



The Psychedelic Renaissance

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Recent studies are finding that psychedelic medicines are effective treatments for mental health disorders such as depression, anxiety, post-traumatic stress disorder and addiction.

Mental health statistics are sobering to read: 45% of Australians will experience a serious mental health illness in their lifetime, suicide is the leading cause of death among young people in Australia, and mental illness is predicted to become the leading cause of disability and disease worldwide by 2020. Awareness, education and better therapeutic solutions are required if we are to alleviate both the suffering of individuals and the burden of mental health disease on society.

To understand the problem, let's investigate the origin. The 100 trillion neural connections mapping each of our brains form a unique neuronal tapestry of learned meaning created

by experience and reinforced by self-narration. Neuronal paths that are frequently activated, by repetitive thoughts or behaviours, steadily become stronger.

But the mind's automated adaptivity can go awry in mental illness, caging sufferers in rigid patterns of thought and behaviour. This is particularly insidious in instances of early trauma, where storylines tend to be relived throughout life. How can we best support patients with mental illness to regain agency and reorient their life path?

Recent research has shown that psychedelics, in combination with psychotherapy, can reduce suicidality, ease end of life anxiety, and offer a road out of both depression and addiction, all with as few as one or two doses. This is in striking

contrast with traditional pharmacotherapy, which usually requires daily dosing of a pharmaceutical medication, such as an antidepressant or anxiolytic, for extended periods.

Recently the US Food and Drug Administration awarded psilocybin (a naturally occurring compound in numerous species of “magic mushrooms”) and MDMA (commonly known as the recreational drug “ecstasy”) breakthrough status as therapies for depression and post-traumatic stress disorder (PTSD), respectively. However, despite the growing recognition of psychedelic medicines in science, their broader acceptance has been limited by cultural misconceptions.

The word “psychedelic” was coined in 1956 by British psychiatrist Dr Humphry Osmond, in correspondence with author and futurist Aldous Huxley, to describe the “mind-manifesting” properties of psychedelics as therapeutic adjuncts. The “psychedelic renaissance” follows the first wave of research that took place after the 1938 synthesis of LSD and the subsequent discovery in 1943 of its profound effects on human cognition and consciousness.

LSD’s structural similarity to serotonin precipitated the first scientific consensus acknowledging the link between brain chemistry and behaviour, giving rise to the field of neuropsychopharmacology. Thousands of research papers were published on psychedelic therapy between 1950 and 1965. Bill Withers, a participant in a study treating alcohol addiction, went on to found Alcoholics Anonymous (AA). His experiences of insight and connection through LSD therapy influenced the AA program.

However, the budding science of psychedelic therapy was largely forgotten after psychedelics became caught in the crossfire of the anti-Vietnam war and hippie movements of the late

1960s, and they became inextricably associated with this counterculture. The first wave of psychedelic research came to a halt in the early 1970s; as President Richard Nixon’s “War on Drugs” prohibited psychedelics, legitimate research and clinical practice suffered deep collateral damage.

Nonetheless, interest remained just below the surface throughout the 30-year moratorium, and a more sophisticated conversation about the use of psychedelic medicines began to evolve with the development of improved research techniques. Since 2001, a significant number of randomised controlled trials (RCTs) has profoundly changed the research landscape and paved the way for psychedelic psychotherapy. In a meta-analysis of 19 studies that included 423 individuals with psychiatric diagnoses (<https://bit.ly/2FvsjDz>), 79% of patients treated with psychedelic medicines showed significant clinical improvement. None of these studies reported any serious adverse effects, toxicities or dependency relating to psychedelics.

The US-based Multidisciplinary Association for Psychedelic Studies (MAPS) has pioneered research investigating MDMA-assisted psychotherapy for PTSD. A Phase 2 study found that 83% of participants no longer met the criteria for PTSD after 12 sessions of psychotherapy, including just two MDMA sessions (<https://bit.ly/2RsXENH>). These effects were largely maintained at a 3½-year follow-up, with only 10% of participants having relapsed. With Phase 3 trials now underway, MAPS expects that MDMA will be approved as a prescription medicine in the USA by 2021.

These results are poignant, as PTSD is notoriously difficult to treat. Patients’ nervous systems are dysregulated by chronic activation of the stress response, and are easily overwhelmed during psychotherapy due to a narrow window of tolerance,



Recently the US Food and Drug Administration awarded psilocybin, a naturally occurring compound in several species of “magic mushrooms”, breakthrough status as a therapy for depression.

Credit: Atomazul/Adobe

specifically relating to the anxiety elicited by re-experiencing, addressing or even discussing the trauma. MDMA engenders a sensation of safety, expanding the window of tolerance and thus allowing patients to work intimately with traumatic memories.

Two recent RCTs of psilocybin-assisted psychotherapy for psychosocial distress associated with terminal illness have been published. The first, at New York University, was a crossover study with 15 active participants and 16 placebo participants (<https://tinyurl.com/y7q5a7oz>). The researchers found that from baseline to a day following the first drug therapy session, 83% of participants in the psilocybin group met the criteria for an antidepressant response and 58% met the criteria for an anxiolytic response, while only 14% in the placebo group experienced remission of each condition. Participants in the psilocybin arm also reported improvements in their physical health and social relationships compared with the control group 6 months after treatment.

The second trial, at Johns Hopkins University, was a double-blind RCT of 56 end-stage cancer patients in which a low dose of psilocybin was used as a control (<https://tinyurl.com/ybv3csue>). More than 80% in the high-dose psilocybin condition exhibited significant reductions in several measures of depression and anxiety, and improved quality of life. These effects were maintained at a 6-month follow-up.

Meanwhile, at Imperial College London, an open-label trial of psilocybin-assisted therapy among 12 participants with treatment-resistant depression (<https://bit.ly/2Mc39KO>) showed promising results, eliciting a significant improvement in eight

of the participants (67%) a week after the psilocybin session. Seven of the participants (58%) no longer met the criteria for depression at a 6-month follow-up. A Phase 2 trial investigating psilocybin for depression is now underway.

An open-label trial at Johns Hopkins University studied psilocybin-assisted psychotherapy for the treatment of tobacco addiction (<https://bit.ly/2MayeyF>), and found that 10 of 15 participants (67%) were abstinent at a 12-month follow-up. This compares with the results of treatment with varenicline, the most efficacious pharmacotherapy for smoking cessation; following treatment, only 25.5% of participants were abstinent at 12 months. A proof-of-concept study of psilocybin-assisted psychotherapy at the University of New Mexico has found similar effects in treating alcohol dependence (<https://tinyurl.com/y9wsjzvo>).

The mechanism of these positive changes is thought, in part, to be mediated by changes in brain network connectivity. The default mode network (DMN) is a hub of functional connectivity associated with introspection and autobiographical memory – our self-story. A 2017 fMRI brain imaging study at Imperial College London (<https://go.nature.com/2DbZAl6>) found that psilocybin acutely decreases functional connectivity in the DMN and increases connectivity between other diverse regions of the brain. The authors propose that psychedelic downregulation of the DMN, along with increased communication throughout the brain, creates a state of cognitive flexibility.

In contrast, addiction, depression and anxiety are characterised by cognitive rigidity and DMN upregulation. It is proposed that psychedelically mediated cognitive flexibility may help break the mind out of a “cognitive rut” and provide the opportunity for a neural “reset” by utilising less developed pathways. By increasing the permeability between conscious and unconscious, between the old and the new, patients discover paths less travelled and craft new ones to update their concept of self.

International research continues to highlight the therapeutic potential of psychedelic medicines to heal mental suffering, cultivating well-being and helping patients reconnect to meaning. Despite this, Australia has so far failed to contribute to this promising field. Research within Australia is vital for the development of psychedelic medicines into regulated therapeutics.

Psychedelics represent a class of medicines that have the potential to shed light on the underlying processes of the mind, the origins of illness and psychological well-being. Just as psychedelic medicines allow patients to re-perceive their lives, we all need to check our biases and re-perceive the importance of psychedelic medicines. By updating our perceptions of psychedelic medicine, we may provide the opportunity for conscious change and a fresh perspective for those who need it most.

Mind Medicine Australia

Mind Medicine Australia is a registered health promotion charity that aims to pave a path for next-generation mental health care in Australia. Responding to the need for a central node for the promotion of regulatory-approved and research-backed psychedelic medicines, Mind Medicine Australia supports the development of government-approved psychedelic therapy in Australia and collaborates closely with Psychedelic Research in Science and Medicine (PRISM), a non-profit research organisation.

Mind Medicine Australia supports a holistic view of health and recognises the whole patient, including experiences, environment, health and pharmacology. We regard mental illness as treatable, not simply amenable to maintenance therapies. Driven by compassion, innovation and empiricism, Mind Medicine Australia seeks to change the mental health paradigm in Australia by pioneering innovative treatment approaches that can translate clinical research into therapeutic practice and positive patient outcomes.

Mind Medicine Australia was launched in February and is seeking strategic partners, donors, volunteers and scientific advisors and researchers who are passionate about changing the paradigm for mental health in Australia.

For more information and to get involved visit www.mindmedicineaustralia.org.au

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