

# Challenges in Integration and Integrated Care

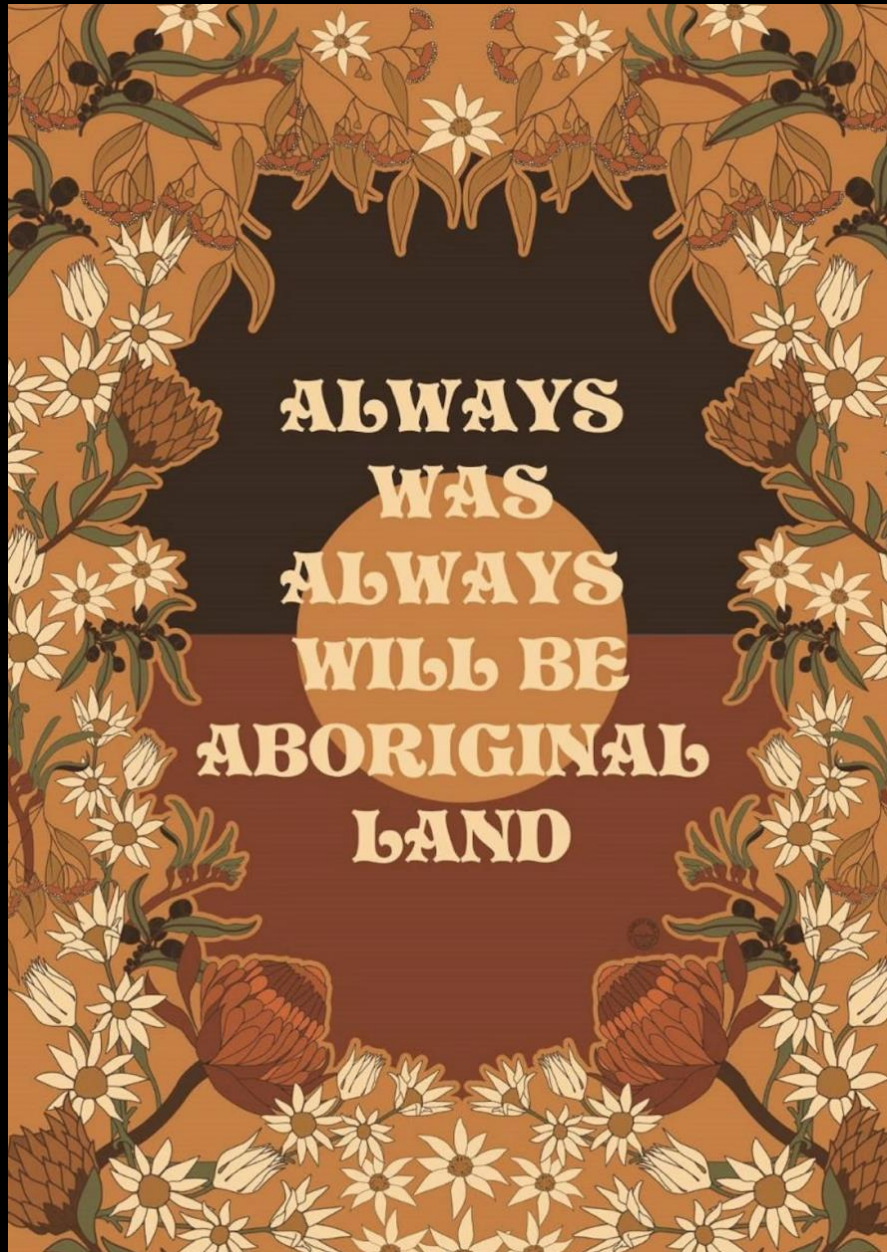
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**easternhealth**



The work I am presenting was conducted on the lands of the Wurundjeri people of the Kulin nation.

I wish to acknowledge them as the Traditional Owners, and to pay my respects to their Elders, past and present.

This land was never ceded.

image credit to @harleyandj

# Disclosures, disclaimers & perspectives

- Addiction psychiatrist & researcher
- Supported by a NHMRC Emerging Leader fellowship (GNT2008173) in methamphetamine use and trauma/PTSD
- CI and site PI on a MRFF-sponsored multisite study of MDMA for PTSD/ Alcohol Use Disorder (MPATHY)
- CI on an Eastern Health Foundation grant on the PANDA pilot study- Psilocybin assisted treatment for Alcohol and Depression
- Member of the RANZCP Psychedelic Assisted Therapy Steering Committee

**background**  
integrated care  
psychedelics & PAT  
**context**  
Australian implementation  
**research**  
evidence base  
safety  
gaps  
**unanswered questions**  
**& challenges**

# background




# Integrated care

- Over **2 in 3** service users in AOD settings have a previous MH diagnosis; nearly **1 in 2** people seeking care in MH services have a co-occurring AOD problem

### Hamilton Centre training program

Hamilton Centre is proud to announce its online training program designed for the Victorian Mental Health and Alcohol and Other Drug (AOD) workforces. Our initial modules are now available.

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## Research

Using evidence to support integrated care and inspire hope for people with co-occurring mental health and substance use conditions, as well as their families and caregivers.

# Integrated care

- Presence of both problems
  - Complicates and impedes recovery from both
- Pressing need for holistic approaches to treatment that acknowledge and actively treat both problems
- For many people, substance use is a solution an underlying problem
- Attractiveness of integrated treatment approaches; and **transdiagnostic** treatments that address underlying challenges (e.g., trauma/ PTSD)



# Integrated care & psychedelics

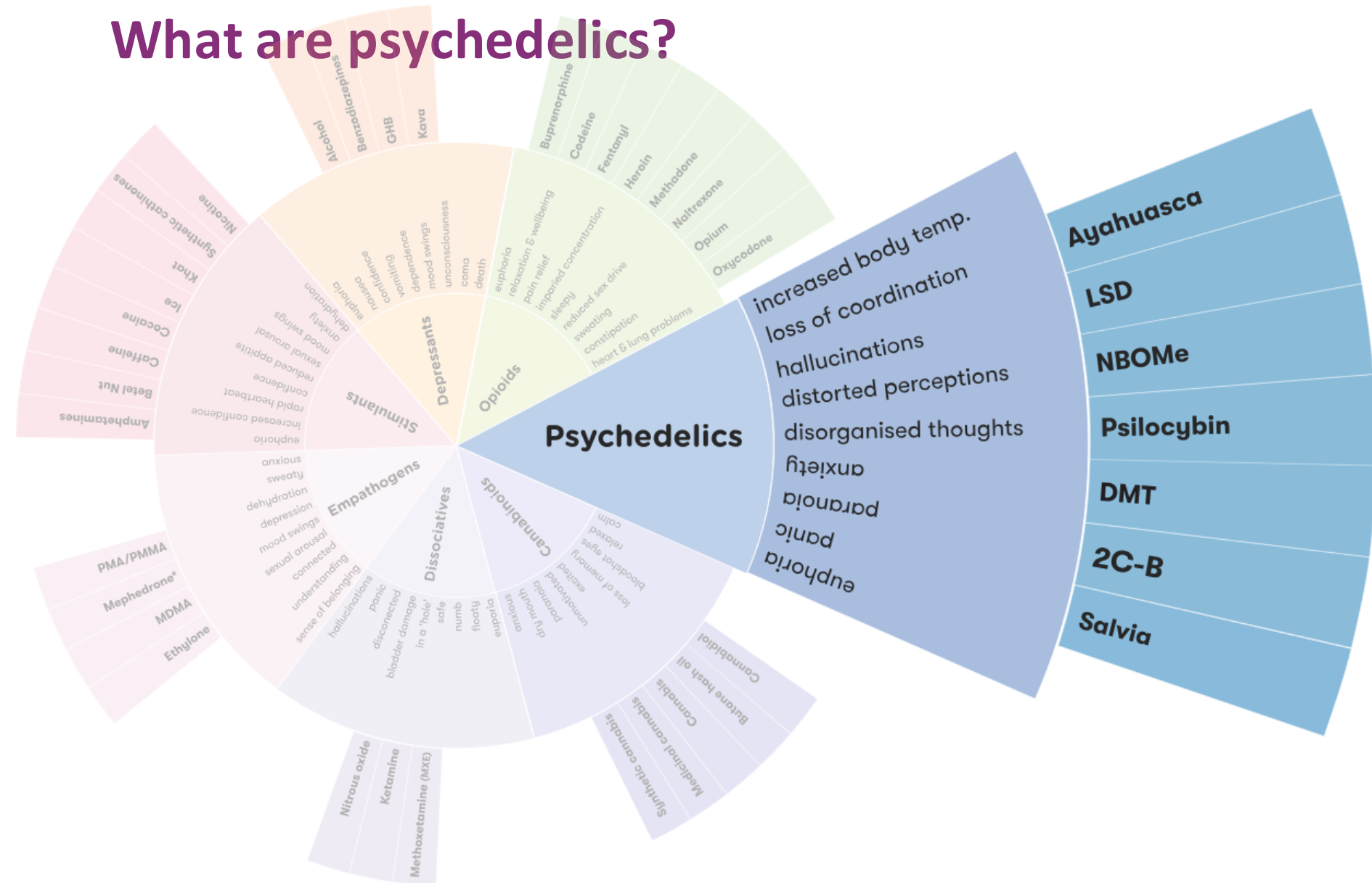
- Transdiagnostic approaches
  - Addressing core constructs or mechanisms of change
- Neurotransmitter systems that underpin both substance use and mental health challenges



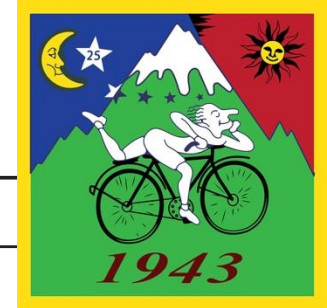


# background psychedelics & PAT

# What are psychedelics?



# What are psychedelics?



**Table 1** Notable Landmarks of Mid-Twentieth Century Psychedelic Research Plus Events of Cultural Significance

Year	Landmark	References
1943	LSD's psychoactive effects discovered by Albert Hofmann (16th and 19th April)	Hofmann, 1980
1947	Werner Stoll publishes first paper on psychological effects of LSD in humans	Stoll, 1947
1950	First English language publication on LSD	Busch and Johnson, 1950
c. 1953	ACNP Founding president Joel Elkes (President in 1961) publishes on LSD after openly self-experimenting with it	Bradley <i>et al</i> , 1953; Roberts, 2008
1954	Aldous Huxley's 'The Doors of Perception' published: documents mescaline self-experiment	Huxley, 1954
1956	Term 'psychedelic' coined by Humphrey Osmond in communication with Aldous Huxley	Huxley, 1980
1957	Term 'magic mushrooms' coined by LIFE magazine	Wasson, 1957
1958	Identification of psilocybin in magic mushrooms by Albert Hofmann	Hofmann <i>et al</i> , 1958
1959	Closed conference held in Princeton on 'the use of LSD in psychotherapy', Jonathan Cole attends, an early ACNP president	Abramson, 1959
1960	First major European conference on psychedelics; Sidney Cohen publishes positive meta-analysis on LSD safety	Passie, 1996; Cohen, 1960
1961	Jonathan Cole (ACNP president 1965-66) expresses 'very mixed feelings on psychedelic research' as critical commentaries emerge	Mangini, 1998
1962	The Marsh Chapel or 'Good Friday' experiment conducted at Harvard under Timothy Leary's supervision but without institutional approval	Pahnke, 1966; Mangini, 1998
1963	Leary dismissed from Harvard; Aldous Huxley and JFK die (both on 22nd November)	Stevens, 1987
1964	Cole takes 'sober look' at psychedelics in JAMA; discussions on LSD take center stage at 1964 APA meeting; Ken Kesey travels across US taking LSD with 'Merry Pranksters'	Mangini, 1998; Cole and Katz, 1964; Stevens, 1987; Wolfe, 1968
1965	Sandoz stop manufacture of LSD and psilocybin	Stevens, 1987
1966	Prohibition of psychedelics and curtailment of research begins in US; Senator Robert Kennedy formally questions this move	Stevens, 1987; Lee and Shlain, 1992
1967	Timothy Leary declares 'turn on, tune in and drop out' at festival in Golden Gate Park	Stevens, 1987
1970	President Nixon signs Controlled Substances Act, LSD and psilocybin made Schedule I	Stevens, 1987; Lee and Shlain, 1992

Abbreviations: ACNP, American College of Neuropsychopharmacology; JAMA, *Journal of the American Medical Association*; NIMH, National Institute of Mental Health.

# What are psychedelics?

**Table 1**

## The classic psychedelics and their natural sources

Chemical name	Common name(s)	Natural sources
5-methoxy- <i>N,N</i> -dimethyltryptamine (5-MeO-DMT)	Toad	Yopo tree ( <i>Anadenanthera peregrina</i> ) seeds Colorado River toad ( <i>Bufo alvarius</i> ) and Sonoran Desert toad ( <i>Incilius alvarius</i> ) skin exudate
<i>N,N</i> -dimethyltryptamine (DMT)	Spirit molecule	Chacruna shrub ( <i>Psychotria viridis</i> ; a component of the ayahuasca brew) and other plant species
Lysergic acid diethylamide (LSD)	Acid	Derived synthetically from ergot fungus ( <i>Claviceps purpurea</i> )
Mescaline (3,4,5-trimethoxyphenethylamine)	Peyote	Cacti species ( <i>Lophophora williamsii</i> , <i>Echinopsis pachanoi</i> , <i>Echinopsis peruviana</i> )
Psilocybin, psilocin	Magic mushrooms, shrooms	<i>Psilocybe</i> mushroom species
<b>Source:</b> Reference 7		

# What are psychedelics?

Class	Primary receptor activation	Onset and duration of action
<b>Indoleamines (aka tryptamines)</b>		
Psilocybin (phosphoryloxy-N,N-dimethyltryptamine)	5-HT <sub>1</sub> , 5-HT <sub>2</sub> , 5-HT <sub>6</sub> and 5-HT <sub>7</sub>	Onset 10–40 min po, peak 90–100 min, duration 4–6 h (most effects abate 6–8 h) Half-life: 2–3 h
Psilocin (active metabolite of psilocybin, 4-hydroxy-DMT)	partial agonists	
N,N-dimethyltryptamine (DMT)	5-HT <sub>1</sub> , 5-HT <sub>2</sub> , 5-HT <sub>6</sub> , and 5-HT <sub>7</sub>	DMT IM onset within 2–5 min and can last 30–60 min
5-methoxy-DMT (5-MeO-DMT)	partial agonists	DMT smoked or inhaled free-base <30 min
Ayahuasca (aya) (DMT from <i>Psychotria viridis</i> plants and <i>Banisteriopsis caapi</i> , containing the potent MAO inhibitors beta-carboline alkaloids)		DMT IV peak 5 min, abate by 30 min Aya: effects within 60 min, peak 90 min, can last 6 h
<b>Phenylalkylamines (synthetic “amphetamines”)</b>		
2,5-dimethoxy-4-iodoamphetamine (DOI)	5-HT <sub>2A</sub> , 5-HT <sub>2B</sub> , 5-HT <sub>2C</sub>	onset 1–2 h, duration 16–24 h
2,5-dimethoxy-4-bromoamphetamine (DOB)	agonists	
Mescaline		Peak within 2 h po, duration up to 8 h
<b>Semi-synthetic Ergolines</b>		
Lysergic acid diethylamide (LSD)	5-HT <sub>1</sub> , 5-HT <sub>2</sub> , 5-HT <sub>6</sub> and 5-HT <sub>7</sub> partial agonists D <sub>1</sub> and D <sub>2</sub> dopamine receptors and adrenergic receptors	po onset 30–45 min, peak 1–2.5 h, duration 9–12 h IV onset 3–5 min, peak 1 h, duration 9–10 h



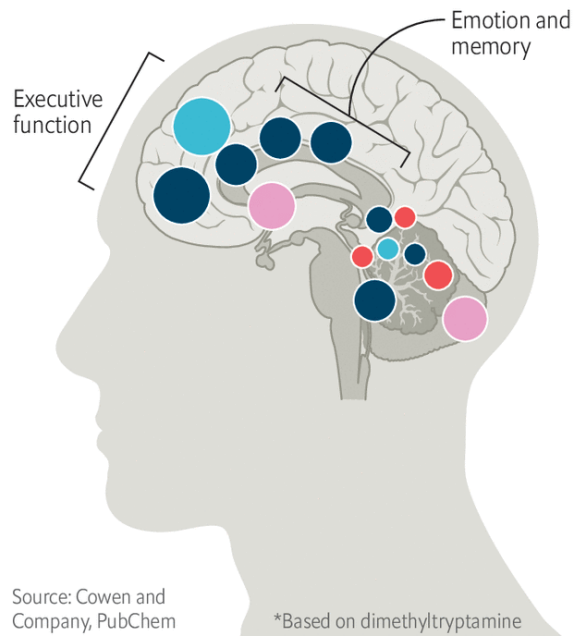
## Tuning in

Psychedelic interactions with brain receptors

Circle size=effect and number of receptors

### Psychedelics

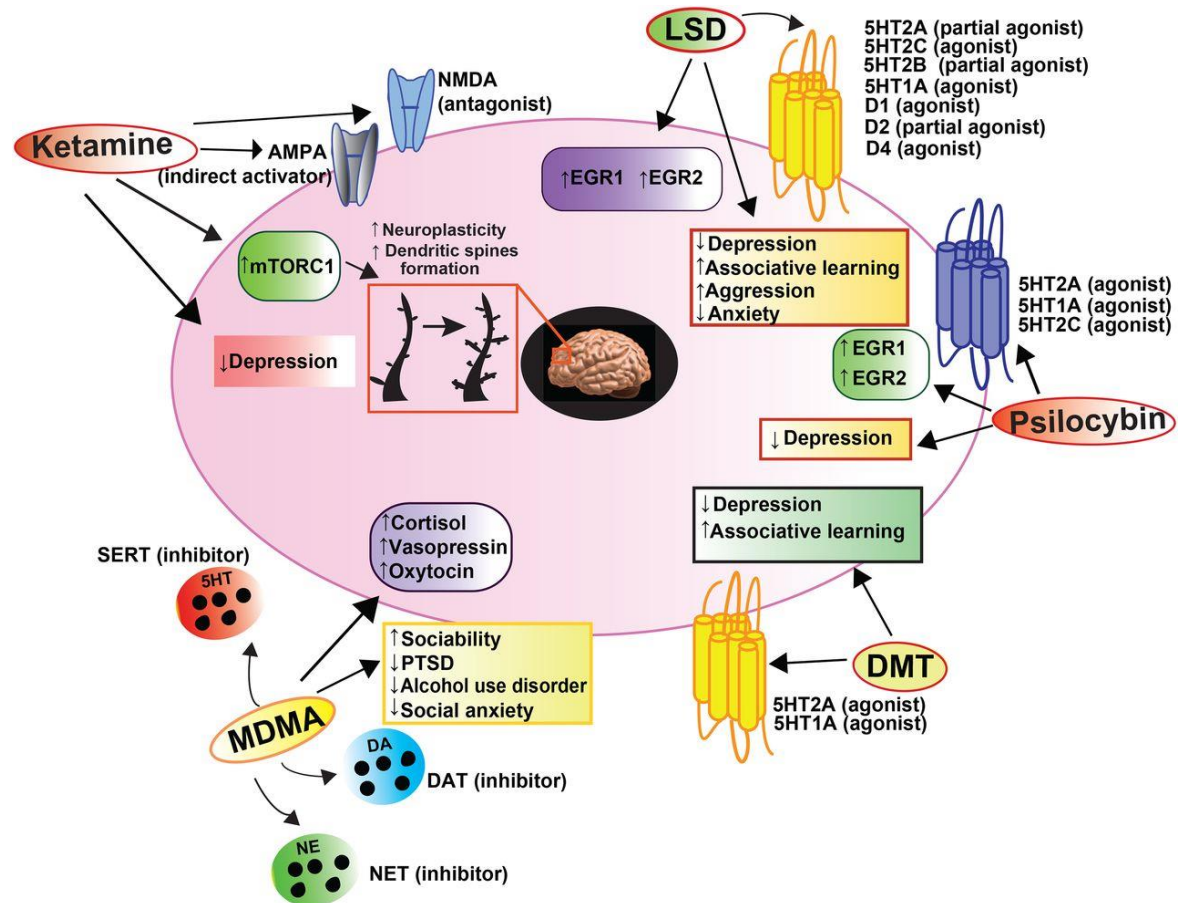
5-MeO-DMT*	● 5-HT2A	● 5-HT1A
Ketamine	● NMDA	
LSD	● 5-HT2A	● 5-HT2B
Mescaline	● 5-HT2A	
Psilocybin	● 5-HT2A	



Source: Cowen and Company, PubChem

The Economist

\*Based on dimethyltryptamine



# MDMA

- MDMA
  - Not a 'classic' psychedelic
  - Actions at 5-HT transporter (SERT)
  - Also blocks DAT (dopamine), and promotes release of oxytocin
  - 'Entactogen', 'empathogen'



# What is psychedelic assisted psychotherapy?

- Crux of the model is that this is psychotherapy with the \*addition\* of a medicine that may enhance therapeutic process
- Used in 2-3 session dosing rather than continual/maintenance model (e.g. antidepressant medication)



## Factors that influence a psychedelic experience.

- 1 Preparation**

Education surrounding the risks, benefits, indications, contraindications, expectations, & intentions prior to the experience. May also benefit from self-exploration, meditation, holotropic breathwork, etc.
- 2 Type of psychedelic**

Understanding the different classes & types of psychedelics, in addition to their respective effects.
- 3 Dose**

Understanding the dose-response & effect of the chosen psychedelic (including microdosing and macrodosing).
- 4 Route of administration**

Understanding the optimal route of administration for the intended purpose (i.e. oral, intravenous, inhaled, intramuscular, etc.).
- 5 Set**

One's mindset, mental state, & intention preceding & during the experience.
- 6 Setting**

The physical & social environment in which the psychedelic experience is occurring.
- 7 Integration**

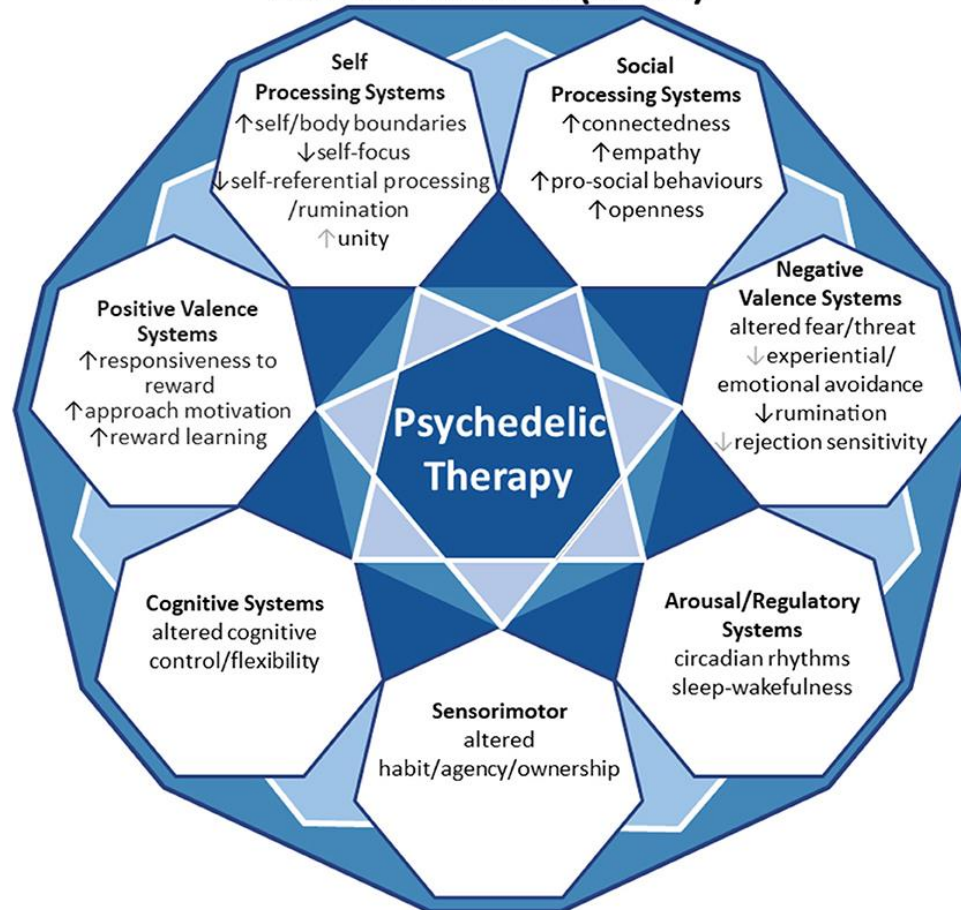
Debriefing & providing support to individuals after the experience.



Lawrence & Carhart-Harris 2019

# How might psychedelics work?

## Psychedelic Therapy and domains of the Research Domain Criteria (RDoC)



# MDMA-AT for PTSD: How might it work?

## *Catalysing therapy*

- Fear extinction learning, memory consolidation; enhancing learning
  - BDNF- mediated?
- Openness
- Self-experience
  - Self compassion
- Promoting therapeutic alliance

# Potential memory mechanisms

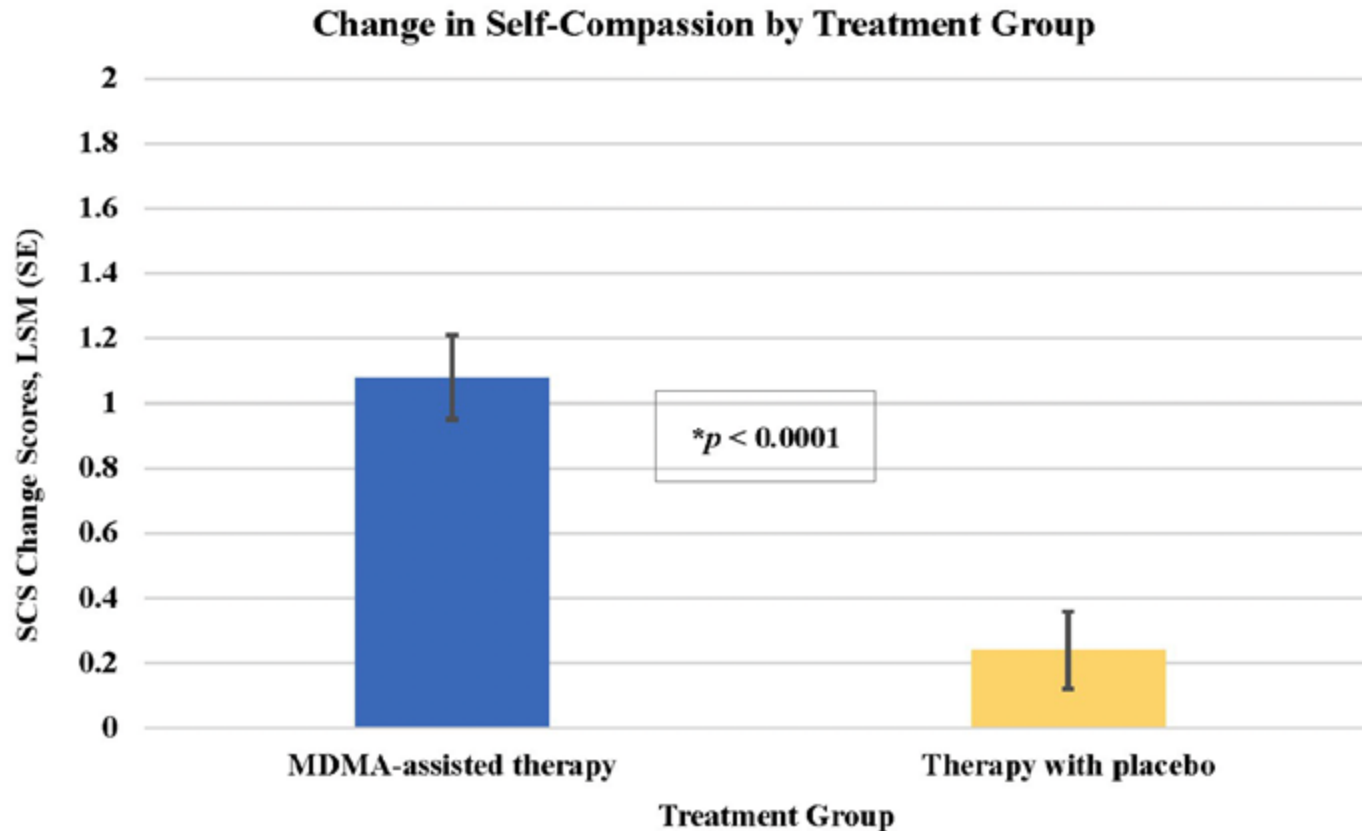
A.A. Feduccia, M.C. Mithoefer

*Progress in Neuropsychopharmacology & Biological Psychiatry 84 (2018) 221–228***Table 1**

MDMA enhances molecules involved in memory, learning, and fear extinction.

MDMA-mediated molecules	Memory, learning, and fear extinction mechanisms	References
Serotonin	<ul style="list-style-type: none"> <li>● Induce affective states to alter fear memories with safety information</li> <li>● Increases DA release</li> <li>● Increases oxytocin release</li> <li>● Modulates MDMA-enhanced fear expression</li> </ul>	(Hogberg et al., 2011; Koch and Galloway, 1997; Thompson et al., 2007)
Dopamine	<ul style="list-style-type: none"> <li>● Increases attention</li> <li>● Induces prediction error</li> <li>● Destabilization of memory traces</li> <li>● Positive behavioral reinforcement</li> </ul>	(Asan, 1997; Esber et al., 2012; Merlo et al., 2015; Schultz et al., 1997)
(Nor)epinephrine	<ul style="list-style-type: none"> <li>● Increases emotional arousal</li> <li>● Enhances learning and memory</li> <li>● Enhances extinction learning</li> <li>● Modulator of cortisol effects</li> </ul>	(Berlau and McGaugh, 2006; Liang et al., 1986; McGaugh, 2000; Mueller et al., 2008; Roozendaal and McGaugh, 1996; Roozendaal et al., 2006a; Roozendaal et al., 2006b)
Acetylcholine	<ul style="list-style-type: none"> <li>● Promotes synaptic plasticity</li> <li>● Increases glutamate release (nAChR)</li> </ul>	(Acquas et al., 2001; Fisher and Dani, 2000; Garcia-Rates et al., 2010; Gray et al., 1996; Nair and Gudelsky, 2006; Radcliffe and Dani, 1998)
Glutamate	<ul style="list-style-type: none"> <li>● Promotes synaptic plasticity</li> </ul>	(Abad et al., 2014)
BDNF	<ul style="list-style-type: none"> <li>● Enhances learning and memory</li> <li>● Modulates synaptic plasticity</li> </ul>	(Abad et al., 2014; Bramham and Messaoudi, 2005; Edut et al., 2014; Edut et al., 2011; Young et al., 2015)
Oxytocin	<ul style="list-style-type: none"> <li>● Mediates socially reinforced learning</li> <li>● Suppresses amygdala activity</li> </ul>	(Eckstein et al., 2015; Ferrier et al., 1980; Guastella et al., 2008; Heinrichs et al., 2004; Hurlmann et al., 2010; Rimmele et al., 2009; Savaskan et al., 2008)
Cortisol	<ul style="list-style-type: none"> <li>● Increases emotional arousal</li> <li>● Modulates learning and memory</li> </ul>	(de Quervain et al., 2011; Hamacher-Dang et al., 2013; Izquierdo et al., 2006; Meir Drexler and Wolf, 2017; Soravia et al., 2006)





**Fig 2. Self-compassion change scores in MDMA-assisted therapy.** Least square means (SE) change in Self-compassion Scale (SCS) from baseline to follow-up by treatment group: MDMA-assisted therapy = 1.08 (0.13) vs. Therapy with placebo = 0.24 (0.12),  $p < .0001$ .

<https://doi.org/10.1371/journal.pone.0295926.g002>

# **context** Australian implementation



# A sequence of events in Australia...

- Oct 2022 initial TGA decision
- Feb 2023 change in TGA decision, with 1 July timeline for implementation

## 'Serious concerns' over TGA's decision making on landmark psilocybin, MDMA ruling

Background Briefing / By [Annika Blau](#) and [Geoff Thompson](#)

Posted Sat 18 Mar 2023 at 6:20am, updated Mon 20 Mar 2023 at 10:56am

*In Brief*

### The down-scheduling of MDMA and psilocybin(e): Too fast and too soon

Steve Kisely<sup>1,2</sup> 

**ANZJP**

*Australian & New Zealand Journal of Psychiatry*  
2023, Vol. 57(7) 933–934  
DOI: 10.1177/00048674231174171

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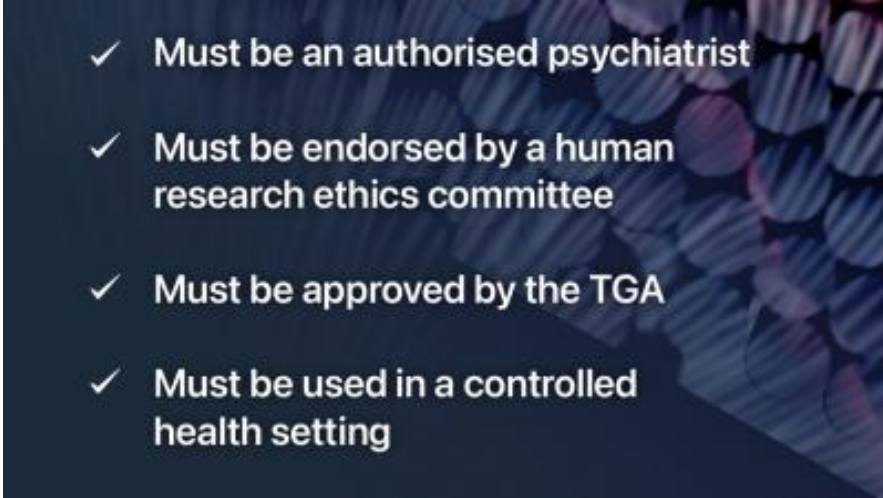


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 **Sage**

# Where are we now?

- Authorised prescriber pathway since 1 July 2023 for psychiatrists
  - psilocybin (TRD)
  - MDMA (PTSD)
- [RANZCP Clinical Memoranda and guide](#)
- [TGA Guide](#)

- 
- ✓ Must be an authorised psychiatrist
  - ✓ Must be endorsed by a human research ethics committee
  - ✓ Must be approved by the TGA
  - ✓ Must be used in a controlled health setting

## RANZCP Psychedelic-Assisted Therapy Steering Group

The steering group is responsible for:

- considering the appropriate level of information and support to provide to members
- providing guidance and recommendations for RANZCP media commentary
- providing relevant information about the prescribing pathway to members and the general public.

[Psychedelic Assisted Therapy Steering Group Terms of Reference](#) [PDF; 121 KB]

The Steering Group is developing additional resources to be released in the coming weeks including principles for best practice and a training framework for psychiatrists.

The PAT Steering Group is also involved in ongoing advocacy around the monitoring and reporting of efficacy and safety outcomes from PAT. The College advocates that data, including on adverse events, must be collected systematically and longitudinally.

## Where are we now?

- **Several private clinics across Australia**  
Metropolitan settings  
(Melbourne, Sydney; Perth)  
Model varies – mostly 1–2 dosing sessions in a package of assessments & 4–6 sessions of therapy
- **Several clinical trials across Australia**  
Indications include generalized anxiety disorder, PTSD, treatment-resistant depression, autism spectrum disorder, eating disorder  
e.g., 4 ANZCTR registered RCTs of MDMA  
e.g., 8 ANZCTR registered RCTs of psilocybin

# Where are we now?

Research

**ANZJP**

## Attitudes toward psychedelics and psychedelic-assisted therapy among potential mental health service users and the general population in Australia

Australian & New Zealand Journal of Psychiatry  
2024, Vol. 58(10) 904–913  
DOI: 10.1177/00048674241261779

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**S Sage**

Zohaib Nadeem<sup>1</sup> , Stephen Parker<sup>1,2,3</sup>, Hugh McGovern<sup>4,5</sup>  
and Lena KL Oestreich<sup>5,6,7</sup>

- Consumer preferences, perceptions and attitudes

*International Journal of Mental Health Nursing*

**WILEY**

International Journal of  
Mental Health Nursing

**ORIGINAL ARTICLE** **OPEN ACCESS**

## The Acceptability of Psychedelic-Assisted Therapy Amongst Mental Health Consumers: Utilising the Theory of Planned Behaviour


Eva Louie<sup>1,2</sup> | Ellen Towers<sup>1</sup> | Alyssa R. Morse<sup>3</sup> | Joshua Watt<sup>1,2</sup> | Zachary Bryant<sup>4</sup> | Paul Haber<sup>1,2</sup> |  
Kirsten Morley<sup>1,2</sup>

# Where are we now?

## Psychotherapy

### A survey of Australian psychiatrists' and psychiatry trainees' knowledge of and attitudes towards psychedelics in the treatment of psychiatric disorders

#### AUSTRALASIAN PSYCHIATRY

Australasian Psychiatry  
 2023, Vol. 31(3) 329–335  
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- Clinician perceptions and attitudes




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**Mark Montebello**  Drug and Alcohol Services, Northern Sydney Local Health District, St Leonards, NSW, Australia; Specialty of Addiction Medicine, Northern Clinical School, The University of Sydney, St Leonards, NSW, Australia; National Drug and Alcohol Research Centre, University of New South Wales, Randwick, NSW, Australia

## ORIGINAL PAPER



WILEY

### Australian psychologists' attitudes towards psychedelic-assisted therapy and training following a world-first drug down-scheduling

Jordan J. Negrine<sup>1</sup> | Cheneal Puljević<sup>2</sup>  | Jason Ferris<sup>3</sup>  |  
 Paul Liknaitzky<sup>4,5</sup> | Christopher Perlman<sup>6</sup> | Timothy Piatkowski<sup>1,7</sup> 

# Where are we now?



“We don’t want to run before we walk”: the attitudes of Australian stakeholders towards using psychedelics for mental health conditions

Breanne E Kunstler<sup>a,b,c</sup>, Liam Smith<sup>a,b</sup>, Christopher J Langmead<sup>b</sup>,  
Denise M Goodwin<sup>a,b</sup>, Breanna Wright<sup>a,b</sup> and Melissa A Hatty<sup>a,b</sup>

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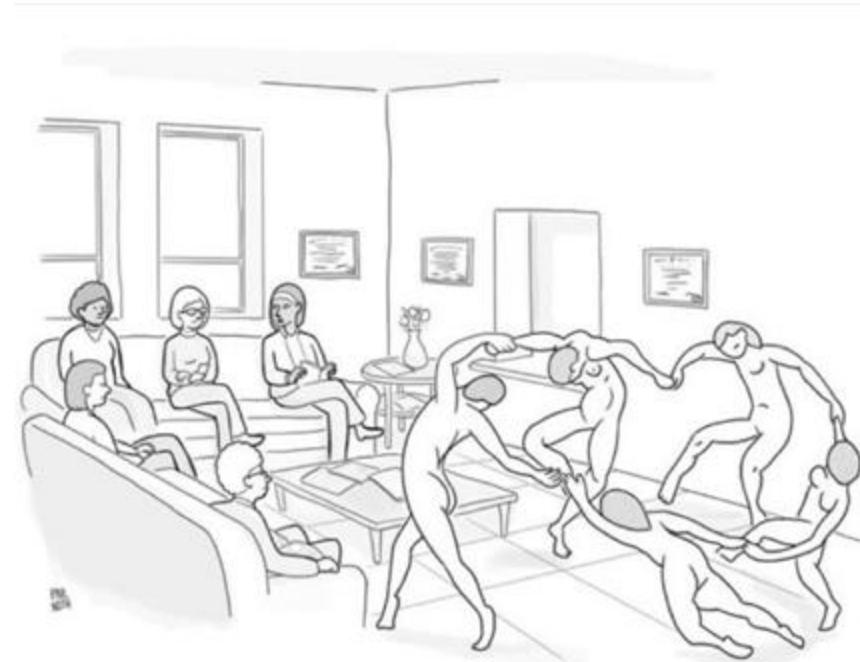
- Policymaker and stakeholder views

# research challenges



# Challenges

- Blinding
  - 90% of participants in recent trials guessed their treatment allocation
- Expectancy effects
- Generalisability- less than 10% of screened participants make it on to these trials



*"So I'm guessing we're in the placebo group."*

# **research effectiveness**

# Mental Health

- Psilocybin for treatment resistant depression
  - Several meta-analyses
    - 7-10 completed RCTs (approx. <500 patients)
    - All with major caveats, moderate risk of bias – meaning low certainty of evidence
    - Evidence to date in favour of psilocybin; limited medium to longer term data
- Metaxa and Clarke. BMJ 2024. <https://doi.org/10.1136/bmj.r111>
- Menon et al. Acta Psychiatrica Scandinavica 2025. <https://doi.org/10.1111/acps.13778>



# Efficacy of psilocybin for treating symptoms of depression

## Summary



Psilocybin treatment showed a significant improvement in depression scores compared with comparators. Greater effectiveness was seen among patients with secondary depression, those who had used psychedelics in the past, and with higher doses

## Study design



Systematic review with meta-analysis | 9 trial arms assessed from 7 trials

## Population



436 adults with clinically significant symptoms of depression

## Comparison

### Intervention

**Psilocybin**  
as standalone treatment,  
excluding micro dosing



### Control

**Non-psychedelic treatments**  
including placebo, niacin,  
and micro doses of psychedelics

## Outcomes

Change in depression score from baseline

Standardised mean difference (Hedge's g) 95% CI\*

Overall	<b>PRIMARY</b>	0.66 (0.46 to 0.86)
Primary depression†		0.62 (0.39 to 0.84)
Secondary depression‡		0.88 (0.42 to 1.33)
Low dose (10-15 mg)		0.57 (0.26 to 0.87)
High dose (20-25 mg)		0.73 (0.47 to 1.00)

< Favours control

Favours intervention >

## Evidence certainty

All studies had a moderate risk of bias individually, given the likelihood that many participants were aware of their assigned intervention, resulting in a **moderate certainty of evidence rating**

# Mental Health

- MDMA for PTSD
  - Several systematic reviews & meta-analyses
  - Yong et al 2025 ANZJP review of meta-analyses

**Results:** Fourteen systematic reviews comprising 20 primary studies involving up to 353 participants were included. All reviews included studies of one-to-three sessions of 50–125 mg MDMA-assisted psychotherapy (some with supplemental dosage) compared to either 25–40 mg of MDMA or inactive placebo with psychotherapy. Four were deemed high quality. Meta-analyses reported substantial benefits of MDMA-assisted psychotherapy in improving post-traumatic stress disorder symptoms (standardised mean difference, 0.8–1.3), response rate (relative risk, 1.3–3.5) and remission rate (relative risk, 2.3–2.9) compared to psychotherapy alone. However, for reviews that assessed the certainty of evidence, the evidence was rated as low to very low certainty due to high risk of bias, indirectness and imprecision. There was moderate-quality evidence that MDMA-assisted psychotherapy was associated with an increased odd of transient adverse events. However, reviews noted reliance on spontaneous rather than systematic adverse event reporting, discrepancies between adverse events reported in published studies and clinical trial registries, and a lack of long-term safety data.

**Conclusion:** Four high-quality systematic reviews suggest low to very low certainty evidence for efficacy outcomes and moderate to very low quality evidence for safety outcomes.



# MDMA – PTSD

**Table 1.** Summary of major outcomes reported in systematic reviews.

Outcomes	Summary of findings
Study characteristics	<ul style="list-style-type: none"> <li>Reported on both the safety and efficacy of MDMA-AP: <math>n = 10</math></li> <li>Reported on safety only: <math>n = 2</math> (Breeksema et al., 2022; Colcott et al., 2024)</li> <li>Reported on efficacy only: <math>n = 2</math> (Hoskins et al., 2021; Luoma et al., 2020)</li> </ul> <p><b>Intervention group:</b> 50–125 mg MDMA-AP (1–3 sessions)</p> <p><b>Comparator group:</b> active placebo (25–40 mg of MDMA) or inactive placebo along with psychotherapy</p> <p><b>Risk of bias assessment tools:</b> Cochrane Risk of Bias tool, modified quality and risk of bias checklist (NHMRC, 1999), Critical Appraisal Skills Programme (CASP), CONSORT Harms 2022, or qualitative assessment</p> <p><b>Certainty of evidence assessment:</b> GRADE approach, ICER Evidence Rating Matrix, AHRQ Methods Guide for Comparative Effectiveness Reviews</p>
Methodology quality (assessed by authors using AMSTAR-2)	high = 4, moderate = 1, low = 3, critically low = 6
Efficacy of MDMA-AP	<p><b>PTSD symptoms:</b> SMD in CAPS score of <math>-0.8</math> to <math>-1.3</math> (Bahji et al., 2020, 2023; Green et al., 2023; Hoskins et al., 2021; Kisely et al., 2023; Mackey et al., 2022; Mustafa et al., 2024; Tedesco et al., 2021)</p> <p><b>Response rates:</b> RR of 1.3 to 3.5 (compared to comparator group) (Bahji et al., 2020, 2023; Kisely et al., 2023; Mustafa et al., 2024; Tedesco et al., 2021)</p> <p><b>Remission rates:</b> RR of 2.3 to 2.9 (compared to comparator group) (Bahji et al., 2020, 2023; Mustafa et al., 2024; Tedesco et al., 2021)</p> <p><b>Loss of diagnosis:</b> RR of 1.70 (compared to comparator group) (Mustafa et al., 2024)</p> <p><b>Depressive symptoms:</b> MD in Beck's Depression Inventory of <math>-10.8</math> to <math>-11.1</math> (Green et al., 2023; Illingworth et al., 2021)</p> <p><b>Daily functioning:</b> MD in Sheehan Disability Scale of <math>-1.5</math> (Mustafa et al., 2024); SMD of <math>-0.4</math> to <math>-0.8</math> (Green et al., 2023; Mustafa et al., 2024)</p> <p><b>Long-term outcomes</b> (change in PTSD symptoms after 2–74 months follow-up): SMD of <math>-0.8</math> to <math>-1.1</math> (Bahji et al., 2020; Tedesco et al., 2021)</p>
Safety of MDMA-AP	<p><b>Any adverse events (immediate):</b> OR of 1.7 to 3.5 (compared to comparator group) (Colcott et al., 2024)<sup>a</sup></p> <p><b>Any adverse effects (up to 7 days):</b> OR of 1.6 (compared to comparator group) (Colcott et al., 2024)<sup>a</sup></p> <p><b>Adverse events of special interest:</b> No significant difference found</p> <p><b>Rate of discontinuation:</b> No significant difference (Colcott et al., 2024) or lower risk of discontinuation in the intervention group: RR of 0.32 (Mustafa et al., 2024)</p> <p><b>Long-term adverse events:</b> 2–4% of adverse events reported after 12 months (Colcott et al., 2024)</p>

AHRQ, Agency for Healthcare Research and Quality; ICER, Institute for Clinical and Economic Review; MD, mean difference; MDMA-AP, MDMA-assisted psychotherapy; OR, odds ratio; SMD, standardised mean difference; RR, relative risk.

The statistical summaries reported for efficacy and safety outcomes are presented at a high level and should be interpreted within the context of each individual review and its certainty of evidence.

<sup>a</sup>Refer to individual review for incidence rate or RR of each adverse event.

# Substance Use Disorder

- Much less evidence
- People with SUD often excluded from MH trials
- Uncontrolled studies, self-reports from self-experience and non-medicalized settings (which may not be transferable)
- Trials for specific SUD indications include
  - psilocybin for alcohol use disorder
  - ketamine for alcohol use disorder
  - psilocybin pilot for methamphetamine use disorder

Current Addiction Reports (2025) 12:15  
<https://doi.org/10.1007/s40429-025-00629-8>



## Psychedelics in the Treatment of Substance Use Disorders and Addictive Behaviors: A Scoping Review

Jérémie Richard<sup>1,2</sup> · Albert Garcia-Romeu<sup>1,2</sup>

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# Bogenschutz (2022) Psilocybin for AUD

## JAMA Psychiatry

### RCT: Psilocybin-Assisted Treatment of Alcohol Use Disorder

#### POPULATION

53 Men, 42 Women



Adults with alcohol dependence  
**Mean age, 45.8 y**

#### SETTINGS / LOCATIONS



**2 Academic centers in New York and New Mexico**

#### INTERVENTION

95 Individuals randomized



##### 49 Psilocybin

Administered orally in 2 all-day sessions (dose range, 25-40 mg/70 kg)



##### 46 Diphenhydramine control

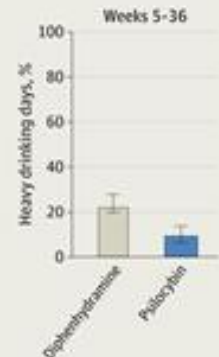
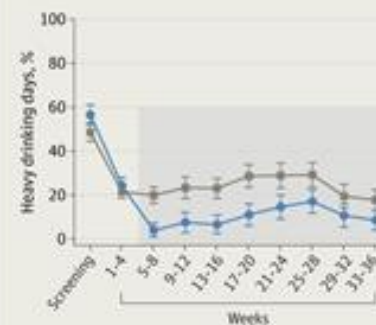
Administered orally in 2 all-day sessions (dose range, 50-100 mg)

#### PRIMARY OUTCOME

Percent heavy drinking days (scale, 0-100), assessed using the timeline followback interview, contrasted between groups over the 32-wk period following the first administration of study medication.

#### FINDINGS

Percent heavy drinking days during the 32-wk double-blind period was lower in the psilocybin group compared with the diphenhydramine group



#### Percent heavy drinking days

**Psilocybin=9.7%**

**Diphenhydramine=23.6%**

Mean difference, 13.9 (95% CI, 3.0-24.7;  $P = .01$ )

Bogenschutz MP, Ross S, Bhatt S, et al. 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. *JAMA Psychiatry*. Published online August 24, 2022. doi:10.1001/jamapsychiatry.2022.2096

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# Integrated care

- No completed studies so far
- Promising indications include
  - alcohol use disorder + PTSD
  - alcohol use disorder + depression
  - methamphetamine + depression
- Major gap in research

# MPATHY study

## mpathy



Lead investigator:  
Kirsten Morley  
University of Sydney

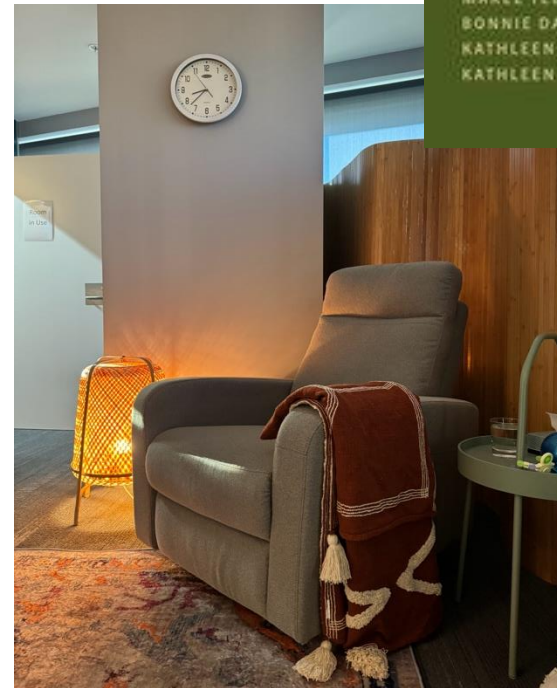
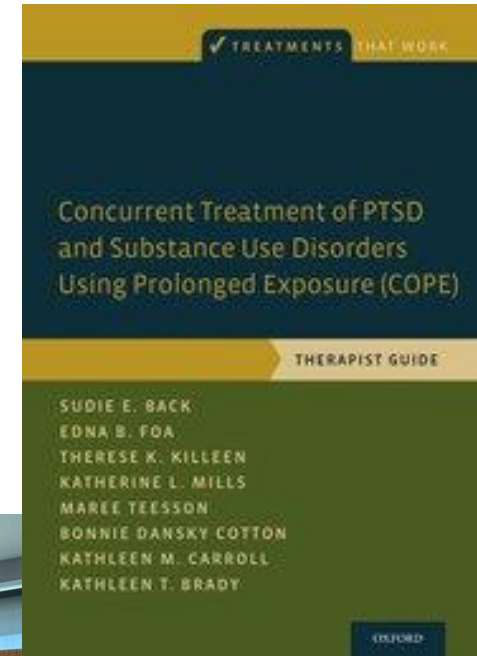
PI (Sydney): Paul Haber  
PI (Melbourne): Shalini Arunogiri

Investigators:  
Kath Mills, Maree Teesson, Dan Lubman, Andrew Baillie, Alyssa Morse, Yong Yi Lee, Sudie Back



# MPATHY

- Evidence based integrated trauma-focused psychotherapy based on prolonged exposure (COPE) and relapse prevention
- Addition of MDMA (x 2 dosing sessions)
- Total of 14 sessions of psychotherapy, incl. 2 MDMA dosing & integration sessions
- Primary outcome PTSD severity;  
Secondary outcome AUD severity



# **research** safety & adverse effects

## Is it safe?

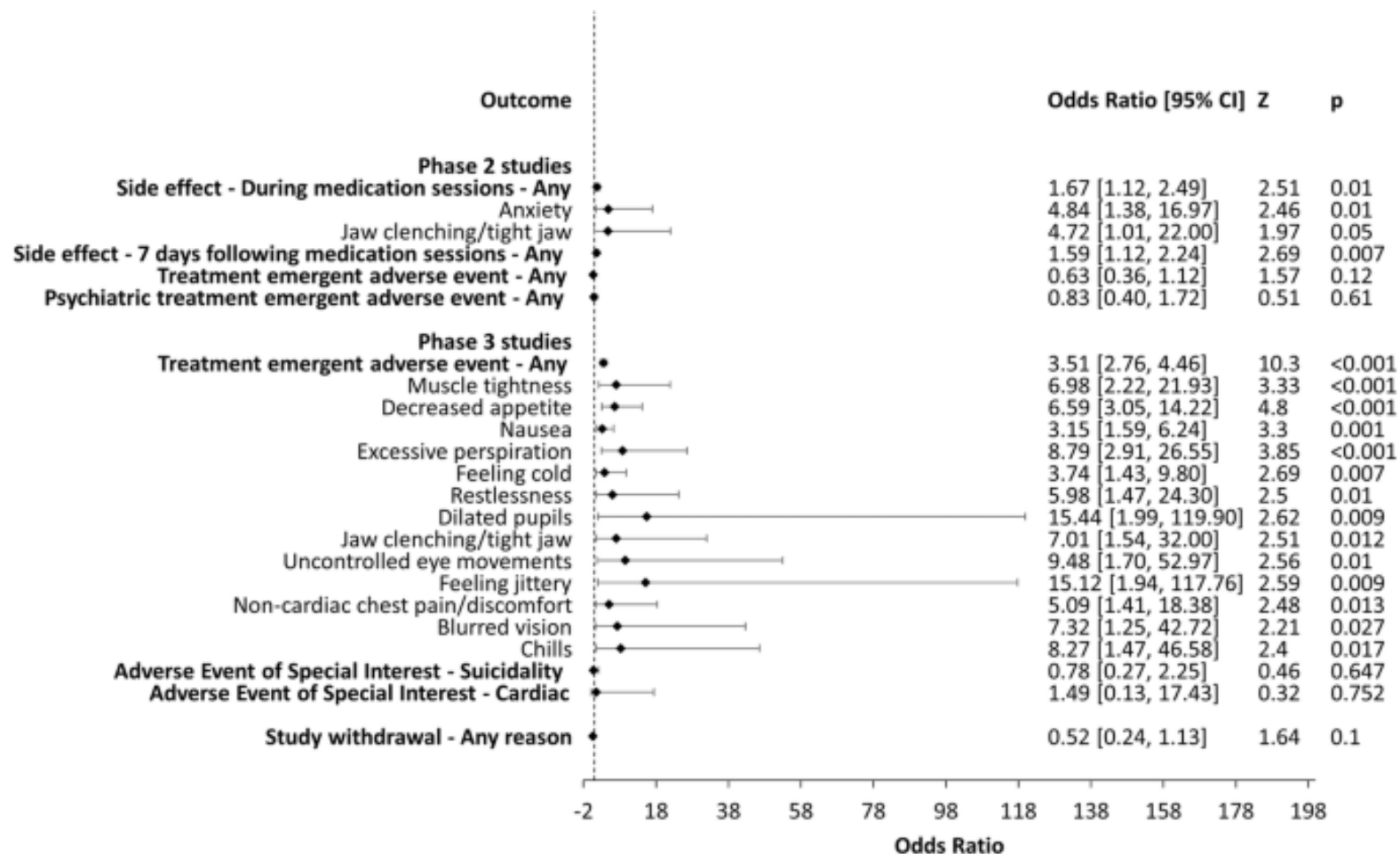
- Current studies have been conducted in very selective clinical trial populations, and largely in psilocybin and MDMA (much less data on other psychedelics)
- Registry and TGA data during this roll out will be **critical** to informing a safety signal in a general (non-clinical trial) population



## ARTICLE OPEN



## Side-effects of mdma-assisted psychotherapy: a systematic review and meta-analysis

Julia Colcott<sup>1,2</sup>, Alexandre A. Guerin<sup>2</sup>, Olivia Carter<sup>1</sup>, Sally Meikle<sup>1</sup> and Gillinder Bedi<sup>2,3</sup>

# research gaps

# Gaps in research evidence

- Major gaps and limitations in existing evidence
  - Very little to no evidence in Australian context to date  
(but several trials currently in planning or underway)



# Gaps in research evidence

- Major challenge in providing informed consent whilst gaps in evidence remain
- Safety; long term follow-up data
- Challenges in implementation
- Current model may not be widely implementable or accessible



# Implementation & Integration

Integration as a task of making sense, making meaning, and applying insights

Implementation as a process of evidence gathering, perspective taking, and application





# Thank you for listening

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## **Thanks to our Melbourne mpathy team**

*Dan Lubman, Daniel Pham, Sarah Catchlove, Liron van Heerden, Taya Grainger, Emily Bove, Anna Bough, Trudi Mckenzie, Temika Mu, Michelle Sharkey, Vicky Phan, Christina Ngo-Nguyen, Adam Milne*

*and to Kirsten Morley, Paul Haber, Katherine Mills, Sudie Back*

