Advances in Complementary and Integrative Medicine

Science Publication Inc.

Brief Report Open Access

# Psychedelic-assisted psychotherapy and its potential to manage demoralisation: A brief exploration of an alternative approach to end of life care

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Received: September 16, 2024; Revised: November 18, 2024; Accepted: March 21, 2025; Published: May 07, 2025

**Abstract**

Australia has become the first country to legalise the use of psychedelics, namely MDMA and psilocybin, for the clinical treatment of post-traumatic stress disorder and treatment-resistant depression. Here, the history of its use, how it works, and the hope it may provide people receiving end-of-life care for depression and demoralisation is briefly explored.

**Keywords** Psychedelic-assisted therapy, demoralisation, end-of-life care

## 1. Background and purpose

### 1.1 Australia cautiously permits psychedelic-assisted psychotherapy

On July 1st 2023, psychedelic substances psylocibin and 3,4-methylenedioxymethamphetamine (MDMA, also known colloquially as "ecstasy") were down-scheduled in Australia for therapeutic use [1]. However, the Therapeutic Goods Administration permitted its clinical use for two indications only: post-traumatic stress disorder (PTSD) and treatment-resistant depression. Owing to its mechanism of action, psychedelics could potentially have a role in mental health conditions which are associated with neurobiological changes including addiction and existential distress namely, demoralisation (discussed further below) [2, 3].

### 1.2 Psychedelics may create optimal conditions for environmental input to have enduring effects on the adult brain

Psychedelics re-open the critical period for social reward learning, which is associated with receptiveness to social and environmental experiences leading to the development of prosocial behaviours such as empathy and neuroplasticity. This means psychedelics may have the potential to re-program neurobiological changes involved in some psychological conditions such as PTSD, depression and addiction. Psychedelics target a wide range of neuroreceptors including 5-$HT_{2a}$ receptors and monoamine transporters, which is involved in the same pathways targeted by antidepressants such as Zoloft® and Aurorix®. Other targets include kappa-opioid receptors and N-methyl-D-aspartate receptors which have a role in anti-nociception and the regulation of neuroexcitatory pathways [4, 5].

### 1.3 Psychedelics have been used as medicine by ancient civilisations

Traditionally consumed to build or reinforce social connectedness as part of spiritual practices, psychedelic herbs have been used for millennia in various parts of the world; ayahuasca in South America, peyote in North America and ibogaine in West Africa. In the modern era, promising research into psychedelics emerged in the 1960s but was embargoed as a political reaction to the so-called 'War on Drugs' [6]. Nonetheless, there is evidence to suggest that psychedelics do not induce the same degree of reward signaling compared addictive drugs such as cocaine, which is desirable for dampening the potential for drug-seeking behaviour typically associated with withdrawal [7, 8]. That said, the use of psychedelics is not without its risks, particularly under uncontrolled conditions. Reported side effects have included psychosis, delusions, depressive symptoms and dysphoria, which emphasises the importance of 'set, setting and integration', which refers to the practice of careful preparation prior to administra-

tion of psychedelic medicines, support during administration, and therapeutic follow-up by experienced professionals [9].

### 1.4 Demoralisation and implications of psychedelic-assisted psychotherapy at the end-of-life

Targeted treatment may be long due for demoralisation, which is more robustly associated with suicidal ideation than major depressive disorder in patients with a serious illness such as cancer [10-13], and perhaps even more so today as patient refusal of life-sustaining treatments, food or water and voluntary-assisted dying are being accepted as medical alternatives. The latest International Classification of Diseases (ICD-11) defines demoralisation syndrome as a mental state of disheartenment, impaired coping, feeling trapped, hopelessness, loss of meaning and purpose in life, desire for hastened death, and functional impairment [14, 15]. It is important to note that demoralisation is clinically distinguishable from depression. Notable distinctions observed in people with demoralisation, includes motivation, experience of pleasure and capacity to react which generally remain intact despite fluctuation in symptoms. Furthermore, symptoms associated with depressive disorders including sleep, appetite, energy and concentration, do not appear to be apparent in people with demoralisation only [14, 16, 17]. Supportive counselling which may involve unstructured, supportive interaction with a caring provider has been suggested as first-line treatment for demoralisation [18].

In a variety of medical settings (including gastroenterology, cardiology, endocrinology, and oncology), a majority of people who experience demoralisation do not satisfy the criteria for depression. Whilst in people with major depression, demoralisation co-existed in more than half of the group. Hence, treatment should be targeted and involve addressing the potential causes of demoralisation in addition to the use of pharmacological treatment for depressive features [14, 19]. The prominence of demoralisation also highlights the significant impact of psychosocial distress and importance of screening for allostatic overload, which corresponds to the biopsychosocial experience that arises when the cumulative demands of external stressors become chronic and exceed a person's capacity to cope [20]. Hence, other environmental factors such as life events, unemployment and adverse living conditions can also contribute to allostatic overload and overall disease burden [21, 22].

A rational approach would involve directly lowering or removing the impacts of the stressors, as well as address the psychosocial stress and the human experience of loss and hopelessness through whole-person approaches such as spiritual care, meaning-centered psychotherapy and dignity therapy [23-28]. Systematic reviews have suggested that spiritual well-being may be a protective factor against demoralisation and brief psychosocial interventions alone may also lead to small improvements [29, 30]. However, there is still work to be done for spiritual care to be integrated into standard medical care, requiring significant individual and systems levels interventions to foster motivation, skill development and supportive work environments [23, 31].

It is worthwhile noting that the positive change in demoralisation rendered by brief psychosocial interventions may be underestimated, as it is generally not a primary outcome of existing studies and participant demoralisation levels have been low at baseline. Nonetheless, emerging evidence suggests psychedelic-assisted psychotherapy as safe and suitable, especially where effective treatments are limited for the treatment of depression, anxiety and existential distress [2]. Furthermore, sustained improvements in demoralisation have been noted for up to 4.5 years after ingestion of a single dose of psilocybin received in conjunction with psychotherapy [32, 33]. Unfortunately, the cost of psychedelic-assisted psychotherapy may be inhibitory for some people (currently estimated to cost between 25k-35k AUD), with the bulk of the costs being linked to the multidisciplinary care to ensure appropriate 'set, setting and integration' for safe administration [34]. In the treatment above, this involved a total of 6 sessions (equivalent to 12 hours) of pre-ingestion preparation and post-ingestion integrative psychotherapy administered over a seven-week period [32]. However, treatment can be expected to become more affordable due to economies of scale that accompanies time and experience [35].

## 2. Conclusion

Future work may focus on the development and implementation of standardised spiritual care and targeted brief psychosocial interventions for people with moderate to severe demoralisation. In the meantime, there is value in exploring psychedelic-assisted psychotherapy as a treatment option for addressing demoralisation.

## Author Contributions

The author did all the research work for this study.

## Competing Interests

No conflicts of interest exist.

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