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Psilocybin for anxiety and depression in cancer care? Lessons from the past and prospects for the future

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This special issue of the *Journal of Psychopharmacology* contains two landmark studies – the most rigorous controlled trials to date using the psychedelic drug psilocybin, the active ingredient of magic mushrooms (Griffiths et al., 2016; Ross et al., 2016). These were conducted in patients with anxiety and depression and existential distress in the context of having a diagnosis of cancer, and they showed that a single psychedelic experience could produce profound and enduring mental health benefits.

To many people brought up in the Reagan drug war era with the ‘drugs fry your brain’ message, psilocybin may seem a strange and possibly even a dangerous drug treatment of serious mental illness. For this reason, we have asked a number of significant figures in relevant research areas to provide commentaries on the two studies. These experts in the fields of psychiatry, trial design and end-of-life care provide their perspective on the research and its implications for clinical practice. The fact that everyone we approached agreed to provide a commentary, despite short notice, is a testimony to the interest that these two studies have sparked.

The honours list of the commentators reads like a ‘who’s who’ of American and European psychiatry, and should reassure any waverers that this use of psilocybin is well within the accepted scope of modern psychiatry. They include two past presidents of the American Psychiatric Association (Lieberman and Summergrad) and the past-president of the European College of Neuropsychopharmacology (Goodwin), a previous deputy director of the Office of USA National Drug Control Policy (Kleber) and a previous head of the UK Medicines and Healthcare Regulatory Authority (Breckenridge). In addition, we have input from experienced psychiatric clinical trialists, leading pharmacologists and cancer-care specialists. They all essentially say the same thing: it’s time to take psychedelic treatments in psychiatry and oncology seriously, as we did in the 1950s and 1960s, which means we need to go back to the future. As the commentaries point out, much more research needs to be done into optimising this approach, evaluating the breadth of possible target disorders and exploring the underpinning mechanisms. But the key point is that all agree we are now in an exciting new phase of psychedelic psychopharmacology that needs to be encouraged not impeded.

When Albert Hoffman discovered the remarkable mind-altering properties of lysergic acid diethylamide (LSD) in 1943, he didn’t have much trouble persuading his bosses at the pharmaceutical company Sandoz (now part of Novartis) that this drug would play a very important role in understanding the nature of mental illness and potentially providing a very novel approach to

their treatment. Through the 1950s and 1960s, Sandoz supplied medical LSD in the form of Delysid that was studied in hundreds of trials in thousands of patients. The US government via the National Institutes of Health funded more than 130 grants in this field. Results were generally reported as positive and encouraging in disorders including anxiety, depression and addiction (Krebs and Johansen, 2012). One of the founders of Alcoholics Anonymous, Bill Wilson, was so impressed by the power of LSD to change alcoholics’ defeatist focus on alcohol and to give them insights into powers beyond themselves that he encouraged treatment research with it.

Having set off this burst of innovation with LSD, Hoffman continued to research psychedelics derived from plant products, and this led to his discovering the chemical structure of active ingredient of ayahuasca (DMT) and magic mushrooms (psilocybin). The kinetics of psilocybin made it a particularly interesting agent to study therapeutically. When given orally, the effects come on in 20–40 minutes and last around three to four hours, a time course much easier to use in the clinic than that of LSD, which can produce effects that last for 12 hours, or DMT, which isn’t orally active and which given intravenously lasts for just 10–20 minutes. Psilocybin also shows a clear dose–effect relationship, and rarely seems to produce ‘bad’ trips. In many ways, it is the ideal psychedelic for treatment trials, which is what Sandoz tried to do when Hoffman characterised it.

Unfortunately, psilocybin got caught up in the backlash against LSD occasioned by the protests against the Vietnam War and the Haight–Ashbury social revolution. So when LSD was banned on the basis of some very dubious so-called research findings of harm, psilocybin and all other known psychedelic drugs became illegal too. There was no evidence of psilocybin being harmful enough to be controlled when it was banned, and since then, it has continued to be used safely by millions of young people worldwide with a very low incidence of problems. In a number of countries, it has remained legal, for example in Mexico where all plant products are legal, and in Holland where the underground bodies of the mushrooms (so-called truffles) were exempted from control.

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It is the safety and ease of practical use of psilocybin that has led to it being resurrected in a series of psychological (Griffiths et al., 2006, 2008, 2011), psychopharmacological (Kometer et al., 2012; Pokorny et al., 2016; Vollenweider et al., 1998), imaging (Carhart-Harris, Erritzoe, et al., 2012a; Carhart-Harris, Leech, et al., 2012b; Carhart-Harris et al., 2013) and small pilot clinical studies (Bogenschutz et al., 2015; Carhart-Harris et al., 2016; Grob et al., 2011; Johnson et al., 2014; Moreno et al., 2006). These have provided the intellectual and safety data underpinning the two current studies that are special in that they are the most rigorous double-blind placebo-controlled trials of a psychedelic drug in the past 50 years. Hopefully, the positive findings that they report will act to spur on other researchers in the field of psychopharmacology, particularly in relation to depression, anxiety and addiction – disorders of enormous personal and social costs, and with many patients who still fail to respond adequately to current treatments, as well as to patients with existential distress.

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