GPSA
GENERAL PRACTICE SUPERVISORS AUSTRALIA

FREQUENTLY ASKED QUESTIONS

PODCAST WEBINAR

Psychedelic-assisted therapy for mental illnesses

Mental illness is now at alarming levels in this country, and the situation is only getting worse.

1 in 8 Australians now on anti-depressants

- 1 in 4 of these is an older person
- 18% increase in last 5 years
- 95% increase in last 15 years

1 in 5 Australian adults has a chronic mental illness

Over 45% of Australians will experience mental illness in their lifetime

Impact on sufferers, family & carers
Mental illness is a primary cause of both suicide and homelessness

Impact on the economy & society in general
A conservative estimate for the total cost to the economy =$220 billion each year

Adults with mental illness are nearly *twice* as likely to be unemployed or out of the labour force

The most common mental illnesses

- Post-Traumatic Stress Disorder (PTSD)
- Other Anxiety Disorders
- Depression
- Substance Use Disorders

Mental illnesses and specific groups

AUSTRALIAN DEFENCE FORCE are known to experience:	FIRST RESPONDERS are no better off:
• 10 times the general population's suicidal ideation	• 1 in 10 first responders have PTSD
• 6 times as many instances of comorbidity	• 1 in 3 suffer from high psychological distress
• roughly 3 times as many presentations for PTSD, Depression episodes and Alcohol disorder	• first responders have suicidal thoughts at 2 times the rate of adults in the general population
• more than double the number of mental disorders	• one (1) first responder takes his or her own life every 6 weeks

Inadequacies of current treatment outcomes

DEPRESSION

- combined remission from Depression using standard SSRIs and psychotherapies is currently (at best) 35%
- between 50%-80% relapse after treatment stops
- side effects of current pharmacotherapies are profound, with weaning off antidepressants a difficult process in itself

PTSD

- pharmacotherapy treatments for PTSD have only a maximum of 20%-30% of success

As shocking as the statistics are, there has been no innovation in treatments, and therefore no improvement in treatment outcomes, over the past 50 years.

Addressing the Issue

Mind Medicine Australia (MMA) is a registered charity whose sole intention is to help those suffering with mental illness. MMA research indicates that Australia is behind the rest of the world in the exploration of new treatments. The organisation aims to turn this around by offering a medicine-assisted therapy that has zero toxicity, is non-addictive and takes only 2-3 doses to achieve high remission rates.

MMA supports using psychedelic-assisted treatments in a clinical environment to cure - not just manage - a range of mental illnesses including using medicinal psilocybin (for Depression, and possibly OCD and addiction) and medicinal MDMA (for PTSD and possibly addiction) with additional interest in other psychedelic medicines including ketamine, ibogaine and DMT.

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FAQ

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Are psychedelic-assisted treatments really safe?

THE BROAD FACTS

Psilocybin and MDMA are currently in the final stages of clinical trials.

Both have been granted Breakthrough Therapy Designation by the FDA in the USA. This means the FDA is fast-tracking them through the approvals process. Once through the phase 3 trials, they will become instantly prescriptible. The Phase 3 trials for MDMA conclude at the end of 2021.

GENERAL INFORMATION	TREATMENT
Medicinal Psilocybin	
• Psilocybin takes people into an altered state, effecting the dissolution of ego. • Negligible physiological harm and toxicity. • Very low potential harm profile. • Non-addictive. • With proper clinical support and screening,it has minimal psychological risks. • Fear, panic and re-traumatisation is almost completely mitigated.	• 1-2 active doses of medicinal psilocybin in protocols. • Best suited for depression, anxiety, eating disorders, OCD. • Increases mental flexibility and sensitises the patient to the therapeutic environment. • Psilocybin provides a profound personal experience through dream like imagery and connected feeling. • It has been proposed that integration occurs in a window after treatment where the patient is more open to change.
Medicinal MDMA	
• MDMA helps people to feel warm, loving and more comfortable to speak about their trauma, bringing down barriers and reducing fear and defensiveness to enable the patient to talk about their trauma without being triggered. • MDMA may be neurotoxic in high doses (i.e. well in excess of therapeutic amounts) but has a strong safety record in medically-controlled environments with clear protocols. • Non-addictive. • In clinical studies of MDMA, in over 3000 participants using medically-controlled doses, only 1 adverse event (heart rate above pre-set limit) and this was rapidly resolved.	• 2-3 active doses of medicinal MDMA in protocols. • Best suited for PTSD or disorders with underlying trauma (such as addiction). • Disarms a hyper responsive nervous system, allowing a patient to safely approach trauma memories without becoming overwhelmed. • Memories are re-encoded without traumatic emotional connection. • Integration supports the patient to process and move through the traumatic event(s) and connect to the present

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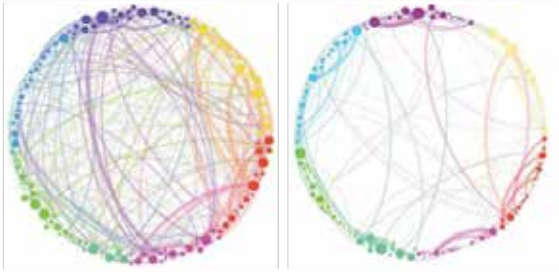
Treating the Cause: Medicinal Psilocybin Assisted-Psychotherapy for Depression

Alters communication between brain networks, such as the Default Mode Network (DMN), which are associated with many mental illnesses.

Enabling patients to 'break out' of repetitive and rigid styles of thinking, feeling and behaving.

Promotes a form of "active coping", restoring patient agency.

Increased communication between brain networks (based on fMRI scans)



Psilocybin **Placebo**

Source: Beckley Foundation, United Kingdom
Based on clinical trials at Imperial College, London

Schenberg, E. E. S. (2018). Psychedelic-assisted psychotherapy... *Frontiers in pharmacology*, *9*, 733.
Petri, G., et al(2014). Homological scaffolds of brain functional networks. *Journal of The Royal Society Interface*, 11(101), 20140873.

THE BRAIN ON PSILOCYBIN Beckley/Imperial Research Programme - A simplified visualisation of connectivity between functional areas and networks in the brain during the resting state under placebo (right) and psilocybin (left). Petri et al. (2014).

Treating the Cause: Medicinal MDMA Psychotherapy for PTSD

MDMA is not ecstasy. Substances sold illegally often have adulterants and are often taken in risky settings with higher doses.

Decreases fear and defensiveness while increasing empathy, trust and safety.

Decreases the activity of the amygdala - associated with traumatic memory.

Not therapy by itself but a catalyst for the therapeutic process.

In a MAPS Phase 2 trial there were 105 participants, all with treatment resistant PTSD (who on average had PTSD for 18 years), led to remission in 52% of cases immediately and in **68% at the 12 month follow up.**

Phase 3 trial taking place at 15 research sites in the U.S., Canada, and Israel. Interim analysis of the data revealed **90% or greater probability that there will be statistically significant results** when all participants have been treated. **MDMA is likely to be prescribable in 18 months in USA.**

Mithoefer, M. C., Feduccia, A. A., Jerome, L., Mithoefer, A., Wagner, M., Walsh, Z., ... & Doblin, R. (2019). MDMA-assisted psychotherapy for treatment of PTSD: study design and rationale for phase 3 trials based on pooled analysis of six phase 2 randomized controlled trials. *Psychopharmacology*, 1-11.

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The treatments

Administered in a medically-controlled environment, psychedelic assisted treatments are facilitated by psychiatrists and psychologists in clinics and hospitals. The location is essential as it must allow for medical supervision (MDs, nurses, monitoring equipment) while the "talk therapy" is conducted alongside the ingestion of the relevant psychedelic compound.

In contrast to the ongoing daily medications required for conventional pharmacology, only 1-3 psychedelic-assisted treatments are needed to achieve the desired outcome.

These treatments emphasise non-avoidance and curiosity, commonly creating substantial increases in self-awareness, self-compassion, insight, connectedness and meaning. Indeed, patients describe these experiences as amongst the most meaningful in their lives, promoting a sense of oneness and connection with everything - which is in stark contrast to the prevalent feeling of disconnection suffered by people with mental illnesses.

There are three (3) distinct therapy phases that take place over several weeks including a) preparation b) acute medicinal experience and c) integration. Between 1- 3 combined pharmacotherapy/ therapy sessions facilitated by a psychiatrist and psychologist and supported by clinical facilities including doctors, nurses and monitoring equipment.

Psilocybin-assisted therapy sessions Johns Hopkins Uni

Clinical Safety Features

MEDICINAL PSILOCYBIN	MEDICINAL MDMA
• Negligible physiological harm and toxicity with very low potential harm profile and **non-addictive**. • With proper clinical support and screening, minimal psychological risks (fear, panic, re-traumatisation) are almost completely mitigated. • A 2015 review found there to be no link between psychosis and psychedelic use.	• **High doses well in excess of therapeutic amounts** may be neurotoxic but strong safety record in a medically controlled environment with clear protocols and **non-addictive.** • In clinical studies of MDMA in over 3000 participants using medically controlled doses, only 1 adverse event (heart rate above pre-set limit) and this was rapidly resolved.

Johansen & Krebs. "Psychedelics not linked to mental health problems or suicidal behaviour: A population study." Journal of Psychopharmacology 29.3 (2015): 270-279

Results that are building momentum

- Trials also planned/underway using **medicinal psilocybin assisted-psychotherapy** for **depression in early-stage dementia** (Johns Hopkins), **anorexia** (Imperial College) and **obsessive-compulsive disorder** (OCD) (MAPS) and **medicinal MDMA-assisted psychotherapy** for **alcohol addiction** (Imperial College). Recently, a pre-clinical trial began to examine psilocybin for weight loss (NeonMind) and schizophrenia.
- Regulatory schemes in the US (Expanded Access), Australia (Special Access) and Israel (Compassionate Use) enable physicians to apply to the Regulator for approval to treat patients suffering from treatment resistant PTSD with Medicinal-MDMA and psilocybin psychotherapy for depression outside of a clinical trial. Switzerland has a similar scheme allowing LSD, Psilocybin and MDMA to be used with psychotherapy.
- Denver (Colorado) and Oakland (California) decriminalised psilocybin possession in 2019, Ann Arbor (Michigan) in September 2020 and Sommerville (Massachusetts) in January 2021.

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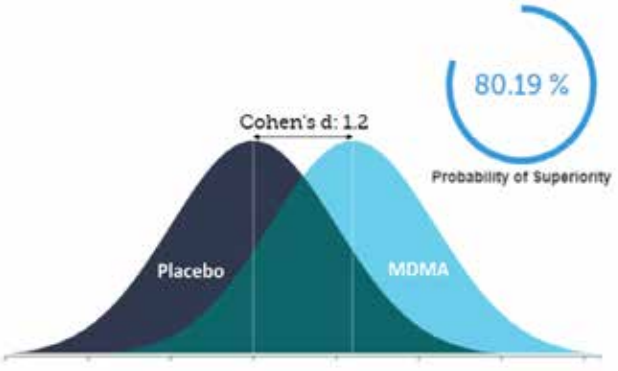
- Oregon (USA) became the first state to legalise psilocybin for therapeutic use in November 2020 and California likely to vote in 2021 on whether to legalise medicinal psilocybin.
- Canadian government allows (August 2020) terminally ill patients to access psilocybin-assisted psychotherapy to help ease anxiety.
- The German government has approved a phase 2B study on psilocybin for treatment-resistant depression and is providing millions of Euros to the project.

Delivering remarkable treatment options

- Most effective treatments for mental illness show *effect sizes* in the order of d=0.5 (where 0.2='small'; 0.5='medium'; 0.8='large' treatment benefit)
- Medicine-assisted psychotherapy effects are 'off the charts'
  - Psilocybin for depression: *d*=2.0-3.1
  - Psilocybin for end-of-life distress: *d*=0.8-1.6
  - Psilocybin for alcoholism: *d*=1.2-1.4
  - LSD for end-of-life distress: *d*=1.1-1.2
  - MDMA for PTSD: *d*=1.17-1.24 (see graph)
- Antidepressants (SSRI's) for depression: *d*= 0.3



Schenberg, E. E. S. (2018). Psychedelic-assisted psychotherapy… Frontiers in pharmacology, 9, 733.
Hengartner, M. P., & Plöderl, M. (2018). Statistically significant antidepressant-placebo differences on subjective symptom-rating scales do not prove that antidepressants work: Effect size and method bias matter. Frontiers in psychiatry, 9, 517.

Australia

Australia has commenced its first trial of the use of psilocybin for end of life anxiety (at St Vincent's Hospital Melbourne). There are substantial plans underway for additional trials in the use of psilocybin for generalised anxiety and MDMA for substance abuse. Monash University in Australia has an active psychedelic research program.

Some barriers currently remain at the State level around Australia because of a legislative failure to distinguish between the recreational and medical use of these substances. Mind Medicine Australia has applied for the rescheduling of psilocybin and MDMA to Schedule 8 (Controlled Medicines) to make medical access around Australia easier. A final decision by the TGA is expected by the end April 2021 - you can keep up to date with this at https://mindmedicineaustralia.org.au/

The role of GPs is to be informed about the treatment options, as an increasing number of patients will ask you about it. As more trials open up (many are expected) GPs can refer patients to them. GPs can also undertake the Certificate in Psychedelic Assisted Therapies (CPAT) - https://cpat.mindmedicineaustralia.org/?source=MMA-website

Does this resource need to be updated? Contact GPSA: P: 03 5440 9077, E: ceo@gpsupervisorsaustralia.org.au, W: gpsupervisorsaustralia.org.au
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