Academic/Research Paper

Psychedelics, used responsibly and with proper caution, will be for psychiatry what the microscope is for biology or the telescope is for astronomy

By Rob Ó Cobhthaigh

Research into the therapeutic use of psychedelics is currently undergoing a major renaissance, after a decades-long hiatus due to the political fallout from the first wave of psychedelic research in the 1950s and 60s

This article will give an overview of the current psychedelic science and examine the promise and challenges of psychedelic-assisted therapy.

It is important for psychotherapists to be aware of the recent developments in psychedelic science for two reasons. Firstly, to be aware of the therapeutic potential of psychedelics as well as their risks, and secondly, to consider how best to support clients who self-experiment with psychedelics to integrate and process their experiences.

Psychedelics are a term meaning "mind manifesting", "denoting a group of chemical compounds that, when taken, dramatically alter consciousness for a period of between one and eight hours" (Forde, 2019 p. 32).

The 'classic psychedelics' (DMT, ayahuasca, LSD, mescaline, peyote, and psilocybin (the active ingredient in 'magic mushrooms')) are seeing an explosion in scientific study of their therapeutic potential.

MDMA and ketamine are not considered classic psychedelics but are included in this article due to their therapeutic properties.

Psychedelic Research

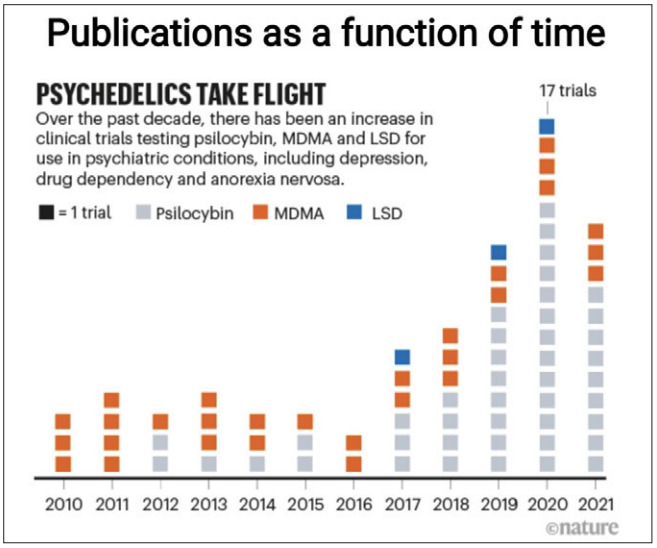
This renaissance is being led by prestigious research institutes such as MAPS (the Multidisciplinary Association for Psychedelic Research), the Johns Hopkins Center for Psychedelic and Consciousness Research in the US, and the Centre for Psychedelic Research at Imperial College, London.

Psychedelics are currently illegal in Ireland under the Criminal Justice (Psychoactive Substances) Act 2010, however a clinical trial is currently taking place in Tallaght Hospital/ Trinity College, Dublin on the use of psilocybin for treatment resistant depression under the supervision of psychiatry Professor Veronica O' Keane. Dr John Kelly calls the initial data "promising", and that "hopefully, eventually we'll have a psychedelic therapy programme within the HSE" (Freyne, 2022).

Given the large number of clinical trials currently underway, it is impossible to give a complete overview of the field, so in this article, I will focus primarily on the use of psilocybin- assisted therapy for depression and MDMA for PTSD. However, research is currently underway on psychedelic-assisted therapy for a very diverse range of mental and physical conditions.

Most notably, major clinical trials are ongoing

studying psilocybin therapy for treatment resistant depression (Phase 3), LSD therapy for generalized anxiety disorder (Phase 2), DMT therapy for major depressive disorder (Phase 2), MDMA for Eating Disorders (Phase 2) and ketamine therapy for alcohol use disorder (Phase 3). While outcomes of these trials should not be prejudiced by high expectations, the very fact that so much time and resources are being channeled into this area indicates the therapeutic potential.



It worth mentioning that studies showing promise in the treatment of major depression, anxiety and cluster headaches with LSD are occurring at the University of Basil, Switzerland; in the treatment of alcoholism with LSD and psilocybin in the US and Switzerland; the easing of end-of-life anxiety with psilocybin for people with life threatening cancer, and the treatment of opioid addiction with Ibogaine in New Zealand and Mexico (Tatala, 2020).

Research has also shown promising results in using psychedelics to treat Alzheimer's and dementia suggesting a "… potential role for both sub-perceptual 'micro'- and psychedelic-doses as a strategy for neuroprotection and cognitive enhancement in prodromal Alzheimer's disease." (Vann Jones, 2020, pg. 2).

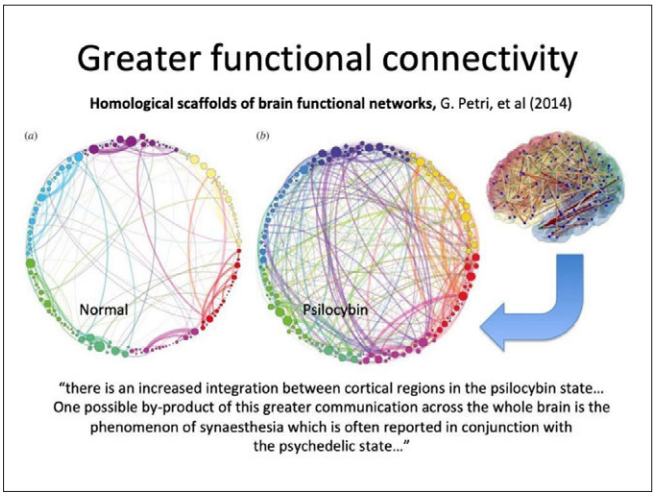
The Therapeutic Promise of Psychedelics

"When delivered safely and professionally, psychedelic therapy holds a great deal of promise for treating some very serious mental health conditions." (O'Hare, 2019, p. 1).

The 'classic psychedelics' have a similar mechanism of action. They are serotonergic agonists which cause activity in serotonin receptors. Most notably,

Neuroimaging studies have consistently shown that psychedelics significantly reduce DMN activity, as does meditation, and that this correlates with the experiencing of ego-dissolution (or losing the sense of self)

they temporarily reset the Default Mode Network (DMN) (Canal 2018). The Default Mode Network is responsible for our sense of ego- self, and our thoughts. Neuroimaging studies have consistently shown that psychedelics significantly reduce DMN activity, as does meditation, and that this correlates with the experiencing of ego-dissolution (or losing the sense of self). This "resetting" of the DMN could be linked to the antidepressant effects of psilocybin. (Carhart-Harris et al., 2012; Carhart-Harris et al., 2018).



A recent study on the "Long-term effects of psychedelic drugs" states that some of the changes that can occur include: enduring changes in personality/attitudes, depression, spirituality, anxiety, wellbeing, substance misuse and mindfulness (Aday et al., 2020, pg. 1).

Psilocybin for depression

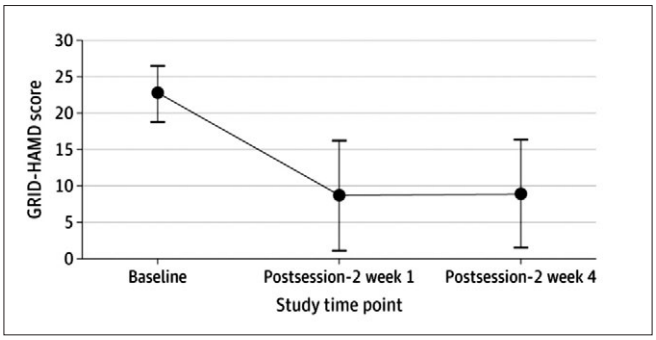
Psilocybin is a naturally occurring psychedelic compound produced by more than 200 species of fungii and has been used by indigenous people for healing for thousands of years (Schultes, 2001). A landmark 2017 study conducted by the Beckley/Imperial Research Programme, published in the *Lancet Psychiatry*, provided the first clinical evidence for the efficacy of psilocybin-assisted psychotherapy to treat depression, even in cases where all other treatments have failed. The findings showed that

Dr Roland Griffiths of Johns Hopkins, showed that psilocybin can induce mystical-type experiences which can have profound and transformative effect on people's lives

"psilocybin was well-tolerated, and induced a rapid and lasting reduction in the severity of depressive symptoms" (Carhart-Harris et al., 2017, pg. 1).

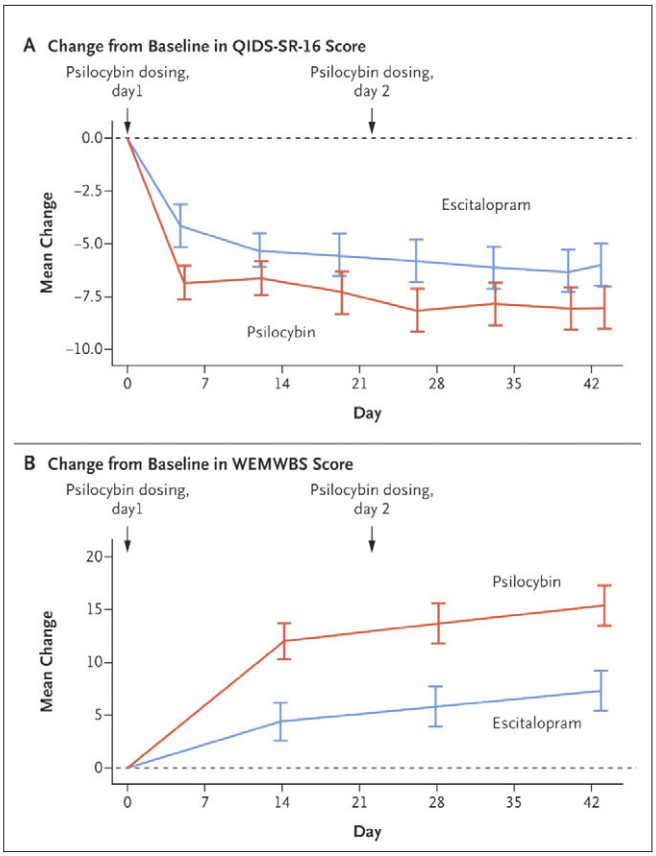
A more recent randomized clinical trial published in the *Journal of the American Medical Association Psychiatry*, found that "psilocybin administered in the context of supportive psychotherapy (approximately 11 hours) produced large, rapid, and sustained antidepressant effects" in patients with major depressive disorder. (Davis et al., 2020, pg. 4)

Decrease in the GRID Hamilton Depression Rating Scale (GRID-HAMD) Scores at Week 1 and Week 4 Postsession-2 Follow-up in the Overall Psilocybin Treatment Sample



Extraordinarily, the effect sizes reported in this study were approximately 2.5 times greater than the effect sizes found in psychotherapy alone and more than 4 times greater than the effect sizes found in psychopharmacological depression treatment studies (i.e. SSRIs).

A major paper in the *New England Journal of Medicine* in April 2021 showed the results of a Phase 2 clinical trial evaluating psilocybin-assisted therapy compared with psychotherapy and escitalopram, a common SSRI antidepressant, in the treatment of major depressive disorder (MDD). It showed that psilocybin-assisted therapy outperformed the SSRI antidepressants on several measures, however the trial data was not as conclusive as some hoped. (Carhart-Harris et al., 2021).



The therapeutic benefits of psilocybin go beyond the treatment of depression. One of the pioneers of psilocybin research, Dr Roland Griffiths of Johns Hopkins, showed that psilocybin can induce mystical-type experiences which can have profound and transformative effect on people's lives : "Fourteen months after participating [in one study], 94% of those who received psilocybin said the experiment was one of the top five most meaningful experiences of their lives; 39% said it was the single most meaningful experience "(Griffiths et al., 2011, pg. 1).

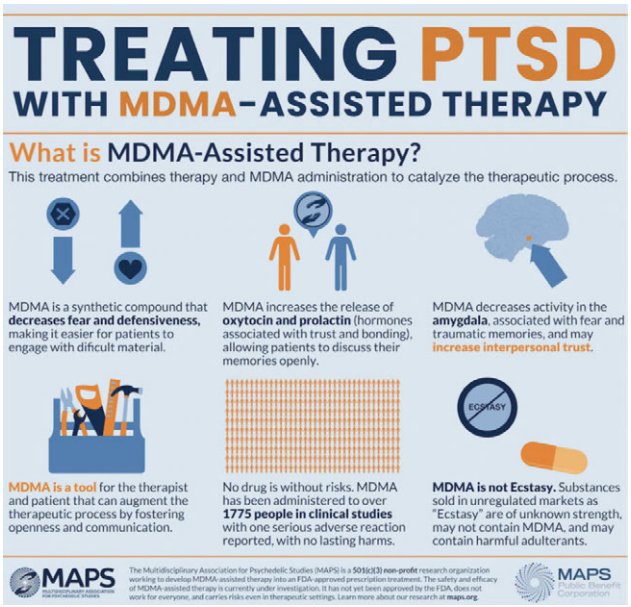
According to Amanda Fielding of the Beckley Foundation: "We've noticed that the people who experience the most ego dissolution, which can be expressed as having a mystical experience, are very often the people who have the best results in treating their condition" (Meehan, 2017, pg. 1)

MDMA for PTSD and Relationship Counselling

MDMA is known for inducing heightened energy levels, euphoric mood, openness, and empathy (Wardle, 2014). Currently, nine study sites in six European countries are involved in the Phase 2 *Open Label Multi-Site Study of Safety and Effects of MDMA-assisted Psychotherapy for Treatment of PTSD*, with a Phase 3 trial planned.

In the US, the Multidisciplinary Association for Psychedelic Studies (MAPS) is undertaking a plan to make MDMA-assisted therapy into a Food and Drug Administration (FDA)-approved prescription treatment by 2023. With preliminary research being extremely promising, the FDA has granted 'Breakthrough Therapy' Designation for MDMA-Assisted Therapy for PTSD.

A major paper published in May 2021 in *Nature Medicine* showed the results of MAPS US Phase 3 clinical trial, showing that 88% of individuals who underwent MAPS' MDMA-AT protocol experienced clinically meaningful reductions in PTSD symptoms. Perhaps even more remarkable was the fact that 67% of participants in the treatment arm no longer met the criteria for a PTSD diagnosis 2 months post-treatment, versus 32% of those in the placebo group (Mitchell et al., 2021).



Other studies have shown the potential of MDMA in enhancing relationship satisfaction, which shows potential application for use in couple's counselling. (Monson et al., 2012): "[People on MDMA] don't have the same level of fear response. They feel more relaxed, so they can tell each other things they might not otherwise be able to talk about," says Katie Anderson, a lecturer at Middlesex University, who has studied MDMA use in couples' therapy. (Anderson et al., 2020, pg. 3).

Psychiatrist Bessel Van Der Kolk, author of the seminal book on trauma, *The Body Keeps the Score* (Van der Kolk, 2014), has described from his own experience how MDMA offers the possibility for people to have a deep inner experience in which they can tolerate things that were intolerable before, and experience perspectives that were previously inaccessible. For deep inner healing to occur, we need to help people get into a state where they can observe what happened to them with a sense of calm and self-compassion, and then put it into the past, where it belongs (Van der Kolk 2018, pg. 1).

But he also cautions about the importance of using these substances in the correct way:

> *At the same time, it's unlikely that MDMA will prove to be the magic pill. It's not the only way to get to that deep state of self-observation and self-awareness. It's very important that people not go wild and create excessive expectations. But does the current work with psychedelics and MDMA have great promise? Absolutely. I'm still worried that people will be careless and take it without well-trained guides. You need to be accompanied by a very good therapist to use these drugs, once they're legal, for optimal therapeutic advantage*. (Van der Kolk, 2018, pg. 1)

Ayahuasca

Ayahuasca, a powerful DMT containing hallucinogenic mix used as a traditional medicine by the indigenous peoples of the upper Amazon, is seeing a huge growth interest for its therapeutic potential. Research is currently on going on the therapeutic use of ayahuasca for addiction, and for certain psychiatric disorders (Frecska et al., 2016; Geddes, 2020).

In one recent study published in *Nature:*

> *Effects of ayahuasca on mental health and quality of life in naïve users" showed that after the use of ayahuasca, more than 80% of those subjects showed clinical improvements in psychiatric disorders that persisted at 6 months. The study showed significant reductions in depression and psychopathology, with long-term users showing lower depression scores, and higher scores for self-transcendence and quality of life, as compared to their peers* (Jiménez-Garrido et al., 2020, pg. 1).

The challenges of psychedelics

I present the current scientific literature with a strong caveat, that if these substances are not administered in a carefully controlled set and setting, in the correct dosages, that they may be harmful and even dangerous. It should be noted that all the scientific research mentioned states the importance of proper screening, preparation, supervision, and integration. In rare instances, psychedelics can evoke a lasting psychotic reaction, more often in people with a family history of psychosis (Barrett, 2016).

That said, a large-scale 2015 meta-analysis by a team of researchers from Johns Hopkins and the University of Alabama showed 'classic psychedelics' to be surprisingly safe (Henricks et al., 2015).

The study analyzed data from more than 191,382 people between 2008 and 2012 during the annual National Survey on Drug Use and Health. More than 13 percent of those surveyed (27,235 people) had used 'classic psychedelics' at some point in their life. The respondents who had used a classical psychedelic were 19 percent less likely to have been in psychological distress during the previous month, 14 percent less likely to have had suicidal thoughts over the last year, 29 percent less likely to have made plans for suicide and 36 percent less likely to have attempted suicide in the past year than the survey respondents who had never used psychedelics.

Data from the first era of psychedelic research supports this idea. Around 10,000 participants are thought to have participated in LSD research in the 1950s and 60s, and the rate of psychosis, suicide attempts and suicides during treatment "appears comparable to the rate of complications during conventional psychotherapy, according to an analysis of data from this era" (Passie, 2008, pg. 2).

Widespread coverage of the new wave of psychedelic research has found its way into the media and popular culture. This is leading anecdotally to a rise in the self-administration of these powerful substances, including the practise of 'microdosing', taking regular, sub-perceptual doses of a psychedelic substance for improved wellbeing. A recent paper in *Nature* co-authored by Paul Stamets, found "psilocybin micro-dosers demonstrate greater observed improvements in mood and mental health at one month relative to non-microdosing controls", although this research needs further study to be conclusive. (Rootman et al., 2022, pg. 1).

According to Dr Mike Scully, Chair of the Addictions Psychiatry Department, at the College of Psychiatrists of Ireland, addiction to psychedelic drugs is very rare.

> *When I was training as a junior doctor, hallucinogenic drugs had a really negative reputation. They were considered habit -forming substances and were said to be very damaging. But when you actually look at the modern literature on psycho-pharmacology, that impression does not appear to be evidence-based*

He goes on to say…

> *I looked at a paper from 2015 published in the Journal of Psychopharmacology, from a large population study of 130,000 adults in the United States, including 19,000 psychedelic users. It failed to find evidence for a link between psychedelic use [of LSD, psilocybin or mescaline], and mental health problems* (Meehan, 2017, pg. 3).

As the pioneer of psychedelic therapy, Dr Stanislav Grof, succinctly said "Psychedelics are tools. There's nothing intrinsically good or bad about them. It's like asking whether a knife is dangerous or useful: it depends on who is using it and for what purpose" (Winter, 2009, pg. 3).

On the therapeutic potential of 'bad trips'

One of the main concerns relating to psychedelics is the fear of a 'bad trip'. These concerns are valid, with the literature showing that about 10-30% of participants in a therapeutic setting have challenging or very challenging experiences. (Barrett et al., 2016). However, the evidence suggests that if meaning can be found for those challenging experiences, a 'bad trip' can still have therapeutic value.

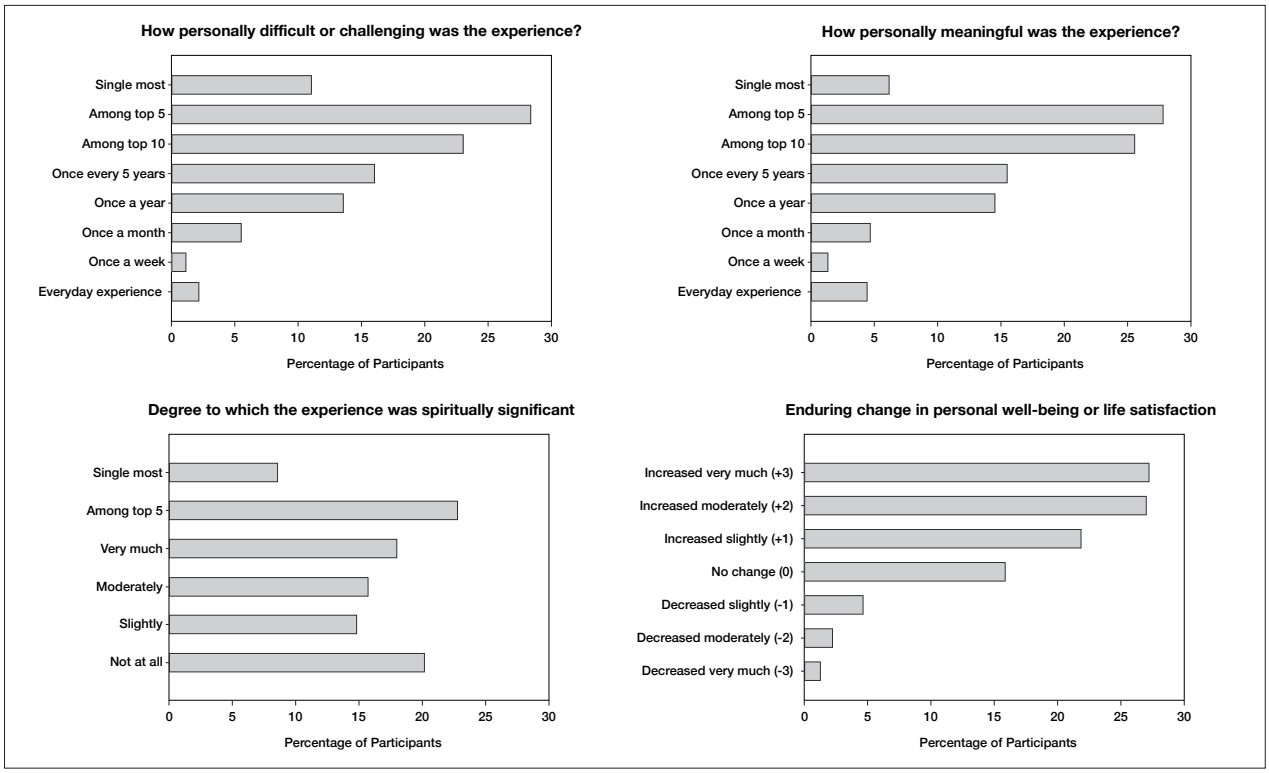
According to MAPS (2020) the type of psychedelic crises that may arise…

> *Old traumas can be remembered and relived. These memories can be of a physical nature (reliving one's birth, childhood abuse and/or illness, memories of famine and/or war, accidents, rape are some of the possibilities of re-emergence). These memories can also be of an intellectual, emotional nature (reliving verbal abuse, a lack of basic emotions, body contact, love, nurture, or a disassociation due to a traumatic experience)* (pg. 1).

Whether these experiences are re-traumatising or beneficial depends largely on the therapeutic container provided.

In a very large study in the *Journal of Psychopharmacology,* 1,993 individuals completed an online survey about their single most psychologically challenging experience (i.e. their worst "bad trip") after consuming psilocybin mushrooms in a non-therapeutic setting (Carbonaro, 2016). Thirty-nine percent rated it among the top five most challenging experiences of their lifetime. The level of difficulty of experience was positively associated with dose, the higher the dose the more likely to have a challenging experience.

Despite these difficulties, 84% endorsed benefiting from the experience and the study concludes that "the incidence of risky behavior or enduring psychological distress is extremely low when psilocybin is given in laboratory studies to screened, prepared, and supported participants." (Carbonaro, 2016, pg. 1). As Vickor Frankl (2006) pointed out, "Those who have a 'why' to live, can bear with almost any 'how'" (pg. 23),



it would seem that helping people find meaning in challenging experiences is the key to unlocking the therapeutic potential of 'bad trips'.

Interestingly, a recent paper in the *Irish Journal of Medical Science* on mental health service user attitudes to psilocybin therapy, showed 72% agreed that psilocybin should be tested for medicinal value, 59 % believed that psilocybin should be granted medical treatment status, and 20% believed psychedelics are unsafe even under medical supervision (Kelly et al., 2021)

Challenges facing the emerging field of psychedelic therapy

In a recent paper *Consciousness, Religion, and Gurus: Pitfalls of Psychedelic Medicine* , Dr Matthew Johnson of Johns Hopkins sees the main challenges as (1) Sloppiness regarding use of the term "consciousness". (2) Inappropriate introduction of religious/spiritual beliefs of investigators or clinicians. (3) Clinical boundaries and other ethical challenges associated with psychedelic treatments.

Johnson goes on to note that …

> *My observation suggests that psychedelic therapy is like putting a magnifying glass on many of the aspects of non psychedelic psychotherapy, including both positive aspects, e.g., the importance of rapport, and negative ones, e.g., potential for abusing a position of expertise or authority* (Johnson, 2020, pg. 3).

Some other major issues facing the emerging field include the challenge of training sufficient numbers of therapists and supervisors, the difficulty in blinding clinical trials, the possible under-reporting of adverse events (AEs) in clinical trials, the issues of generalisability and expectancy in clinical trials, the issue of relapse for clinical trial participants, the medicalisation of sacred indigenous medicines, potential for re-traumatisation during the psychedelic experience, and the question of how to safely navigate sexual trauma in the psychedelic space (Ó Cobhthaigh et al., 2020). Much work is currently ongoing to address these issues.

Irish psychiatrist Dr Roberta Murphy of Imperial College, London published a paper in March 2022 in *Frontiers in Pharmacology* investigating for the first time the relationship between the therapeutic alliance and rapport, and the quality of the acute psychedelic experience and treatment outcomes, as well as the need to better understand the therapeutic mechanisms of action in psilocybin-assisted therapy (Murphy et al., 2022). The paper found evidence of an effect of therapeutic alliance and rapport on the quality of the psychedelic experience, which in turn was associated with changes in depressive symptom severity 6 weeks later. As with all forms of therapy, the therapeutic relationship really matters.

The renaissance in psychedelic science

poses opportunities but also challenges for the psychotherapy profession. What role, if any, will psychotherapists in Ireland play in the therapeutic use of psychedelics? Do psychotherapists have a role in mitigating the risk for clients of the potential harmful effects of psychedelic self-experimentation? What role, if any, will psychotherapists play in helping clients integrate psychedelic experiences? And how will the training of psychedelic-assisted therapists integrate into the current models of psychotherapy? These questions have no easy answers and require serious consideration.

The psychedelic renaissance raises major legal, ethical, and educational considerations for the mental health field in general. Psychedelics are not a magic bullet, a panacea, but there are grounds for cautious optimism. As psychedelic-assisted therapy becomes more mainstream in the US and Europe, the considerations arising from this psychedelic renaissance will become more prevalent in Ireland. For this reason, it is important that the psychotherapy profession be prepared.

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