (MEQ; Barrett, Johnson, & Griffiths, 2015)
- Challenging Experience Questionnaire (Barrett et al., 2016)



Instrument	Acronym	Factors	Reliabilities	Validity	Author(s)
Mystical Experience Questionnaire	MEQ	1. Mystical 2. Positive Mood 3. Time and Space 4. Ineffability			MacLean et al., 2012; Barrett et al., 2015
Challenging Experience Questionnaire	CEQ	1. Grief 2. Fear 3. Death 4. Insanity 5. Isolation 6. Physical distress 7. Paranoia			Barrett et al., 2016



Mystical Experience on Sessions Days Predicts Later Therapeutic Outcomes



Yaden & Griffiths, *ACS*, 2020

Five Dimensional/ Eleven Factor Altered States of Consciousness (5-DASC; Dittrich, 1998; Studerus et al., 2010)



Instrument	Acronym	Factors	Reliabilities	Validity	Author(s)
Five-Dimensional Altered State of Consciousness	5D-ASC	1. Oceanic Boundlessness 2. Anxious ego dissolution 3. Visionary Restructuralization 4. Auditory alterations 5. Reduction of vigilance			Dittrich et al., 2010
Eleven-Dimensional Altered State of Consciousness	11D-ASC	1. Experience of Unity 2. Spiritual Experience 3. Blissful State 4. Insightfulness 5. Disembodiment 6. Impaired Control and Cognition 7. Anxiety 8. Complex Imagery 9. Elementary Imagery 10. Audio-Visual Synesthesia 11. Changed Meaning of Percepts			Studerus et al., 2010

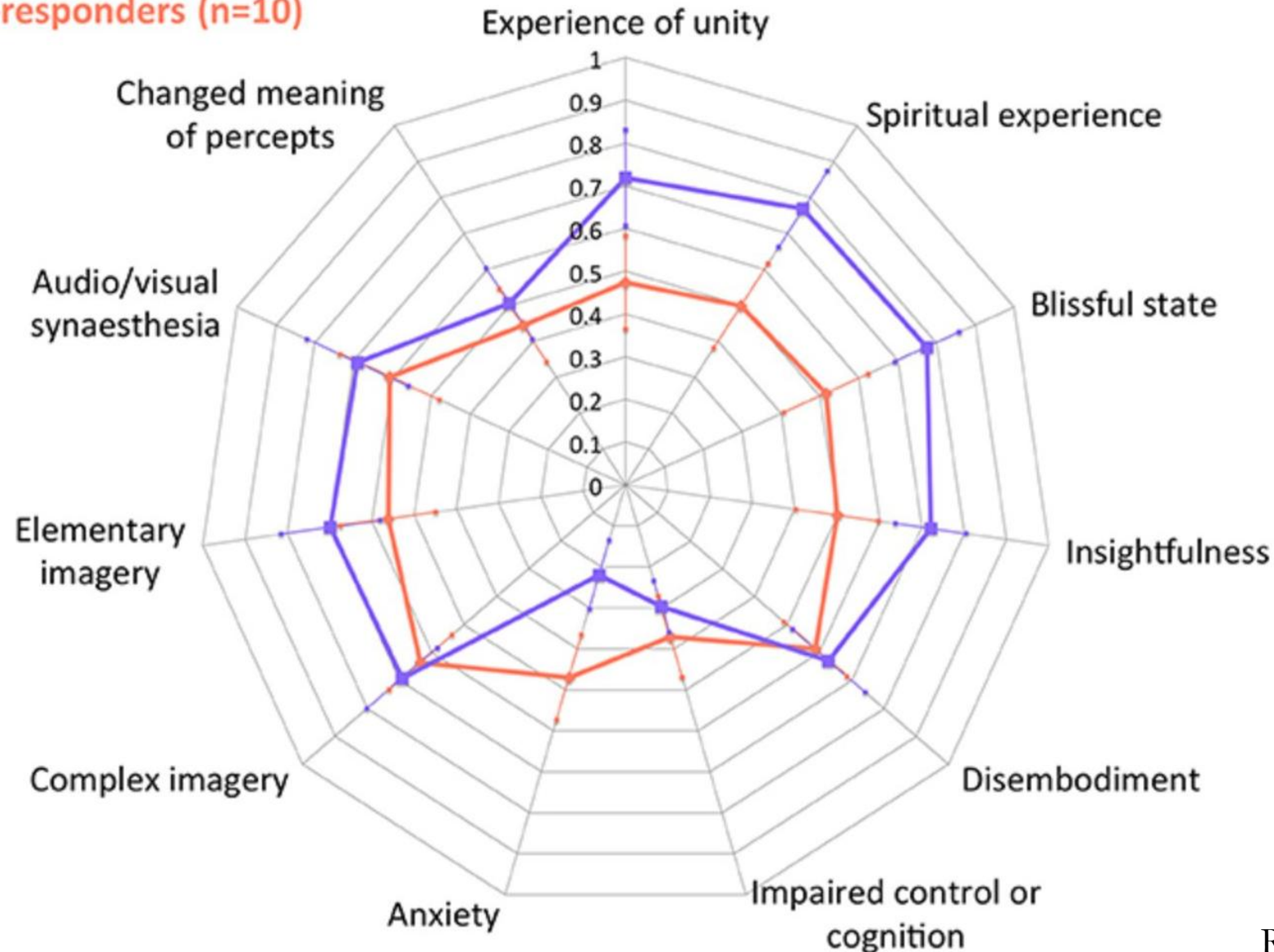
Responders (n=9)

Non-responders (n=10)



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Roseman, Nutt, & Carhart-Harris, 2018

Ego Dissolution Inventory (EDI; Nour, Evans, Nutt, & Carhart-Harris, 2016)

Emotional Breakthrough Inventory (EBI; Roseman et al., 2019)



Instrument	Acronym	Factors	Reliabilities	Validity	Author(s)
Ego Dissolution Inventory	EDI	1. Ego Dissolution 2. Ego Inflation			Nour et al., 2016
Emotional Breakthrough Inventory	EBI				Roseman et al., 2019



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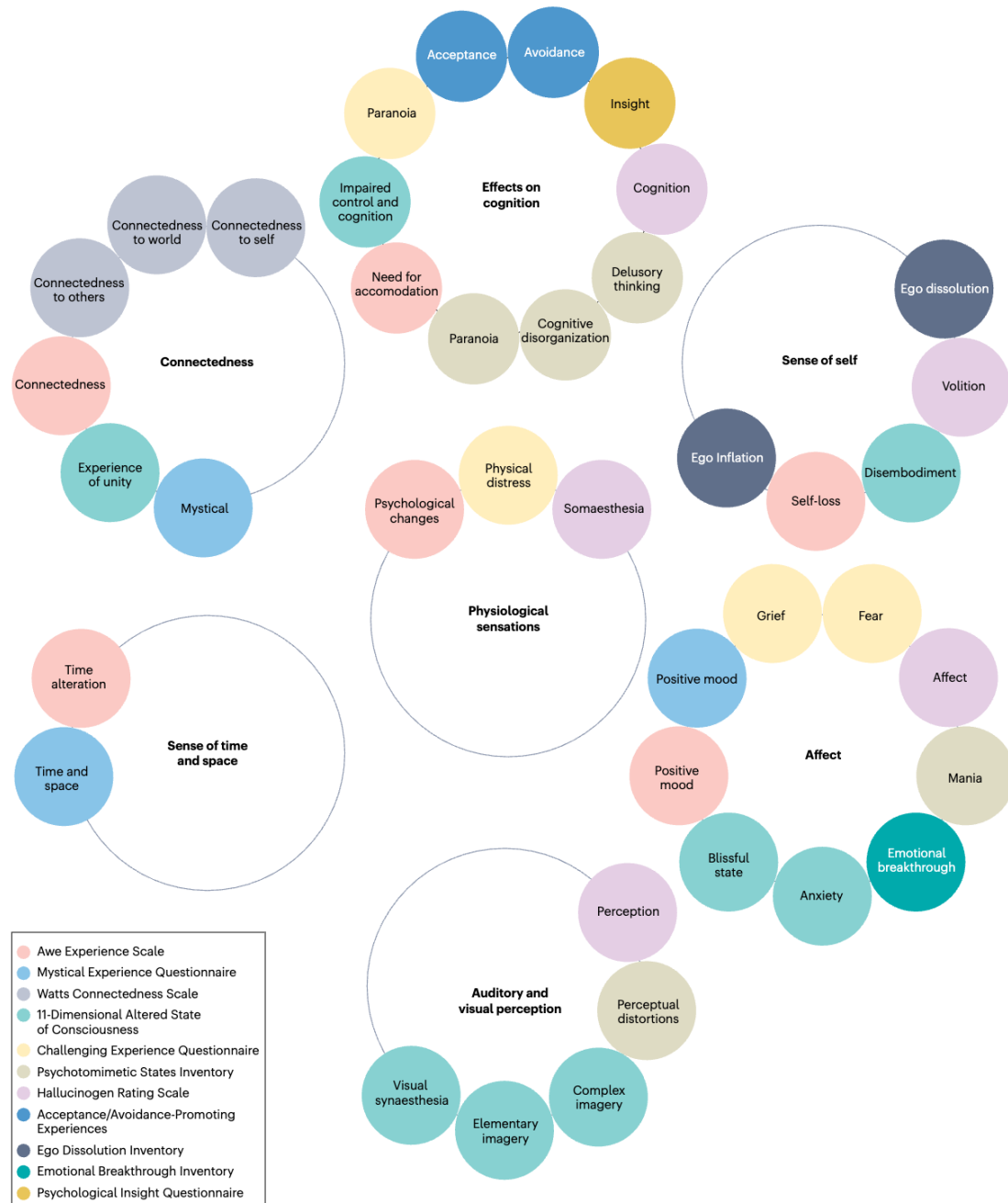
Mystical and Other Alterations in Sense of Self: An Expanded Framework for Studying Nonordinary Experiences

Ann Taves 

Department of Religious Studies, University of California, Santa Barbara

“To better understand the nature and effects of unusual experiences, such as alterations in the sense of self, we need self-report measures that distinguish between generically worded experiences and the way they are appraised in terms of valence, significance, cause, and long-term effects in different contexts.”

Taves, Psychological Science, 2019



Yaden, Goldy, Weiss, & Griffiths, 2024, Nature Rev Psych

Clinically relevant acute subjective effects of psychedelics beyond mystical experience

David B. Yaden¹✉, Sean P. Goldy¹, Brandon Weiss¹ & Roland R. Griffiths^{1,2}

“We discuss how to balance the **limitations of existing measures** with methodological advances in practice and elaborate on well-known methods and other psychological processes that can help inform the creation of new measures. We suggest actionable recommendations for how the field can transcend current conceptualizations and provide guidance on best practices until the **next generation of measures** is validated.”

Yaden, Goldy, Weiss, & Griffiths, 2024, Nature Rev Psych



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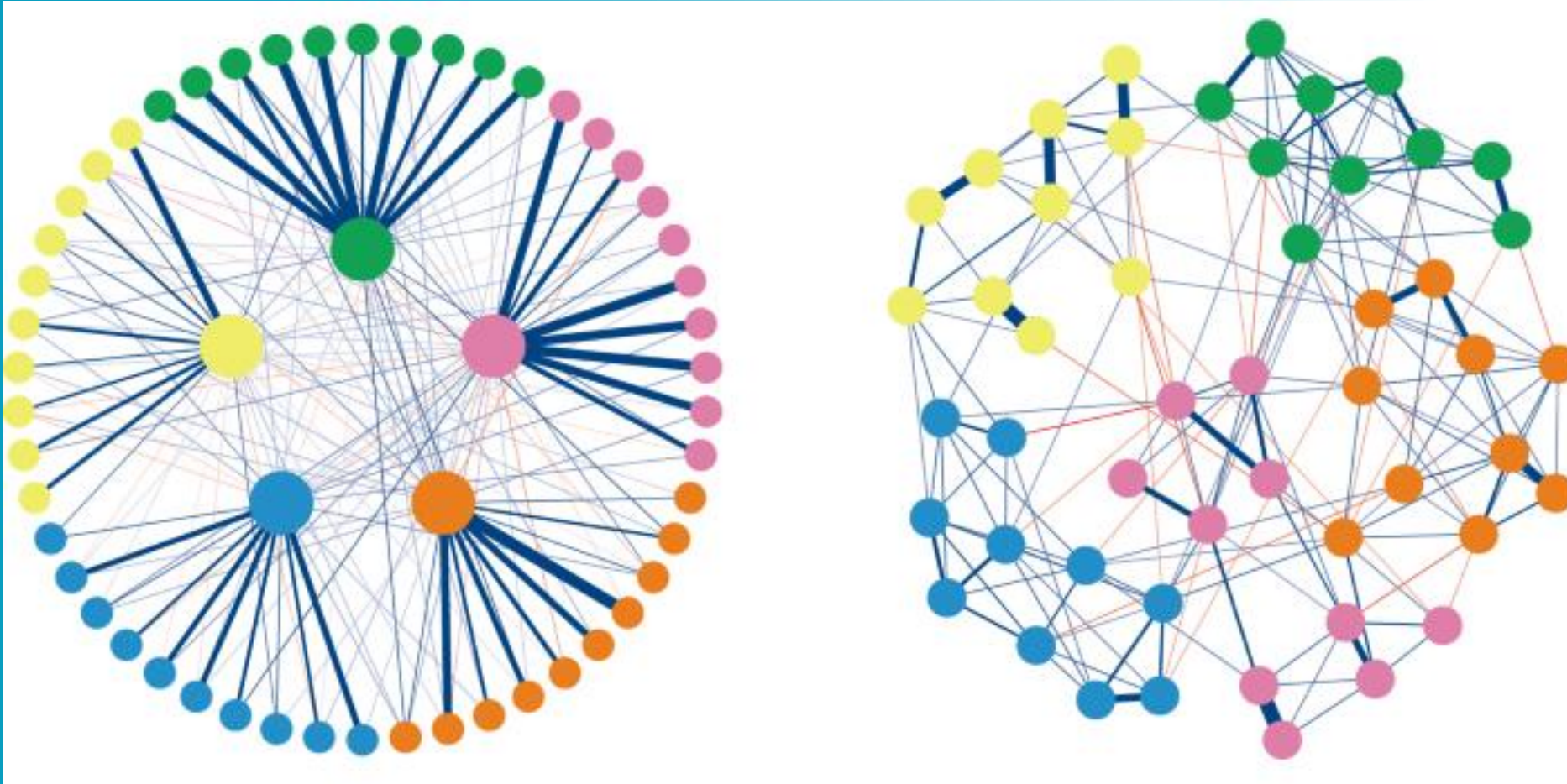
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THE NEXT GENERATION





Quantitative: Large-Scale Factor Analysis and Network Analysis



Yaden, Goldy, Weiss, & Griffiths, 2024, Nature Reviews Psychology

Qualitative: Cognitive Interviewing



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PSYCHIATRY ACADEMY

Probe	Description	Example
Paraphrase	Participant restates the entire item in their own words to help the researcher understand if it is understood as intended	In your own words, what do you think this item means?

Wolf et al., 2023, PsyArXiv (pre-print)



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HEALTH CARE
ACADEMY



Graziosi et al., 2023, Journal of Psychoactive Drugs

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W.E.I.R.D.

Henrich, Heine, & Norenzayan, 2010, Behavioral and Brain Sciences

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Acute Subjective Effects of Psychedelics within and Beyond WEIRD Contexts

Marianna Graziosi M.A. ^{a,b}, Manvir Singh Ph.D.^c, Sandeep M. Nayak Ph.D.^b, and David B. Yaden Ph.D.^b

^aDepartment of Clinical Psychology, Hofstra University, Hempstead, NY, USA; ^bCenter for Consciousness and Psychedelic Research, Johns Hopkins University, Baltimore, MD, USA; ^cUniversity of California, Davis, CA, USA



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Graziosi et al., 2023, Journal of Psychoactive Drugs

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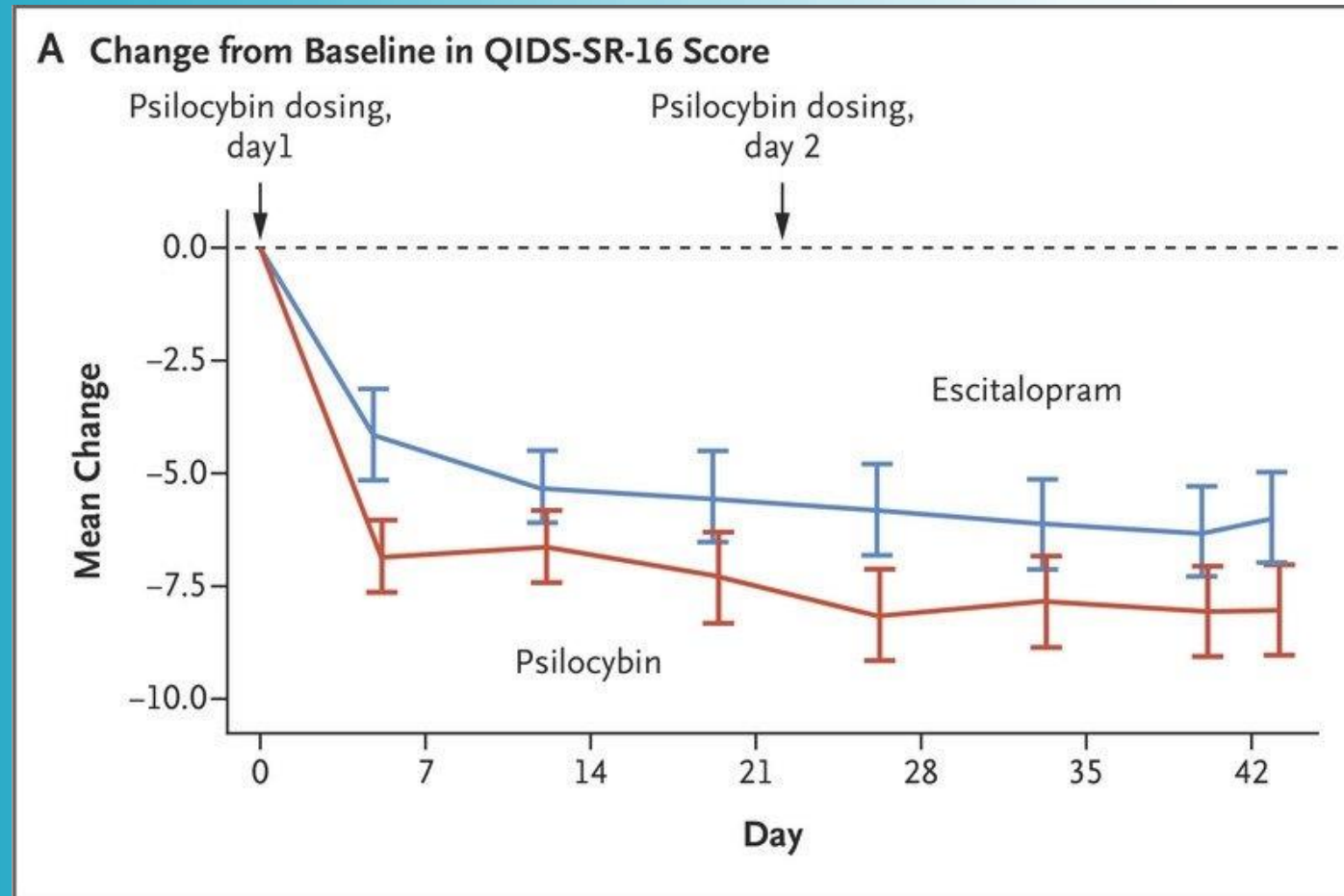
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Depression – Psilocybin vs. SSRI



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Carhart-Harris et al., 2021, NEJM

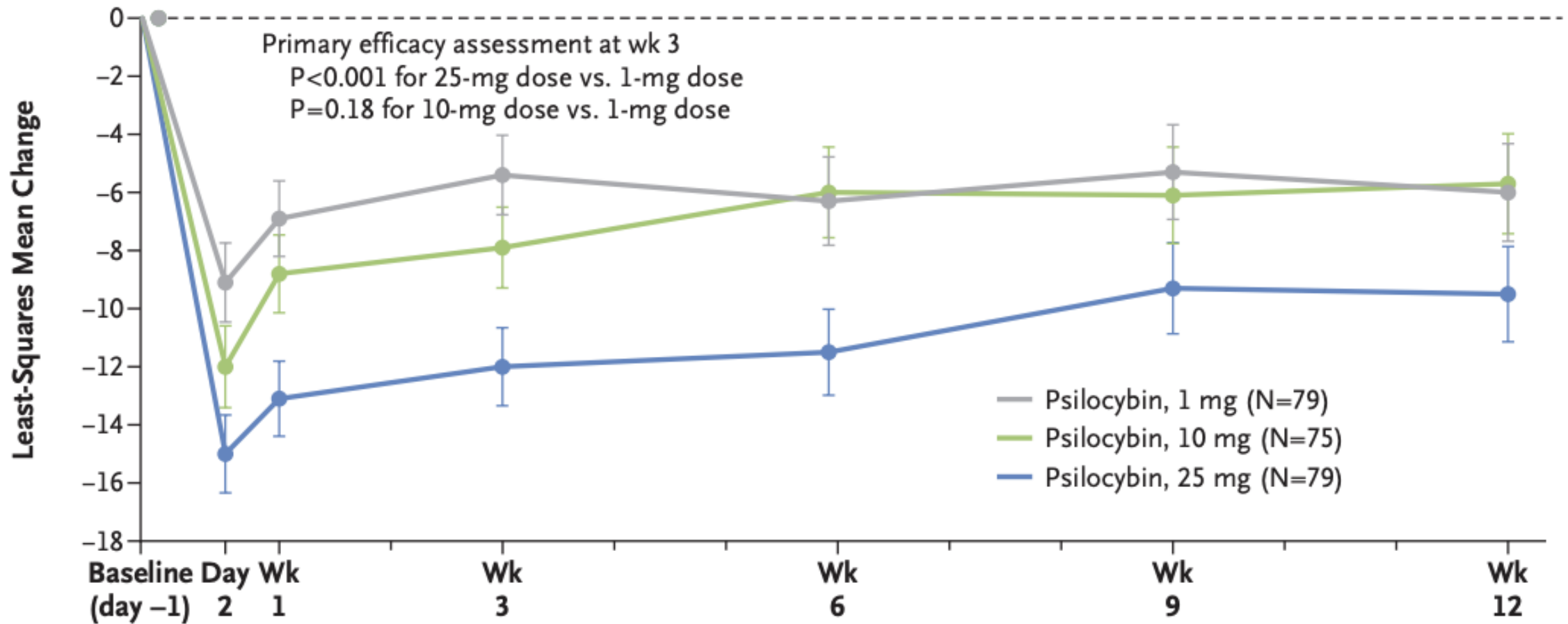
N = 59

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

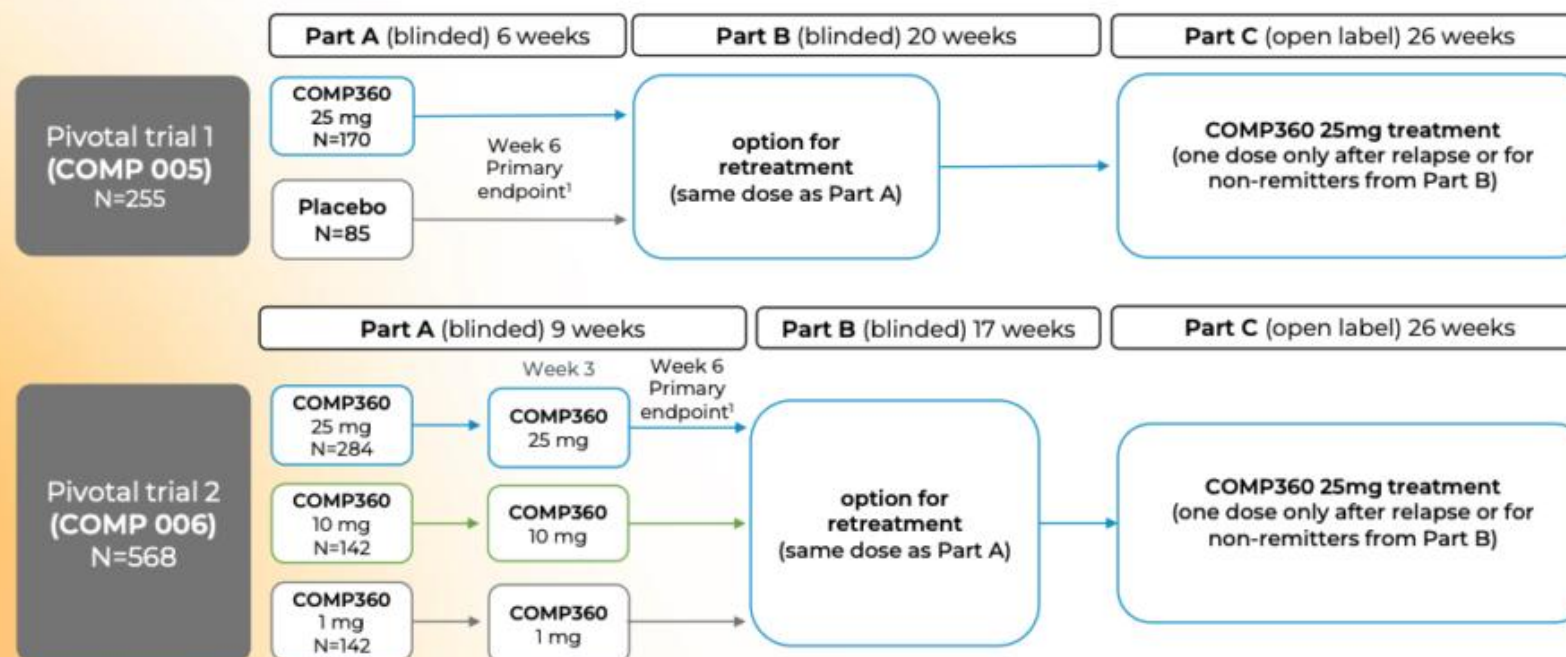


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Phase 3 program: Overview of pivotal trial designs

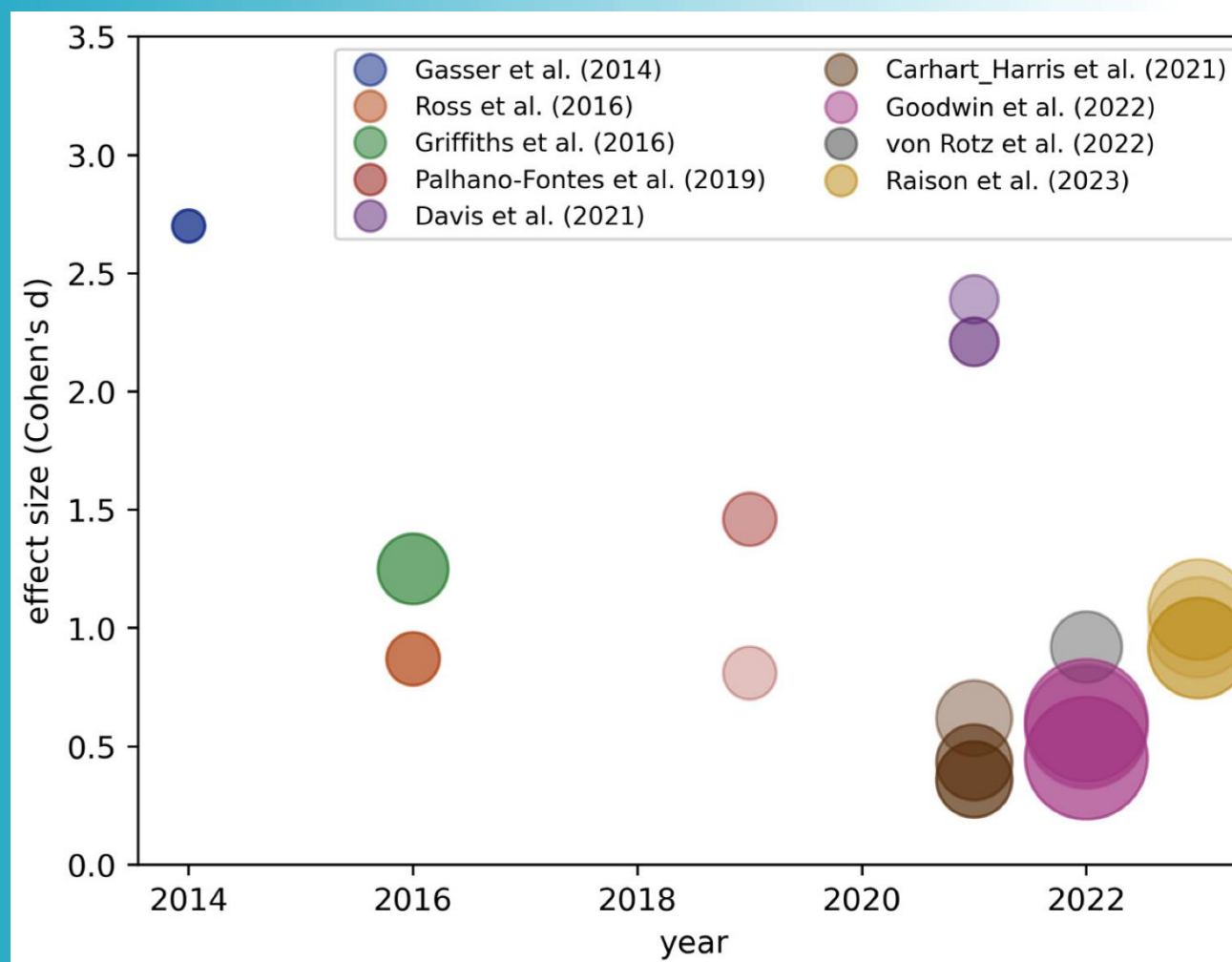


The participant population (TRD definition and core inclusion/exclusion criteria) remains unchanged compared to Phase 2b

1. Primary endpoint = change from baseline in MADRS total score at Week 6. 2. Remitters are defined as patients with MADRS total score ≤ 12 and no single item ≥ 4 . Note that it can take several weeks to organise a dosing session for non-remitters from Part A or Part B so re-dosing does not necessarily happen immediately at the start of Part B or Part C, respectively.

6 | © Compass Pathways





Adverse Events in Studies of Classic Psychedelics

A Systematic Review and Meta-Analysis



Key Points

Question What is the nature, frequency, and severity of adverse events (AEs) reported in studies of classic psychedelic administration in monitored clinical or research settings?

Findings Reports of serious AEs (SAEs) and nonserious AEs (NSAEs) requiring medical or psychiatric attention in classic psychedelic research were rare. In this systematic review and meta-analysis of 3504 participants from 114 studies, SAEs were reported for no healthy participants and approximately 4% of participants with preexisting neuropsychiatric disorders; however, for most studies, there was concern for underdetection or incomplete AE reporting.



Table 3. Adverse Events Reported on Day 1, from Day 2 up to Week 3, and after Week 3 up to Week 12 (Safety Population).^a

Adverse Event	Psilocybin, 25 mg (N = 79)	Psilocybin, 10 mg (N = 75)	Psilocybin, 1 mg (N = 79)
	number (percent)		
Day 1			
Any adverse event	48 (61)	35 (47)	30 (38)
Any severe adverse event	3 (4)	6 (8)	1 (1)
Adverse events occurring in ≥5% of participants in any group			
Headache	19 (24)	11 (15)	13 (16)
Nausea	17 (22)	5 (7)	1 (1)
Euphoric mood	4 (5)	5 (7)	3 (4)
Fatigue	5 (6)	2 (3)	4 (5)
Insomnia	2 (3)	3 (4)	5 (6)
Anxiety	3 (4)	6 (8)	0
Mood altered	4 (5)	3 (4)	0
Dizziness	5 (6)	1 (1)	0
Paresthesia	2 (3)	4 (5)	0
Abnormal thinking	0	4 (5)	0
Any serious adverse event	0	0	0
Day 2 up to wk 3			
Any adverse event	44 (56)	36 (48)	35 (44)
Any severe adverse event	7 (9)	5 (7)	1 (1)
Adverse events occurring in ≥5% of participants in any group			
Headache	9 (11)	5 (7)	9 (11)
Insomnia	4 (5)	5 (7)	8 (10)
Anxiety	4 (5)	6 (8)	3 (4)
Fatigue	6 (8)	2 (3)	3 (4)
Suicidal ideation	5 (6)	4 (5)	2 (3)
Depression	3 (4)	3 (4)	4 (5)
Mood altered	4 (5)	0	1 (1)
Any serious adverse event	4 (5)	4 (5)	0
Suicidal ideation	2 (3)	2 (3)	0
Intentional self-injury	2 (3)	1 (1)	0
Hospitalization	0	1 (1)	0
After wk 3 up to wk 12			
Any adverse event	23 (29)	24 (32)	24 (30)
Any severe adverse event	2 (3)	3 (4)	0
Adverse events occurring in ≥5% of participants in any group			
Headache	3 (4)	2 (3)	6 (8)
Any serious adverse event	4 (5)	3 (4)	1 (1)
Suicidal behavior	3 (4)	0	0
Intentional self-injury	0	1 (1)	1 (1)
Adjustment disorder with anxiety and depressed mood	1 (1)	0	0
Depression	0	1 (1)	0
Drug withdrawal syndrome†	1 (1)	0	0
Suicidal ideation	0	1 (1)	0

Table 3. Adverse Events Reported on Day 1, from Day 2 up to Week 3, and after Week 3 up to Week 12 (Safety Population).*

Adverse Event	Psilocybin, 25 mg (N = 79)	Psilocybin, 10 mg (N = 75)	Psilocybin, 1 mg (N = 79)
Any severe adverse event	2 (3)	3 (4)	0
Adverse events occurring in $\geq 5\%$ of participants in any group			
Headache	3 (4)	2 (3)	6 (8)
Any serious adverse event	4 (5)	3 (4)	1 (1)
Suicidal behavior	3 (4)	0	0
Intentional self-injury	0	1 (1)	1 (1)
Adjustment disorder with anxiety and de- pressed mood	1 (1)	0	0
Depression	0	1 (1)	0
Drug withdrawal syndrome†	1 (1)	0	0
Suicidal ideation	0	1 (1)	0

Goodwin et al., 2022, NEJM



Adverse Events Should Not Be Surprising in Psychedelic Research

Rebecca Ehrenkranz,^{1,*} Manish Agrawal,² Sandeep M. Nayak,¹ and David B. Yaden¹

Abstract

Research has demonstrated both risks and benefits to using psychedelics as a therapeutic intervention for a variety of mental health conditions. In recent years, the public discourse around psychedelic treatments has been largely positive and focused on benefits more than risks. We believe the field would benefit from more balanced attention to the risks as well as benefits of psychedelics within the scientific community and broader public. Coverage of psychedelic science has swung between a pendulum of extremes,



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History repeating: guidelines to address common problems in psychedelic science



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- 1. Valid Inferences:** Conclusions supported by data?
- 2. Conflicts of interest:** Are the relevant COIs reported?
- 3. Safety and adverse events:** Are adverse events transparently reported?
- 4. Control group:** Is a comparison group included?
- 5. Sample size:** Is the study sufficiently powered (large enough)?
- 6. Selection bias:** Is the sample generalizable?
- 7. Study duration:** Was there a sufficiently lengthy follow-up?
- 8. Breaking blind problem:** Has functional unblinding been measured?
- 9. Placebo effects:** Have participant expectations measured?
- 10. Mechanisms of action:** Are speculations about mechanisms warranted?

van Elk & Fried, 2023, Therapeutic Advances in Psychopharmacology



Psychedelic Randomized Controlled Trial (RCT) Process and Problems



Aday et al., 2022, Psychopharmacology



Study Design

- Use 3-arm and/or sequential parallel designs to isolate placebo effects
- Consider pragmatic clinical trials and natural experiments as alternatives to RCTs
- Use active placebos with psychoactive effects



Psychedelic Randomized Controlled Trial (RCT) Process and Problems



Psychedelic Randomized Controlled Trial (RCT) Process and Problems

Recruitment & Enrollment

- Exclude participants with previous history of use with psychedelics and/or the active placebo
- Manage participant expectations by maintaining neutral tone and uncertainty regarding treatment efficacy in recruitment materials
- Incomplete disclosure may be used regarding number of treatment arm conditions



Psychedelic Randomized Controlled Trial (RCT) Process and Problems

Preparation

- List treatment and active placebo drug effects together unspecified, and explain drug effects neutrally
- Consider incomplete disclosure regarding the number of treatment arm conditions
- Note to participants that there is significant variability in drug intensity between individuals
- Measure participant expectations prior to dosing

Aday et al., 2022, Psychopharmacology



Psychedelic Randomized Controlled Trial (RCT) Process and Problems

Dosing

- Use single dose administration design
- Measure participant and clinician guess regarding treatment arm allocation after dosing



Integration

- Maintain neutrality regarding treatment arm guess when interacting with participants



Psychedelic Randomized Controlled Trial (RCT) Process and Problems



Statistical Analyses

- Examine associations between expectations and masking with treatment outcomes
- Evaluate and report treatment expectations and masking success
- Compare effect sizes against “placebo benchmark”



Psychedelic Randomized Controlled Trial (RCT) Process and Problems



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?





Conclusion

“We owe it to the next generation of researchers and clinicians, and the millions of patients with mood and substance use disorders who may benefit from these treatments, to ensure that no exceptions be made in the standards of research or clinical application for psychedelics, regardless of their seemingly exceptional potential.”

Yaden, Yaden, & Griffiths, JAMA Psychiatry, 2021



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* **PSYCHEDELICS** may have some therapeutic potential. However, there are some cautions to keep in mind.



Thank you!



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PSYCHIATRY ACADEMY

- Postdoctoral Research Fellowships
- Research Program Coordinators
- Collaborations

www.HopkinsPsychedelic.org
www.YadenLab.com



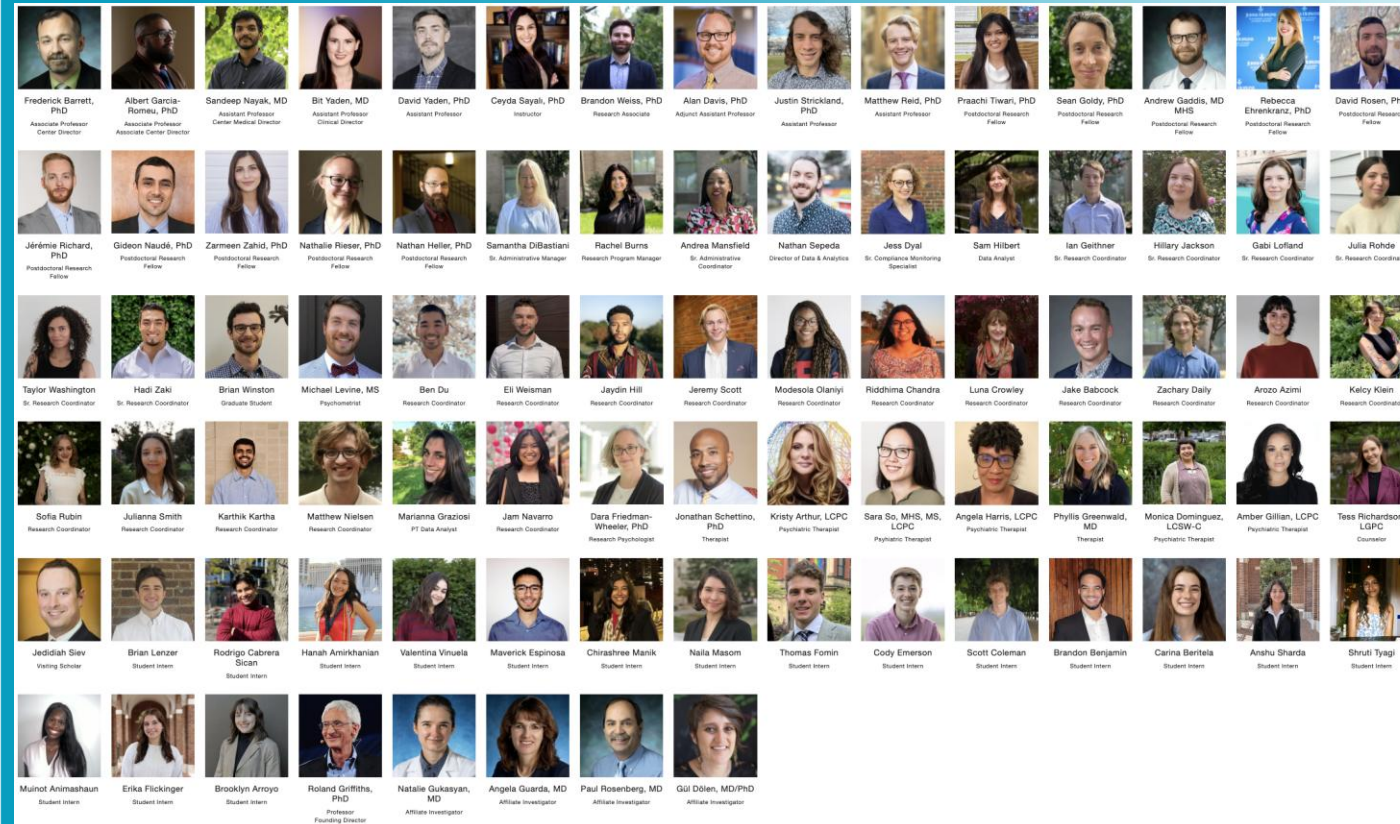
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