The last three decades have witnessed the dawning of the ‘Psychedelic Renaissance’, a return of biomedical research investigating psychedelic compounds as therapeutic tools in psychiatry. Evidence is accumulating that highlights the therapeutic efficacy of administering human-grade psychedelic compounds in controlled clinical settings. Countries such as Brazil, Canada, Israel, Spain, Switzerland, the United Kingdom and the United States are leading this field of research, delivering upwards of 50 clinical trials and pre-clinical trials with high translational power in the last three decades. However, Australia and New Zealand are currently failing to acknowledge such evidence and, as a result, are falling behind in this crucial time of biomedical research and innovation.

The debate regarding psychedelics presented so far in the *Australian and New Zealand Journal of Psychiatry* has highlighted that the reasons for this failure are mostly political: government bodies still stigmatise psychedelic compounds as illegal drugs of abuse with no therapeutic applications, and academic conservatism leads institutions to be wary of potential controversy that could arise from involvement in this field of research (Puspanathan, 2017). Therefore, since Australian academic research relies on the government funding model (National Health and Medical Research Council/Australian Research Council), with limited additional project funding available within universities, no research in this crucial area has thus far been possible.

The author presents the new perspective that psychedelic compounds activate cellular programmes involved in the treatment and remission of several mental illnesses including (but not limited to) cell survival, neuroplasticity and neuroimmunomodulation, while causing fewer side effects compared to routinely prescribed psychiatric medications. The author suggests that an evidence-based approach towards the molecular effectiveness of psychedelic compounds in psychiatry is required in order for funding and academic bodies to rise above stigma, soberly acknowledge and integrate the evidence generated by emerging research, and adjust their policy and outlook accordingly. This could lead to a shift in governmental, public and academic acceptance of this kind of research, and to the allocation of governmental funding for the fostering of world-class psychedelic research in Australia and New Zealand.

**Recent research on the therapeutic benefits of psychedelic compounds**

Contemporary research on psychedelic compounds corroborates the reports of anxiolytic and antidepressant effects in studies performed before the blanket ban was laid upon psychedelic research in the late 1960s. Recent randomised controlled trials (RCTs) have highlighted therapeutic benefits of 

3,4-methylenedioxymethamphetamine (MDMA) for treatment-resistant post-traumatic stress disorder and autism, and psilocybin for smoking cessation. In a recent RCT, a Brazilian treatment-resistant depression cohort was dosed with ayahuasca, a psychedelic tea used in the Amazon for medicinal and spiritual purposes (Palhano-Fontes et al., 2018). The authors reported that a single dose resulted in rapid antidepressant effects compared to placebo. This is remarkable considering the depressive history of these patients; on average, major depressive disorder had persisted for 11 years and four medications had been trialled with no benefit (Palhano-Fontes et al., 2018). Such fast-onset antidepressant effects contrast with the delayed onset of routine antidepressants, which ranges from days to weeks.

Despite the obvious advantages of a fast-acting therapy for MDD, the question remains as to whether the improvements in depressive symptomatology are long-lasting, or temporary. Another RCT performed in the United States suggests that psychedelic therapy, when combined with psychotherapy, creates psychological improvements which are sustained over time (Griffiths et al., 2016). In this study, patients with life-threatening cancer, and anxiety and depression associated with their...
condition, were administered psilocybin, the psychoactive compound found in ‘magic mushrooms.’ A single dose of psilocybin coupled with psychotherapy elicited rapid, robust and sustained improvements in cancer-related anxiety and depression. The patients reported decreased cancer-related existential distress, increased life quality and spiritual wellbeing, and an improved attitude towards death. Remarkably, such improvements were still present 6 months after the experimental session (Griffiths et al., 2016).

**Molecular mechanisms underpinning the therapeutic benefits of psychedelic compounds**

If psychedelic compounds may be useful in psychiatry, it is vital to understand the molecular mechanisms underpinning their therapeutic benefits, in order for legislative and funding bodies to acknowledge their usefulness. In fact, this kind of evidence could form a catalyst in de-stigmatising and normalising psychedelic compounds as therapeutic agents. A recent breakthrough study deciphered some of those molecular mechanisms (Ly et al., 2018). In this study, psychedelics were shown to promote functional and structural neural plasticity. The main findings include increased neuritogenesis, spinogenesis and synaptogenesis in vitro and in vivo. These morphogenetic changes are driven by an increase in brain-derived neurotrophic factor (BDNF), which regulates neuronal plasticity by activating mechanistic target of rapamycin (mTOR), a key signalling cascade modulated by standard antidepressant and antineurodegenerative drugs (Ly et al., 2018).

Given the observed effects on neuroplasticity and immunomodulatory pathways, it cannot be excluded that psychedelics could prove useful in treating diseases underlined by neurodegeneration, such as Alzheimer’s and Parkinson’s disease. While further studies are needed to validate these findings, the rationale is compelling for expanding the reach of psychedelic research to neurodegenerative states.

**The risk of adverse effects of psychedelic compounds in psychiatry**

Although the results so far discussed suggest a wealth of therapeutic benefits that could be harnessed in disease treatment, it is also important to consider the potential negative effects of psychedelic compounds (Nichols, 2016). While psychedelics present low toxicity and are non-addictive, reported mild side effects in clinical settings involve (a) dose-related transient headaches, (b) anxiety, (c) confusion, (d) nausea and vomiting. More serious side effects have been reported following recreational use in uncontrolled settings and include (a) acute panic, which can lead to dangerous behaviour, (b) the exacerbation or manifestation of psychiatric conditions and (c) the manifestation of long-lasting perceptual disturbances (Nichols, 2016). Importantly, given the potential of psychedelic compounds to facilitate access to traumatic memories, psychological support should be provided before, during and after treatment.

Finally, anecdotal evidence indicates that underground psychedelic-assisted therapy has been taking place around the globe since the 1950s. Australians with psychiatric illnesses are becoming impatient with the lack of opportunity to engage in clinical trials and are seeking out psychedelic therapists in the underground. While positive outcomes are often reported from these sessions, the clandestine nature of the movement and the lack of standardised human-grade compounds may paradoxically hinder academic research on psychedelics by generating further negative publicity. This strengthens the argument that it would be timely to foster biomedical research into psychedelic therapy, which could lead to its acceptance and legalisation, while removing the need for such an unregulated underground movement.

**Outlook and conclusion**

Mounting evidence indicates that psychedelic therapy represents an extremely promising line of research. Countries involved in psychedelic research may find themselves at the forefront of a paradigm shift in modern psychiatry. Given the state-of-the-art biomedical, molecular and imaging facilities in Australia and New Zealand, and given our role as top researchers in other fields of medical research, it would be relatively easy for us to become new and key players leading global psychedelic research. In conclusion, Australia and New Zealand require a sober, evidence-based governmental, academic and public acceptance of psychedelic therapy as a tool in the treatment of various disorders affecting the global population. Academic institutions should rise above the stigma and support investigators ready to pursue research on psychedelic compounds. This could result in the allocation of government funding to research groups interested in investigating the therapeutic potential of psychedelic compounds in Australia and New Zealand, which could ultimately lead to improved therapeutic strategies in treating mental illness.

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**ORCID iD**

Antonio Inserra [https://orcid.org/0000-0002-7261-5659](https://orcid.org/0000-0002-7261-5659)
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