Position statement

Psychologists and psychedelic-assisted therapy

December 2021 | Australian Psychological Society
Executive summary

Psychedelic substances are a group of drugs which are known for their hallmark induction of non-ordinary states of consciousness. Used by Indigenous and First Nations peoples for thousands of years, psychedelics only piqued the interest of western psycho-medico research in the mid-20th Century. Early systematic research was halted in the 1970s until the recent ‘renaissance’ in the past 15-20 years. Currently, psychedelic substances are strictly controlled outside designated clinical research trials. Psychedelics are typically separated into four groups (1) classic psychedelics, (2) empathogens or entactogens, (3) dissociative anaesthetics and, (4) other hallucinogens. Focussing on the first two classes, this position statement describes the current understanding of the cognitive, perceptual, social, and emotional effects of psychedelics, and importantly, evidence for their effect on symptoms of mental health disorders. Psychedelic-assisted (psycho)therapy is being considered largely due to the significant proportion of patients who are considered ‘treatment-resistant’.

It is well accepted that psychedelics are not treatments in and of themselves, they are an adjunct tool for therapy. Early promising evidence has prompted the US Food and Drug Administration to grant ‘breakthrough therapy designation’ to MDMA-assisted therapy for the treatment of post-traumatic stress disorder (PTSD) and psilocybin-assisted therapy for the treatment of treatment-resistant depression. Current research investigating the therapeutic potential of LSD, ayahuasca, and ibogaine are limited but may prove to be promising as more evidence becomes available.

Typically, psychedelic substances are well tolerated in clinical settings and result in few adverse events. However, ibogaine appears to have a riskier safety profile. Strict screening, monitoring and dose control is required which limits the settings in which psychedelic-assisted therapy should be undertaken. Cost, availability, and training would also still limit the implementation of psychedelic-assisted therapy if it were to be rescheduled. The limitations of current research include, inter alia, (1) knowledge of appropriate dosing protocols, (2) selection bias, (3) screening and generalisability, (4) small sample sizes, (5) inadequate blinding and controls, (6) relatively short follow-ups, and the (7) unknown different effects of psychotherapy.

The APS is interested in all emerging evidence-based treatment options, particularly for patients who do not respond to current evidence-based treatments. Given this, the APS acknowledges the therapeutic potential of psychedelic-assisted therapy and supports ongoing research in this field. Until there is sufficient compelling phase 3 clinical evidence, and systematic research to overcome the current limitations, however, the APS would not, at this stage, endorse the widespread use of psychedelic-assisted therapy. Critically, if psychedelic-assisted psychotherapies were to become available in Australia, and the TGA takes a similar position to the FDA, psychologists should play a lead role, as regulated practitioners, in providing psychedelic-assisted therapy to vulnerable patient populations. Training and professional development should be provided in collaboration with health professional associations. This is to ensure evidence-based approaches are taken and propagated and to ensure that the strict treatment protocols are followed and necessary patient screening is undertaken.
1. Introduction

1.1 An estimated one in five Australians reported having a mental disorder in the previous 12 months, and almost half of all Australians have been affected at some point in their lifetime. It is estimated that in 2018-19, mental ill-health and suicide cost the Australian economy up to $70 billion and up to an additional $150 billion when disability and premature death due to mental illness are also considered. Despite the availability of evidence-based treatments, it appears that many patients (possibly up to 30%) remain ‘treatment resistant’ and still suffer significant burden which can have staggering quality of life and economic consequences.

1.2 Psychedelics are substances which can be divided into four types of drug: (1) classic psychedelics (e.g. ‘magic mushrooms’ (psilocybin) or Lysergic acid diethylamide (LSD)), (2) empathogens or entactogens (e.g. 3,4-methylenedioxymethamphetamine (MDMA)), (3) dissociative anaesthetics (e.g. ketamine) and, (4) other hallucinogens. The current position statement will focus on the first two classes as they tend to be separated in the literature and clinical memoranda. It is important to note that MDMA is technically not a psychedelic but is similar in terms of subjective effects, potential therapeutic effects, and current Therapeutic Goods Administration (TGA) and international drug scheduling (the current status of psychedelic substances will be described in more detail in Section 3).

1.3 Despite currently being illegal, there are significant numbers of Australians already taking psychedelic substances to ‘self-medicate’ to treat symptoms of mental health disorders.

1.4 In a 2020 Global Drug Survey, 6,500 of 110,000 respondents stated that they were using psychedelic substances as a self-treatment of psychiatric illness or emotional distress: most commonly depression, anxiety, or relationship issues. The report suggests that the most used substances were LSD (34% of reported psychedelic use), MDMA (25.3%), psilocybin (‘magic mushrooms’) (20.4%), and ketamine (13%). Such underground use precludes the appropriate pharmacological, medical, and psychological safeguards which may explain the relatively high number of emergency visits of psychedelic users.
2. Background

2.1 Psychedelic substances have been used in spiritual and therapeutic practices by Indigenous and First Nations peoples for thousands of years\textsuperscript{14-17}. Some argue that psychedelics may be the oldest psychoactive substances used by humans\textsuperscript{17}.

2.2 It is only in the second half of the 20\textsuperscript{th} Century, that psychedelic substances piqued the interest of western psycho-medico research. LSD was first synthesised in 1938 but was largely forgotten due to it being "physiologically unremarkable"\textsuperscript{16} (p. 2). In the mid-1940s the archetypical psychological effects of psychedelics were documented in western contexts\textsuperscript{16}. Research investigating the potential therapeutic benefits of psychedelic substances steadily gained popularity in the 1950-60s. In that time, the experiences of over 40,000 patients were documented in 1,000 papers\textsuperscript{18}.

2.3 Despite emerging evidence, clinical research investigating the therapeutic potential of psychedelics was stopped due to the world-wide classification of psychedelic substances in Schedule I of the 1967 United Nations Convention on Drugs\textsuperscript{19}. This almost eliminated clinical research into their therapeutic potential until the recent renewed interest spurred by the need to consider alternative treatment options. Termed the ‘renaissance’ of psychedelic research, interest in the field has been increasing steadily for the past 15-20 years.
3. Current status of psychedelic substances

3.1 In Australia, psychedelic substances are currently classified as Schedule 9 (prohibited) substances by the Therapeutic Goods Administration (TGA) as listed in the *Poisons Standard February 2021*. Schedule 9 substances are considered to have a "high propensity for dependency and abuse" and are not available for clinical use outside State or Territory approved clinical research trials. However, in September 2021, the TGA released the final report from independent experts who considered current evidence regarding the safety and clinical utility of MDMA and psilocybin. They concluded that "MDMA and psilocybin may show promise in highly selected populations but only where these medicines are administered in closely clinically supervised settings and intensive professional support". The report informed the TGA’s decision to not reclassify MDMA and psilocybin to be Schedule 8 (controlled) substances which was released in December, 2021. In some States and Territories, it is possible for psychiatrists to apply to the TGA on a case-by-case basis under the Special Access Scheme-B to prescribe MDMA and psilocybin.

3.2 The USA Food and Drug Administration (FDA) has classified psychedelics as illegal Schedule 1 substances which have "no currently accepted medical use and a high potential for abuse". In the UK, psychedelics are classified as Class A drugs which strictly prohibits their sale and possession. Similarly, psychedelics are currently Class A controlled drugs in New Zealand except ibogaine which is a prescription medicine.

3.3 Like Australia, psychedelic treatments in the USA are not permitted outside an Institutional Review Board approved clinical trial. However, two conjoint psychedelic substances and psychotherapy treatments have been given ‘breakthrough’ designation, suggesting they have the potential to be safer and more effective than current treatments:

a. MDMA-assisted psychotherapy for the treatment of PTSD
b. Psilocybin-assisted psychotherapy for the treatment of treatment-resistant depression

Breakthrough designation expedites the approval and distribution of treatments once clear evidence from controlled clinical trials is available.

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1 The term psychotherapy (or therapy) is used in this statement to be consistent with the international research literature, however, the APS would consider this to be psychological treatment.
4. Current evidence of psychological and therapeutic effects

4.1 Table 1 provides a detailed overview of the effects of psychedelics on psychological processes and effects on mental health disorders.

4.2 Psilocybin exerts a number of effects on cognitive and perceptual processes, has been associated with blissful feelings and a greater sense of well-being, and anxiety and confusion or thought disorder. There have been multiple studies providing emerging evidence that psilocybin-assisted therapy had benefits in reducing symptoms of depression and/or anxiety in patients with treatment-resistant depression and cancer patients.

4.3 Similarly, MDMA has been shown to affect a number of positive cognitive and emotional processes including reported increased access to emotional material. Unfortunately, MDMA may also induce anxiety and mild cognitive or psychomotor impairments. Some of the hallmark effects of MDMA are the subjective social relatedness effects such as enhanced sociality and closeness to others and a blunting of an ability to decode negative expressions.

4.4 Patients with treatment resistant PTSD experienced a decrease in PTSD symptoms after MDMA-assisted therapy and the reduction in PTSD symptoms appear to be sustained. In a randomised, double-blind placebo-controlled phase 3 study, MDMA-assisted therapy was found to reduce PTSD symptoms and reduced functional impairment compared to placebo with therapy in patients with severe, including co-morbid PTSD.

4.5 The evidence supporting the therapeutic applications of LSD, ayahuasca and ibogaine is less convincing although may emerge with additional research. Some early evidence is listed in Table 1.
5. Psychedelic-assisted therapy

5.1 Critically, the current evidence suggesting promising effects of psychedelics are almost solely in conjunction with psychotherapy which has led to the largely accepted view that psychedelics are not a viable treatment in and of themselves. It is thought that psychedelics enable the surfacing of previously unavailable emotional material which can then be processed and integrated. The precise mechanisms of each component of psychedelic-assisted therapy are still not well understood and require additional research.

5.2 Central to the psychedelic-assisted psychotherapeutic approach is the importance of set (i.e., psychological expectations), setting (i.e., physical environment) and having a trust-based therapeutic clinician-patient relationship. Effects of psychedelic substances do appear to be context dependent, which is consistent with the traditional religious and spiritual uses. Studies which have de-emphasised the importance of context setting, have typically not reproduced the strength of positive effects, which has made it difficult for psychedelic research to demonstrate ‘pure’ pharmacological effects in efficacy testing. For example, one study cited the strength of their results in affecting trait-based measures could have been due to the importance of the research context, which encouraged the integration of spiritual values into daily life (e.g. prosocial values, cultivating a sense of wonder).

5.3 Typically, psychedelic-assisted therapy paradigms include very few doses of psychedelic substances and the following therapy sessions:
   a. Preparatory session(s) – which involves understanding the patient’s history and intentions and educating the patient on the likely experience during the active session.
   b. Psychedelic active session(s) – Typically, patients are accompanied by a male-female therapist dyad which is unfortunately deemed necessary due to previous reports of sexual abuse during MDMA-assisted therapy. Although potentially profound and leading to long-term positive effects, it is important to acknowledge that this session could be very challenging due to the emotional material that may surface.
   c. Integration session(s) – arguably the most important step, this includes the interpretation of the material raised during the active session and the integration of this experience into long-term positive change.

5.4 The typical psychotherapeutic approach has been non-directive, supportive psychedelic or psycholytic therapy which is seen as facilitating the experience rather than directing it. Many believe in the importance of therapists undertaking the experience themselves as a personal practice to fully appreciate the profundity of the psychedelic-assisted therapeutic approach.

5.5 Both the FDA and TGA acknowledge the importance of close professional involvement as being a critical component of successful psychedelic-assisted therapy. Specifically, the FDA requires that the two therapists:
   • “Are mental health care practitioners and (have) a professional licence in good standing” (p. 4)
   • Have demonstrable clinical psychotherapy or mental health counselling experience
   • Have a Masters’ level qualification.

As recommended by Tai et al, it is not necessary that a psychiatrist is a member of the therapist dyad, but one must be present during an active psychedelic session in case of a psychiatric or medical adverse event.
6. Known risks and side effects

6.1 When considering the side effects of psychedelic substances, it is important to distinguish between use in clinical and research settings compared to street use. Research on the street use of psychedelics is fundamentally uncontrolled and the drugs are often contaminated by other substances.

6.2 Given the emerging nature of the field, research in clinical settings must adequately screen for high-risk individuals, including patients with:
   a. **Personal or family history** of psychosis
   b. **Personal history** of mania, violence towards others, acute suicidality, current substance abuse (unless this is the target of the intervention), serious cardiovascular (including uncontrolled hypertension), liver, renal, or neurological comorbidity, current or expected pregnancy.

6.3 The similarity of some effects of psychedelic substances with some symptoms of psychosis has been concerning for researchers and so long-term perceptual disturbances are of particular interest (e.g. hallucinogen persisting perception disorder) when evaluating their safety.

### Classic Psychedelics

6.4 In clinical settings, psilocybin appears to be well tolerated and adverse events with participants taking psilocybin appear to be rare. An analysis of 110 healthy participants found no evidence of hallucinogen persisting perception disorder, prolonged psychosis or other long-term impairment. However, psychedelic effects on personality and mood appear to be dose-dependent which suggests that care must be taken to ensure the dose is controlled.

6.5 Similarly, LSD appears to be well tolerated in controlled settings with healthy participants and participants with life-threatening diseases.

6.6 Apart from inducing vomiting in approximately 50% of participants, ayahuasca was well tolerated in research settings. It is important to note, however, that clinical research involving ayahuasca is still limited by the precise understanding of the ingredients and concentrations of compounds of the decoction.

6.7 In contrast to other psychedelics, ibogaine has the potential to generate life-threatening cardiac arrhythmias and so more research is required to understand its therapeutic potential, particularly in patients with pre-existing cardiovascular comorbidities.

### MDMA

6.8 There have been many reported psychological side effects of street use of ‘ecstasy’ (MDMA) in the literature and importantly, it appears that some of these effects are sustained after periods of abstinence. Other serious physical side effects have also been observed. The observed cardiovascular effects of MDMA, however, may be toxic in crowded and/or hot places or when combined with physical activity. Other research, however, suggests that acute complications caused by ecstasy intake are epidemiologically rare, and results are often confounded by users taking multiple illicit drugs. Specific does-response relationships for individuals may also vary, according to genetic differences, and previous exposure to the drug—meaning that it is difficult to predict toxic reactions of individuals.
6.9 Using a field study design, Halpern et al.\textsuperscript{81} found little evidence of neurocognitive differences of users versus non-users of ecstasy who have had minimal exposure to other drugs. Apart from differences in poorer strategic self-regulation, ecstasy users did not appear to demonstrate residual neuro-toxic cognitive effects.

6.10 Studies of MDMA in animals have indicated that controlled high doses of MDMA which lead to deficits in serotonin neurons can have lingering effects on behaviour but that change is not necessarily neurotoxic (i.e. leading to cell death)\textsuperscript{82}. Importantly, MDMA administered in controlled clinical research settings appears to be well-tolerated\textsuperscript{21,49,55,57,83} and have few harmful side effects\textsuperscript{21,44,49,50,53,57,80}. Recent phase 3 results did not indicate an increase in suicidality in patients with PTSD undergoing MDMA-assisted therapy\textsuperscript{57}. 
7. Limitations of current research

Apart from the lack of detailed understanding of the psychological mechanisms underpinning psychedelic-assisted therapy, there are a number of limitations with the current research which need to be addressed:

7.1 **Knowledge of appropriate dosing protocols** – animal models have often been used as the rationale or background to studies involving psychedelic substances. Animal studies often use very high doses (per kg weight) and the results may not generalise to human populations. Although there is significant volume of literature describing the effects within the ‘therapeutic window’, there is still limited knowledge of the effects above and below that range. Recent research is, for example, investigating the effects of microdosing on wellbeing or creativity and still requires further investigation.

7.2 **Selection bias** – in the limited number of active research trials, participants often volunteer or ‘self-refer’ and contact study co-ordinators directly. Such a bias may mean that results are limited to participants who are open to psychedelic experiences or other homogenous factors may play a role.

7.3 **Screening and generalisability** – for safety reasons, patients who have a family history of psychosis, may be pregnant, breastfeeding, have hypertension or heart disorders are typically excluded from clinical trials. Ultimately, it means that the generalisability of results may be limited in those populations. This has important implications if psychedelic treatments were to become widely available.

7.4 **Small sample sizes** – due to the preliminary nature of much of the research conducted to date, there are typically very small sample sizes. If anything, however, this may under-power the ability to detect experimental effects, but is also less likely to produce robust data regarding safety and tolerability.

7.5 **Inadequate blinding and controls** – due to the often visibly evident effects of psychedelic medications, it is difficult to blind study administrators from experimental groups, which may introduce expectancy effects. Similarly, it is difficult for participants to be blind to their experimental condition, as they may not experience any psychedelic effects in the control conditions. The increased use of ‘active placebo’ conditions may assist, as will true placebo-dose conditions to ensure that low doses of substances are psychopharmacologically active.

7.6 **Relatively short follow-ups** – due to the preliminary nature of the majority of the research, there are still limited longitudinal clinical studies to assess the effects of psychedelics in the long-term.

7.7 **Unknown differential effects of types of psychotherapy** – most psychedelic-assisted therapy research utilises non-directive, supportive psychotherapy. Future research should elucidate the utility of other guideline recommended psychotherapeutic approaches in combination with psychedelic substances and investigate the mechanisms by which therapeutic effects of psychedelics are realised.
8. The future of psychedelics in Australia

8.1 There is an increasing investment in the therapeutic potential of psychedelics and a number of charities and other organisations forming in Australia which are promoting the research\(^\text{6,9-53}\) and legalisation and adoption of psychedelic substances into mainstream healthcare\(^\text{6,9-94}\).

8.2 The Australian Medical Research Future Fund - Clinical Trials Activity Initiative - 2021 Innovative Therapies for Mental Illness - Grant Opportunity released an additional $15M in March 2021 to “assess the safety and efficacy of innovative therapies using hallucinogens and stimulant drugs supported by psychological/psychiatric care for treatment resistant mental illness, compared to standard therapies clinical trial research being undertaken in Australia”\(^\text{95}\).

8.3 If psychedelic substances were to be rescheduled as ’Controlled Substances’ (Schedule 8) and available for clinical use, there would be additional barriers which could limit their widespread use:

a. **Cost** – similarly to medicinal cannabis, if psychedelic substances were to be used more widely, pharmaceutical grade substances are likely to be highly regulated and expensive\(^\text{16,23}\).

b. **Training** – the emerging evidence suggests that the therapeutic benefits of psychedelic substances work in conjunction with psychiatric and psychological treatment to help prepare, guide, and integrate participants’ psychedelic experiences\(^\text{62}\). As described in Sections 5 and 9, psychologists could play a crucial role in psychedelic-assisted therapy. Adequate training and professional development to prepare the psychology workforce would be required to ensure that the strict treatment protocols are followed, and necessary patient screening is undertaken.

c. **Availability of appropriate settings** – at least initially, it will be important that psychedelic-assisted therapy will be conducted in hospitals and other controlled settings to enable appropriate monitoring and ensure access to medical and acute psychiatric/clinical psychological assistance if adverse effects occur.

8.4 The worldwide advancement of personalised medicine is also starting to influence healthcare in Australia. It is foreseeable that the development of individual mental health treatment plans will consider genetic information, medical and psychological history, success of previous treatments, personal preferences, and individualised risk profiles to determine the optimal treatment approach. If psychedelic-assisted therapy was to become available in Australia, it would be important to consider these factors in determining the suitability of the treatment for individuals.
9. The APS position

9.1 The APS welcomes the emergence of safe, evidence-based treatment options to address the shortcomings of currently available medication options for individuals with mental health disorders. Psychologists are ethically bound by the principle of beneficence. The APS has a duty to support the development of emerging evidence-based treatments and clinical trial research into promising therapeutic options, provided they are conducted with patient well-being and safety being paramount.

9.2 The APS is encouraged by the emerging evidence which has led to the FDA 'breakthrough designation' for MDMA-assisted psychotherapy to treat PTSD, and psilocybin-assisted psychotherapy to manage treatment-resistant depression. Both offer many advantages over other alternate treatment options for refractory mental health conditions (e.g. electroconvulsive therapy or ketamine infusion therapy).

9.3 Despite the promising early evidence from the recent ‘renaissance’ of scientific research into psychedelics, understanding of the psychological processes of change underlying the observed benefits is limited. Until positive evidence is available from Phase 3 clinical randomised control trials, there is insufficient evidence for the APS to endorse the widespread adoption of psychedelic-assisted therapy, or other therapeutic options involving psychedelic substances.

9.4 It would be premature for the APS to support the use of psychedelic substances without data regarding the efficacy, safety, potential for abuse, and tolerability of these substances in vulnerable patient populations. Given the recent surge in interest in this field however, the APS anticipates that it may reconsider the position on a regular basis as additional evidence becomes available.

9.5 Every therapeutic intervention carries some element of risk, however, not intervening or using ineffective treatments also carries its own risk. Rates of suffering, relapse, and even suicide, for individuals with treatment resistant psychological disorders are still unacceptably high. It is for this reason that the APS supports ongoing systematic research investigating the therapeutic applications of psychedelics. Given the inhomogeneity of different psychedelics’ effects and safety and efficacy profiles, it is not appropriate to treat them the same. Specific research is required to determine each substance’s therapeutic potential.

9.6 It important to consider, however, that throughout the decades, there have been a number of ‘waves’ of public excitement and expectation that new treatment options will be the mental illness panacea. There are valid arguments to suggest that there is a current overreliance on medications to ‘fix’ mental health disorders. Not only do all psychoactive medications carry their own risks and side effects, improvements that occur as a result of taking medication can help fuel an external attribution of change (i.e. symptoms improved due to an external factor – a drug) rather than an internal one. Such an attribution can help perpetuate a dependence on medications and/or result in relapse. This can be further exacerbated by the anticipation of any discontinuation (e.g., withdrawal) effects or tolerance to effects with sustained use.
9.7 Psychedelic-assisted therapy has the potential to mitigate some issues related to tolerance and attribution as manualised protocols suggest low numbers of doses of psychedelic substances (typically 1-3 doses) and the therapy component of the treatment is emphasised. In addition, current evidence suggests that psychedelics typically do not induce physical dependence, although tolerance to effects may be problematic in sustained use. It is important that future research rigorously investigates the issues of tolerance, physical and psychological dependences when studying psychedelic-assisted therapy to treat mental health conditions.

9.8 As the interest in the therapeutic potential of psychedelic substances continues to increase in Australia, the specific role of psychologists will also evolve. The importance of close "clinically supervised settings" and "intensive professional support" as described by the independent panel for the TGA, suggests that health professionals will be critical in this field. Critically, we would assume that if psychedelic-assisted therapies were to become available, a similar approach to the FDA will be taken. As described in Section 5, therefore, only highly trained, experienced, and presumably regulated mental health professionals should be providing psychedelic-assisted therapy. Therefore, psychologists should play the crucial, lead role in delivering psychedelic-assisted treatment. This is due to the profundity of the experience in addressing and accessing highly emotional, and often traumatic, material. An in-depth understanding of psycho-emotional processes and their interaction in mental-health treatment, while undertaking a trauma-informed approach will be necessary to ensure patient safety and treatment efficacy.

9.9 As Australian psychologists' peak body, the APS aligns with the Royal Australian New Zealand College of Psychiatrists (RANZCP) and other health professionals' peak bodies to be a collaborative voice to determine how treatment is developed and regulated in Australia and what role psychologists have in providing these services. Given our evidence base, experience, and training in working with vulnerable patient populations, it is imperative that psychological expertise is utilised in the development of this emerging field. In addition to undertaking a lead role in the delivery of psychedelic-assisted therapy, we would also consider the role of psychologists would be to participate in inter-disciplinary relationships with a view to establishing joint educational opportunities and knowledge sharing. As the RANZCP and other professional bodies' positions solidify, we endeavor to work collaboratively to ensure the best health outcomes for Australians.

9.10 Currently, most of the training of psychedelic-assisted psychotherapists is conducted in the context of clinical trials. This has the advantage of being informed by the latest evidence-base. If psychedelic-assisted therapy was to become mainstream, training and professional development will be required to adequately prepare the workforce. This must be undertaken in collaboration with regulated professional organisations, to ensure the best-practice, evidence-standards are maintained and propagated throughout the professions. Professional guidelines and stringent screening protocols would also need to be developed.

9.11 The cost and practical constraints related to the delivery of psychedelic-assisted therapy suggest that, currently, it is unlikely that such treatment could become a ‘frontline’ option and would more likely be deployed for patients with treatment-resistant mental health disorders.
### Table 1 - The effects of psychedelics on psychological processes and effects on mental health disorders

#### Classic psychedelics (5-HT<sub>2A</sub> receptor agonists<sup>17,105-107</sup>)

<table>
<thead>
<tr>
<th>Psilocybin - present in the Psilocybe mushroom species&lt;sup&gt;108&lt;/sup&gt;</th>
<th>Effects on psychological processes</th>
<th>Effects on mental health disorders</th>
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<tr>
<td></td>
<td>Cognition</td>
<td>Perception</td>
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<td></td>
<td>• Mystical experience&lt;sup&gt;35&lt;/sup&gt;</td>
<td>• Changes in perception e.g. synesthesia&lt;sup&gt;26&lt;/sup&gt;</td>
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<td></td>
<td>• Transcendence of time and space&lt;sup&gt;35&lt;/sup&gt;</td>
<td>• Visual pseudo-hallucinations and illusions&lt;sup&gt;26&lt;/sup&gt;</td>
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<td></td>
<td>• Sense of meaning and insight&lt;sup&gt;36&lt;/sup&gt;</td>
<td>• Labile mood (e.g. blissful or joyful feeling)&lt;sup&gt;36&lt;/sup&gt;</td>
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<td></td>
<td>• Increased spirituality&lt;sup&gt;36&lt;/sup&gt;</td>
<td>• Mystical experience&lt;sup&gt;35&lt;/sup&gt;</td>
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<td>• Changes in perception e.g. synesthesia&lt;sup&gt;26&lt;/sup&gt;</td>
<td>• Mystical experience&lt;sup&gt;35&lt;/sup&gt;</td>
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#### Effects on mental health disorders

- In an open-label feasibility study, psilocybin assisted therapy had benefits in reducing depressive symptoms in patients with treatment-resistant depression<sup>38</sup>.
- Similarly, other feasibility studies with minimal psychotherapy suggested that anxiety and mood were significantly improved in cancer patients after taking psilocybin<sup>37,38</sup>.
- Using a randomised controlled crossover design, psilocybin-assisted therapy (preparation, medication dosing and postdosing integration sessions) resulted in decreased anxiety and depression in cancer patients<sup>52</sup>.
- Combined with nondirective interpersonal support, psilocybin has been shown in an open-label pilot study to aid smoking cessation<sup>120</sup> and additional research is underway<sup>110</sup>.
- In an open label proof of concept study using psilocybin-assisted therapy (motivational enhancement therapy, preparation sessions, psilocybin-assisted therapy sessions, and debriefing sessions), alcohol-dependent participants reported increased abstinence<sup>111</sup> sparking phase two research<sup>112</sup>.
- Preliminary evidence suggests that psilocybin can relieve symptoms of obsessive-compulsive disorder<sup>113</sup>. Current research to explore this is underway<sup>114,115</sup>.
- Additional research is investigating the use of psilocybin to treat substance use disorders<sup>116</sup>, anorexia nervosa<sup>117</sup>, depression in Alzheimer’s disease<sup>118</sup>, inter alia.
- Current research in Australia is focussing on the potential of psilocybin-assisted therapy in reducing anxiety in end-of-life patients<sup>119</sup> and the psychological and neural effects of microdosing with psilocybin<sup>84</sup>.

#### Lysergic acid diethylamide (LSD)

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<th>Lysergic acid diethylamide (LSD)</th>
<th>Effects on psychological processes</th>
<th>Effects on mental health disorders</th>
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<td></td>
<td>Cognition</td>
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<tr>
<td></td>
<td>• Increased cognitive flexibility&lt;sup&gt;91&lt;/sup&gt;</td>
<td>• Changes in perception e.g. synesthesia&lt;sup&gt;26&lt;/sup&gt;</td>
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<td></td>
<td>• Increased openness&lt;sup&gt;50,91,122&lt;/sup&gt;</td>
<td>• Mystical experience&lt;sup&gt;35&lt;/sup&gt;</td>
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<td></td>
<td>‘Loosened’ cognition&lt;sup&gt;91,121&lt;/sup&gt;</td>
<td>• Transcendence of time and space&lt;sup&gt;35&lt;/sup&gt;</td>
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<td></td>
<td>Insightfulness&lt;sup&gt;122&lt;/sup&gt;</td>
<td>• Sense of meaning and insight&lt;sup&gt;35&lt;/sup&gt;</td>
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Table 1 - The effects of psychedelics on psychological processes and effects on mental health disorders continued

<table>
<thead>
<tr>
<th>Ayahuasca – botanical brew containing dimethyltryptamine and harmine</th>
<th>Effects on mental health disorders in conjunction with psychotherapy</th>
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<tr>
<td>• A pilot study suggested that LSD-assisted therapy can significantly reduce anxiety in patients with life-threatening diseases.</td>
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<td>• Positive and sustained effects on mood and attitudes of LSD may open possibilities for the treatment of mental health disorders.</td>
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<td>• LSD may influence the processing of negative stimuli which play a role in mood and anxiety disorders.</td>
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<td>• Future research will focus on LSD effects on anxiety and the effects of microdosing of LSD.</td>
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<tr>
<td>• Mystical and noetic experiences</td>
<td>• Auditory and visual hallucinations</td>
</tr>
<tr>
<td>• Increased mindfulness</td>
<td>• Altered spatial perceptions</td>
</tr>
<tr>
<td>Ibogaine – psychoactive plant alkaloid</td>
<td>Effects on mental health disorders</td>
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<tr>
<td>Effects on mental health disorders</td>
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<tr>
<td>• Preliminary studies investigating ibogaine treatment found reduced sustained opioid use and withdrawal symptoms and depressive symptoms in substance dependent participants.</td>
<td></td>
</tr>
</tbody>
</table>
Table 1: The effects of psychedelics on psychological processes and effects on mental health disorders. This is not intended to be an exhaustive literature review. The results included have been selected to provide a sense of the effects of the substances and the current state of research investigating their impacts on mental health disorders. Layout adapted from Reiff et al.7

<table>
<thead>
<tr>
<th>Entactogens</th>
<th>3,4-methylenedioxymethamphetamine (MDMA)</th>
<th>Effects on psychological processes</th>
<th>Effects on mental health disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td>Cognition</td>
<td>Perception</td>
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<td></td>
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<td>Positive emotional effects</td>
<td>Negative emotional effects</td>
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<td>• Slight perceptual alterations (not hallucinations)44,45</td>
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<td></td>
<td>• Decreases in neuroticism43</td>
<td>• Euphoria44–46</td>
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<td>• Feelings of authenticity42</td>
<td>• Enhanced well-being45</td>
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<td>• Increased access to emotional material47,48</td>
<td>• Sense of a greater meaning in life47</td>
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<td>• Anxiety41,42,48–50</td>
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<tr>
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<td></td>
<td>• Feelings of being insightful44</td>
<td>• Confusion or ‘drunken’ feeling45,45</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Difficulty concentrating50</td>
<td>• Closeness to others41,52</td>
</tr>
</tbody>
</table>

• In two pilot randomised-controlled trials, patients with treatment resistant PTSD experienced a decrease in PTSD symptoms after MDMA-assisted therapy53,54.
• Importantly, the reduction in PTSD symptoms appeared to be sustained more than a year after the MDMA session56.
• In a phase 2 double-blind randomised-controlled trial, military veterans, firefighters, and police officers with treatment-resistant PTSD reported a reduction in PTSD symptoms and were more likely to be in remission after undergoing manualised MDMA-assisted therapy49. The high MDMA dose group also exhibited a reduction in depression symptoms and the moderate and high dose groups reported improved sleep quality, dissociative symptoms and gains in psychological, occupational and social functioning68. Similar reduction in symptoms and remission rates were found in another phase 2 study55.
• In a randomised, double-blind placebo-controlled phase 3 study, MDMA-assisted therapy was found to reduce PTSD symptoms and reduced functional impairment compared to placebo with therapy in patients with severe, including co-morbid PTSD57.
• In another study, increased openness facilitated by MDMA-assisted therapy predicted reduction in PTSD symptoms43.
• Results from a pilot randomised double-blind study suggest that MDMA-assisted therapy reduced social anxiety symptoms in adults with autism spectrum disorder10.
• In a randomised pilot study, MDMA-assisted therapy trended towards reducing trait anxiety in patients with a life-threatening illness, as well as decreasing depression symptoms and improving sleep quality47.

Table 1: The effects of psychedelics on psychological processes and effects on mental health disorders. This is not intended to be an exhaustive literature review. The results included have been selected to provide a sense of the effects of the substances and the current state of research investigating their impacts on mental health disorders. Layout adapted from Reiff et al.7.


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