We declare no competing interests.

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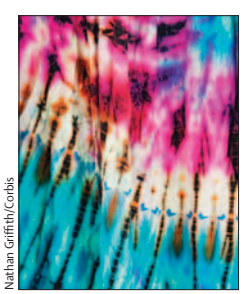
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Turn on and tune in to evidence-based psychedelic research



Nathan Griffith/Corbis

For many people, words such as psychedelic and LSD (lysergic acid diethylamide) refer only to dangerous drugs of abuse. Less well known is that tens of thousands of patients were treated effectively with psychedelic drugs in the 1950s and 1960s,[1] and that these drugs had almost become part of mainstream medicine by the time they became demonised and research was halted for 40 years.

Once again, psychedelic drugs have become a topic of research, with a plethora of new projects across the world. Several charitable and non-government-funded organisations have flourished in recent years, financing international psychedelic studies. The Multidisciplinary Association for Psychedelic Studies, the Heffter Research Institute, and the Beckley Foundation are investigating the potential role for psychedelic-assisted psychotherapy to manage treatment-resistant psychiatric disorders. The classical psychedelic drugs, LSD and psilocybine (the active component in so-called magic mushrooms), are physiologically safe,[2] have a low dependency risk,[3] and might be effective and safe adjuncts to psychotherapy for patients with a range of psychiatric disorders when used at therapeutic doses and in controlled conditions. These psychedelic drugs might also provide existential support and opportunities for personal growth and development.[4,5]

For the **Multidisciplinary Association for Psychedelic Studies** see http://www.maps.org

For the **Heffter Research Institute** see http://www.hefter.org

For the **Beckley Foundation** see http://www.beckleyfoundation.org

Use of psychedelic drugs for the treatment of addictions has been explored since the 1950s. Indeed, Bill Wilson, the founder of Alcoholics Anonymous, was a keen supporter of LSD therapy. A meta-analysis[6] of LSD-based therapy for alcoholism in the 1950s and 1960s gathered several heterogeneous studies. None was as methodologically robust as contemporary research studies, but when analysed together they showed a significant effect size. 60 years later, with pharmacological treatments for alcohol and opiate addictions remaining relatively poor,[7] researchers are now revisiting psilocybine-assisted psychotherapy for the treatment of alcohol dependency.[8] For example, ketamine-assisted psychotherapy yielded positive results in Russia in the 1990s. Evegeny Krupitsky and Alexander Grinenko[9] compared 111 patients with alcohol addiction given ketamine-assisted psychotherapy with 100 patients with alcohol addiction given conventional management. 66% of patients given ketamine-assisted psychotherapy remained sober after 1 year, compared with 24% of the control group.

Anxiety disorders are particularly amenable to psychedelic therapy because the drugs allow the patient to safely revisit painful memories that otherwise block progress with traditional psychological therapies.[10,11] 3,4-methylenedioxymethamphetamine (MDMA) has been used in psychotherapy for patients with post-traumatic stress disorder (PTSD), in which it enables patients to address traumatic memories without any overwhelmingly negative side-effects.[12] A 4 year follow-up[13] of a cohort of treatment-resistant patients with PTSD who were given a single course of MDMA-assisted psychotherapy showed sustained

remission of PTSD. Clinical phase 3 development of MDMA is now on the horizon, with projects underway in Australia, Canada, Israel, Jordan, the UK, and the USA.[14] Patients undergoing MDMA therapy reported a reduction in coincidental tinnitus, so this association is now being investigated.[15] The empathogenic qualities of MDMA[16] are being explored as a way to improve Theory of Mind in patients with anxiety associated with autism.[17]

The function of the psychedelic experience in management of issues associated with death has been studied intensely in the past. Stanislav Grof, Joan Halifax, and Elizabeth Kuber-Ross[18] pioneered the use of LSD-assisted psychotherapy for patients with cancer in the 1960s. Results from two contemporary randomised trials, one using psilocybine[10] and another using LSD,[11] showed successful treatment of anxiety in end-stage cancer. Obsessive-compulsive disorder, which shows substantial resistance to treatment, has been treated successfully with psilocybine-assisted psychotherapy.[19] The anecdotal phenomenon that cluster headaches can be relieved by recreational use of LSD and psilocybin has led to a randomised trial to test this hypothesis.

Psychedelic drugs are also being investigated to advance neuroscience. Results of magnetoencephalography and functional MRI studies[20] at Cardiff University and Imperial College, London, showed that psilocybin and LSD decreased blood flow and reduced electrical activity in the medial prefrontal cortex. These results suggest that the subjective effects of psychedelic drugs are caused by decreased activity and connectivity in the brain's key connector hubs, enabling a state of unconstrained cognition—a contemporary neurobiological perspective of Aldous Huxley's so-called reducing valve hypothesis and an important advance in understanding of the neurophysiological substrates of consciousness. Whether psilocybine-assisted psychotherapy could be developed as a treatment for resistant depression is being investigated (Nutt D, personal communication).

Anthropological links between spirituality and the use of natural hallucinogens exist. Results from a double blind randomised trial with psilocybine in the 1960s showed spontaneous mystical experiences in participants who were otherwise naive to psychedelic drugs. A team at Johns Hopkins University is now exploring how a psychedelic-induced mystical experience can positively affect maladaptive personality traits, with a view to manage addictions.[21]

Despite a controversial history, these drugs could have an exciting future. Important reports[22] challenge the dated belief that MDMA at therapeutic doses causes lasting neurotoxic effects, and results from a large population study[23] of 20 000 users of recreational psychedelic drugs showed no evidence of substantial mental health problems in these people. If the medical profession can continue to concentrate on evidence-based data and avoid the pitfalls and negative bias of the past (panel), the future for psychedelic drug research looks promising.

Panel: Barriers to psychedelic research and mainstream medical practice

Psychedelic drugs-assisted studies are not well funded. The pharmaceutical industry lends little support for psychedelic research. The drugs themselves (LSD, MDMA, psilocybin) are all off patent, the recommended doses are low and infrequent, and they do not require repeated long-term use. Consequently, most funding comes from private and charitable donations, which is slow and laborious.

The saying that "psychotherapy must only occur with the sober patient" is a challenge to psychotherapists and psychologists who are unaccustomed to working with patients in the unique psychedelic mental state.

The War On Drugs of the past 40 years has created negatively biased risk information, which labels any drug with a history of recreational misuse as of limited therapeutic value. Peculiarly, this view does not seem to apply to opiates, even though they are far more toxic and addictive than psychedelics.[24] This erroneous belief requires challenging. Epidemiological and pharmacological evidence indicates that psychedelic drugs can be safe and effective in controlled clinical conditions. Indeed, psychedelic drugs satisfy risk-benefit analysis more robustly than many other medications used in psychiatric practice.

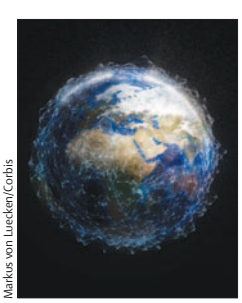
Historical associations with uncontrolled recreational misuse and hedonistic approaches have negatively biased general opinion about psychedelic substances, and this bias might prevent many clinicians from getting involved in psychedelic research. This opinion needs to be challenged by contemporary, sober, and evidence-based approaches.

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Health equity and mental health in post-2015 sustainable development goals



Markus von Luecken/Corbis

Published **Online** November 26, 2014 http://dx.doi.org/10.1016/S2215-0366(14)00094-7

A major attraction of the Millennium Development Goals (MDGs) and a reason for their widespread acceptance was the clear focus on achievement of equity.[1] However, a major criticism of the goals, in so far as they relate to health, is the absence of a clear and categorical commitment to specific normative goals for mental health. This omission is striking since mental illnesses contribute to nearly a quarter of total years lived with disability across all disorders worldwide,[2] but receive disproportionately low policy and budgetary attention, especially in low-income and middle-income countries, where only 0·5–1·9% of the overall health budget is allocated to mental health.[3]

Since the launch of the MDGs, several important developments have occurred that point to a growing recognition of the need to pay greater attention to mental health in the overall development agenda. The WHO Executive Board resolution of January, 2012,[4] and the more recent adoption by WHO of a Comprehensive Mental Health Action Plan 2013–20[5] are examples. Notably, evidence[6] for effective and affordable interventions for the most common mental health disorders has also become increasingly compelling. As a result, a post-2015 global effort to set new developmental goals might offer an important opportunity to galvanise this growing international attention to mental health. Such attention would commit governments (including those of low-income and middle-income countries) and international development organisations to scale up treatment and services for psychosocial disabilities. The notion of "no health without mental health",[7] embraced and promoted by WHO, is an attestation of the primacy of mental health to any consideration of achieving health for all. It is more than an attestation: it is a reminder that if equity in health is a goal, attention to mental health cannot be ignored.