

**An exploration of the relationship between psychedelic drug use,
mystical experiences, mindfulness, and mental health.**

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Thesis declaration form

I confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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Overview

Research into psychedelic drugs and their therapeutic potential has gained increasing attention in recent years, however an understanding of the psychological mechanisms by which these substances exert their influence is not yet fully established. The purpose of this thesis was to better understand the relationship between psychedelic drug use and the psychotherapeutic constructs implicated in explaining their proposed benefits.

This volume is comprised of three parts. Part One presents a review of relevant literature, pertaining to the question of which psychotherapeutic constructs may be relevant to psychedelic experiences and their effects. The relevance of constructs such as 'mindfulness' and 'psychological flexibility' are considered, as well as the role of psychedelic-induced 'mystical experiences'.

Part Two of the thesis describes an exploratory cross-sectional study, gathering data from a large sample of recreational psychedelic drug users using an internet-based survey. This study explored the association between lifetime psychedelic drug use, mystical experiences, mindfulness and depression, and examined the pathways between demonstrated effects.

Finally, a critical appraisal of the process of conducting the research is provided. This includes personal reflections on the undertaking of research within the subject area of psychedelics, as well as a consideration of the process of establishing a direction for the study from a psychological position.

Impact Statement

A revival of interest in the therapeutic potential of psychedelic drugs has been seen in recent years, with an evidence-base for their application in the treatment of mental health problems expanding. Whilst benefits have been demonstrated in depression and addiction, for example, the mechanisms by which psychedelics exert their therapeutic effects are not yet fully understood. Evidence to date has explored aspects of the acute psychedelic experience (i.e. 'mystical experiences') which appear to be important in explaining their therapeutic effects. Likely change processes at a neurobiological level have also been identified, however psychological mechanisms remain unclear. The role of mindfulness has very recently been investigated with regard to psychedelics, with studies suggesting increases in this capacity following their use. The aim of this study was therefore to explore the relationship between mindfulness-related constructs, mental health, psychedelic use, and psychedelic-induced mystical experiences.

It is envisaged that findings will contribute to a growing understanding of the psychological pathways involved in psychedelic effects and potentially inform future research on their therapeutic use. By providing preliminary exploratory data from a large sample of psychedelic users, support may be provided for future research on the relevance of mindfulness-related psychotherapeutic constructs, both enabling an understanding of the mechanisms of change in psychedelic therapy and improving our understanding of the recreational use of these drugs.

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Part 1: Literature Review

'Third-Wave' psychotherapeutic constructs and their relevance to the psychedelic experience.

Abstract

This literature review takes the form of a conceptual introduction, providing an comprehensive overview of those constructs investigated as part of the empirical study of this thesis (see Part 2). An introduction to classic psychedelic drugs and psychedelic experiences is provided, including a consideration of mystical and/or challenging or difficult experiences. The evidence regarding therapeutic outcomes following psychedelic use is discussed, as well as an overview of theories which seek to explain these effects. A proposed overlap between psychedelic experiences and meditative practices is examined, and relevant aspects of ‘third wave’ cognitive-behavioural psychotherapeutic approaches are identified, such as ‘mindfulness’ and ‘psychological flexibility’ (core components of Acceptance and Commitment Therapy (ACT)). The value that these psychotherapeutic constructs may hold in understanding, supporting and integrating psychedelic experiences is explored, and discussed in relation to both acute and sustained effects.

Having highlighted the relevance of mystical experiences and mindfulness-related capacities with regard to psychedelics and their therapeutic potential, this review concludes by outlining the aims of the empirical study presented in Part 2.

Introduction

The use of psychedelic drugs was explored in psychiatry and psychotherapy in the early 1950s through to the mid-1960s (Carhart-Harris & Goodwin, 2017), however, shifting social norms and political pressures led to a hiatus of research in the field. Policy was implemented categorising classic psychedelic drugs as causing serious harm, with high potential for abuse and as having no accepted medical use (Misuse of Drugs Act 1971; Controlled Drugs (Penalties) Act, 1985). The so-called “war-on-drugs” began and thus politically, and socially, these substances came to be accepted as harmful, and research into their potential benefits was largely abandoned.

In recent years however, there has been a resurgence of interest within the psychiatric and psychological community and a re-evaluation of the potential benefits of classic psychedelic compounds. These include psilocybin (the active ingredient found in ‘magic mushrooms’), LSD (lysergic acid diethylamide), DMT (N,N-Dimethyltryptamine; the psychedelic ingredient in the South American beverage ‘ayahuasca’) and mescaline (found in the peyote and San Pedro cacti). The present revival has enabled a body of research comprising psychological, pharmacological, and neurological studies of classic psychedelics and their use (Carhart-Harris & Goodwin, 2017). Despite ongoing regulatory barriers, the research community continues to grow its evidence-base, demonstrating potential acute and lasting beneficial consequences of these drugs, hopeful that such demonstrations, along with evidence of limited adverse effects, will shift public and political discourse away from a largely harm-focused narrative.

Of particular interest is the emergence of studies of mystical and transcendental psychedelic-induced experiences, which suggest an overlap with some aspects of meditative practices and the constructs underpinning “third-wave” psychotherapeutic approaches (e.g. ‘Mindfulness Based Cognitive Therapy’ (MBCT), ‘Mindfulness Based Stress Reduction (MBSR) and ‘Acceptance and Commitment Therapy’ (ACT),). This review will give a brief overview of these approaches, and summarise the relevant constructs which underpin them, including an outline of ‘mindfulness’, ‘decentering’, ‘acceptance’ and ‘psychological flexibility’. Specifically, these constructs will be discussed with regard to the drug-induced psychedelic experience, given their implication in understanding the sustained effects of psychedelic drugs. Hypothesised mechanisms of action, including the phenomenological role of ‘mystical’ or ‘peak’ experiences and how these may relate to third-wave psychotherapeutic constructs, will be explored. Other third-wave psychotherapeutic approaches, such as Compassion Focused Therapy or Dialectical Behavioural Therapy, whilst likely of interest and relevance, are not discussed in this chapter. The decision as to which approaches to include was guided by the available literature and evidence. As an emerging field of study, to date there has been little empirical consideration of other third-wave therapies (e.g. CFT/DBT) with regard to psychedelics, and as such only those approaches with an existing emerging evidence-base (i.e. MBCT/MBSR/ACT) are discussed.

To better understand the relationship between psychedelics and several of the core constructs explored and identified within this review, the empirical study (Part 2) developed a cross-sectional internet-based survey to gather data from psychedelic drug users regarding their patterns of use, the nature of their

psychedelic experiences, as well as their traits and mental health. This study intended to provide an understanding of the associations between key variables implicated in the potential benefits of psychedelics, as determined by this review's consideration of the current theoretical and research landscape. This study may therefore contribute to a growing foundation of understanding and knowledge, upon which future work can begin to establish a reliable pathway of effects.

The Psychedelic Experience

Understanding Psychedelic Experiences

To understand the ways in which particular psychotherapeutic constructs may be relevant to drug-induced psychedelic experiences, it is necessary to first understand the nature of said experiences. "Classic psychedelics", i.e. serotonergic psychedelics with a similar neurochemical mechanism of action to lysergic acid diethylamide (LSD), typically refers to DMT (commonly prepared as a brew known as 'ayahuasca'), psilocybin (the active ingredient in 'magic mushrooms' and truffles), mescaline (ingested via the Peyote or San Pedro cacti), and closely related synthetic analogues. Whilst psychedelic drugs are commonly associated with the counter culture movement of the 1970's and recreational use in western societies, all but LSD have been historically used in ceremonial settings in South America and Mexico and continue to be part of modern day retreats in countries where their use is legal as part of a psychedelic sacrament. The effects of these drugs includes profound alterations in perception (including sensory illusions, modified sense of time/space, blurred self/other boundaries, and frank hallucinations), affect (from euphoria to terror) and cognition (from desired attributes of creativity and insight to increased confusion) (Dos Santos & Hallak, 2020).

Aside from drug dosage, the importance of context in determining the nature of psychedelic experience is highlighted amongst researchers, with a focus on one's *set* and

setting. A person's set refers to that which they bring internally to the experience; their mood, personality and pre-existing expectations and assumptions. The setting, however, refers to the external environment in which the experience takes the place; the people present, the atmosphere. It is understood that the therapeutic potential of psychedelic compounds may rely on these key contextual determinants (Carhart-Harris et al, 2018). It is generally accepted that without this important consideration, the psychedelic experience may not only be ineffective in terms of eliciting desirable outcomes, but actively harmful. Preliminary findings from the psychedelic research group at Imperial College London demonstrate that 'readiness to surrender' to the experience, holding an intention in mind, having an expectation for the experience, and being in a therapeutic setting predict a 'peak' or 'mystical' experience, rather than a 'challenging' psychological experience, colloquially known as a 'bad trip' (Carhart-Harris et al, 2018).

'Mystical experiences' (i.e. a profound sense of unity, sacredness, truth, and transcendence of time and space; Stace, 1960) can reliably occur under high doses of psychedelics. Whilst these experiences are not exclusive to psychedelic drugs and can occur spontaneously in religious, spiritual, or awe-inspiring contexts, research has demonstrated that a high dose of psilocybin can induce a 'complete' mystical experience in up to 61% of participants (Johnson et al, 2019). The definition and occurrence of a 'complete' mystical experience is informed by the Mystical Experiences Questionnaire (MEQ30), a widely used and validated measure (Griffiths et al, 2006; MacLean et al, 2012; Barrett et al, 2015). Using this tool, a score of ≥ 60 percent on each of the measure's four factors ('mystical', 'positive mood', 'transcendence of time and space', 'ineffability') is indicative of a complete experience, with stronger effects observed with higher doses (Griffiths et al, 2011; Barrett et al, 2015; Carbonaro et al, 2018). In an analysis of mystical experiences induced by psilocybin (as measured by the MEQ30), 66% of 119 healthy volunteers rated the experience as being one of the top five most personally meaningful experiences in their life.

Of these 119 volunteers, 68% placed the occasion within their top five most spiritually significant experiences, whilst 70% felt there to have been a positive change in their behaviour, which was attributable to the experience (Barrett and Griffiths, 2017). Further studies relating to mystical experiences, their acute and sustained effects, and their hypothesised mediating role in positive change, will be discussed in more detail below.

In addition to the above aspects of the psychedelic experience, a number of factors have been highlighted as relating to a 'difficult' (distressing or emotionally 'challenging') psilocybin-induced experience. Barrett et al (2017) demonstrated seven factors (grief, fear, death, insanity, isolation, physical distress and paranoia) to be associated with the difficulty, meaningfulness and spiritual significance of the overall experience (Barrett et al, 2017). These outcomes were measured using a set of self-report items developed and administered in laboratory studies of psychedelics and their effects (Griffiths et al, 2006; 2011), using an anchored Likert-scale to assess the overall impact of a psychedelic session. Barret et al's (2017) findings demonstrate that participant's ratings of these seven challenging factors during the psychedelic session was related to the perceived impact of the overall psychedelic experience. Not only does risk exist in regards to the potential for short-lasting challenging psychological experiences, but there are also some instances of physical and potentially fatal harm, such as the recent case of a 19 year old British man who died after participating in an ayahuasca ceremony in Colombia (Morris, 2018). Furthermore, individuals may experience a rare phenomenon known as Hallucinogen Persisting Perception Disorder (HPPD), whereby distressing recurrence of perceptual disturbances can re-emerge months after psychedelic drug use (Martinotti et al, 2018). It should be noted however, that HPPD and fatal consequences of hallucinogen use are extremely rare, and exemplars of this drug class are considered to be among the least harmful of all licit and illicit recreational drugs (Nutt et al., 2007). Of further note, is that acute challenging experiences and positive (mystical) experiences are not mutually exclusive. Supplementing

anecdotal reports, Carbonaro et al (2016) demonstrated through an online survey of 1993 individuals that despite experiencing a psychologically challenging experience (participant's reported on their worst "bad trip"), 84% endorsed having benefitted from their experience with psilocybin mushrooms. Thus, the psychedelic experience may be understood as more nuanced than a simplistic 'good' vs 'bad' dichotomy.

Applications and Evidence for Therapeutic Potential

Countering the commonly held view that psychedelic drugs cause physical and/or psychological harm, is evidence from a large-scale population survey in the USA demonstrating that lifetime classic psychedelic use is associated with a significantly reduced likelihood of psychological distress and suicidal thinking, planning, and attempting. Other illicit drug use, however, increased the likelihood of the same outcomes, when other factors (e.g. age, gender, ethnicity, education, marital status, lifetime illicit substance use, risky behaviour) were controlled for (Henricks et al, 2015). Similar population studies also illustrate that lifetime use of classic psychedelics is not associated with an increase in prevalence or severity of mental health problems. Rather, psychedelic use is instead associated with a reduced chance of inpatient mental health treatment, with the use of psilocybin carrying a decreased likelihood of serious psychological distress, psychiatric inpatient treatment or medication, within the past year (Johansen & Krebs, 2015). Further supporting this notion, longitudinal research of ceremonial drinkers of Ayahuasca does not show increased levels of psychopathology with repeated use. Interestingly, whilst naïve ayahuasca users do demonstrate clinical improvements after their first use, long-term users have reduced depression scores and increased quality of life scores compared to these one-time users (Jimenez-Garrido et al, 2020).

Further evidence for improved psychosocial outcomes have been demonstrated by Pisano, Putman & Kramer et al (2017), whose analysis of population data from the US

National Survey on Drug Use and Health collected over a period of 5 years, illustrated that classic psychedelic drug use is associated with a decreased risk of opioid abuse and dependence (in contrast to other illicit drug use, which was found to be associated with an increase in this risk). Benefits of psychedelic drug use have also been shown amongst those known to the criminal justice system, with evidence of a reduced incidence of intimate partner violence amongst US prisoners (Walsh et al, 2016), and reduced recidivism amongst offenders with a history of substance abuse (Hendricks et al, 2014). Other socially relevant outcomes include the finding that psychedelic use is associated with decreased criminality, specifically, decreased odds of theft, assault, property crime and violent crime (Hendricks et al, 2018). Despite promising findings, it is noted that these studies are correlational in design and causal associations with these outcomes have not yet been established through longitudinal experimental studies.

Evidence also suggests an association between psychedelic drug use and personality change, particularly relating to changes in 'openness' or 'self-transcendence' (Nour et al, 2017; Maclean et al, 2011; Bouso et al, 2015), with evidence of causal inference provided by experimental design (Maclean et al, 2011). In the treatment of substance dependence, changes in personality have been suggested to be a key mechanism of change with regard to the proposed positive impact of psychedelic drug use. It is proposed that these alterations in personality enable the mindset and skillset necessary to implement and maintain abstinence or recovery (Sessa & Johnson, 2015; Bogenschutz & Pommy, 2012). A further association has been demonstrated between psychedelic drug use and 'nature relatedness', that is, connection to and concern for the natural environment (Nour et al, 2017; Lyons & Carhart-Harris, 2018). Nature relatedness has separately been found to be associated with positive affect, vitality and life satisfaction (Capaldi et al, 2014) and lower levels of anxiety (Martyn & Brymer, 2016). Though, again, it is unclear at present whether these variables are causally related and whether a chain of effects exists between

psychedelic drug use, nature relatedness and positive mood-related outcomes. More broadly than the above effects, individuals who use psychedelics with the purpose of enhancing self-knowledge demonstrate better coping (Moro et al, 2011), and long term ayahuasca use has been shown to elicit better psychosocial adaptation on measures of life purpose and subjective well-being when compared to non-ayahuasca using controls (Bouso et al, 2012).

Importantly, psychedelic drugs also appear to have clinical and therapeutic value. This was suggested by early research (from the 1960's and 70's) on the treatment of alcoholism (Krebs and Johansen, 2012). More recent studies have demonstrated promising results in treating depression (Carhart-Harris et al, 2018; Osorio et al, 2015; Palhano-Fontes et al, 2019) OCD (Moreno et al, 2006), death anxiety and low mood related to life-threatening illness (Grob et al, 2011; Griffiths et al, 2016; Ross et al, 2016), as well as improved outcomes in drug dependence (Sessa & Johnson, 2015; Bogenschutz & Pommy, 2012; Pisano et al, 2017), alcoholism (Bogenschutz et al, 2015) and smoking cessation (Johnson et al, 2017a; 2017b). However, only few of these studies employ rigorous methodological controls and are instead naturalistic and observational in nature. Future clinical trials will complement these studies to further our understanding of any causal nature and clinical potential of these relationships (dos Santos et al, 2020).

Researchers in this field highlight the possible therapeutic value of psychedelic substances to address an unmet need, by repurposing psychedelic drugs for the treatment of disorders and distress currently not alleviated by contemporary medical management or talk therapies (Carhart Harris & Goodwin, 2017). Taken together, the above literature suggests a potentially protective, rather than predominantly harmful, effect of psychedelic drug use –naturalistically and experimentally – both relative to other drug use, and non-drug taking controls.

The Role of Mystical Experiences

As discussed earlier, mystical experiences are a phenomenon proposed to often occur during high dose psychedelic experiences, characterised by a profound unity with all that exists, a felt sense of sacredness, a sense of the experience of truth and reality at a fundamental level (noetic quality), a deeply felt positive mood, transcendence of time and space, and difficulty explaining the experience in words (ineffability) (Stace, 1960).

Preliminary evidence suggests that the occurrence of this experience during psychedelic drug use is associated with positive outcomes, such as self/community reports of positive changes in attitudes and behaviour (Griffiths et al, 2006; Griffiths et al, 2011), persisting increases in the personality domain of 'openness' (MacLean et al, 2011), and improvements in treatment-resistant depression (Roseman et al, 2018). Positive correlations and partial mediation have also been demonstrated between the intensity of psilocybin-induced mystical experiences and improvements in depression and anxiety in cancer-related distress (Griffiths et al 2016; Ross et al 2016) as well as improvements in levels of alcohol dependency (Bogenschutz et al, 2015). Mystical experiences induced by psilocybin have further been demonstrated to mediate the ascription of meaning and spiritual significance when these outcomes are measures at 14-month follow-up, following high doses of psilocybin (Griffiths et al, 2008).

Another related, yet distinct, construct is 'ego-dissolution'; that is, an altered sense of self and a blurred distinction between self/other representations (Nour et al, 2016). Indeed, narrative reports of subjective experience have alluded to this breakdown of one's ordinary character of normal waking consciousness (Milliere, 2017). Ego-dissolution has been found to occur under higher doses of psychedelics, as well as with increased experience intensity, occurring as part of 'peak' or mystical experiences described above (Nour et al, 2016). The degree of ego-dissolution one experiences has been shown to correlate positively with the extent of a positive and lasting impact on well-being (Nour et

al, 2016). This is consistent with research demonstrating that the degree of ego-dissolution during the psychedelic experience predicts changes in openness, nature relatedness and liberal non-authoritarian views (Nour et al, 2017). Changes in affect and mindfulness – amongst other outcomes – the day after and 4-weeks after an Ayahuasca ceremony, were correlated with the level of ego-dissolution experiences during the ritual, whilst controlling for previous experience with the drug (Uthaug et al, 2018). This particular relationship is of note for this review, given that similar ‘ego-less’ alterations in self-consciousness have been demonstrated in deep meditative states (Dor-Ziderman et al, 2013). This overlap has inspired curiosity in the scientific community regarding a common core phenomenology regarding drug-induced and meditative ego-dissolution (Milliere, 2017).

Theories of Psychedelic Therapy

The question of which particular acute effects of psychedelic drugs (both neurochemically and subjectively) enable therapeutic benefits and clinical improvement has been met with scientific efforts to understand and present theories of their mechanisms. From the theories of psychedelic research in the 19th/20th Century (i.e. Model Psychoses Theory, Filtration Theory, and Psychoanalytic Theory), to the 21st century cognitive neuroscience accounts (Entropic Brain Theory, Integrated Information Theory, and Predictive Processing), commonalities and enduring theoretical features have been observed (Swanson, 2018). Relating to these theories, Swanson (2018) presents four shared features. First, is the notion that psychedelic drugs prevent an evolutionarily adaptive ‘filtering’ or otherwise ‘constraining’ of mental phenomena (such as perception, emotion and cognition), by supressing those brain mechanisms which apply said constraints. Second, is the hypothesis that said brain mechanisms are capable of both over- or under- performing; with an ‘overactive filter’ eliciting too much constraint on the mind and promoting an existence characterised by rigidity and neuroticism, and an ‘underactive filter’ eliciting too little limitation on conscious awareness resulting in confusion, instability

or what may be understood as psychotic presentations. Third, is thus the idea that both the acute psychedelic experience and chronic psychoses share the ‘unconstrained’ mental processes. Finally, fourth, is the consideration that psychedelic drugs hold therapeutic potential as a direct result of their inhibition of these constraining mechanisms, enabling a conscious awareness that is less limited. Advances in science throughout the 21st century enabled the study of the neurophysiological and neurochemical correlates of the psychedelic experience, and the linking of this with phenomenology. For instance, ‘Entropic Brain Theory’ has been proposed as an account of psychedelic effects, stating that the cognitive flexibility and perceptual destabilisation experienced by users corresponds to increases in ‘entropy’ (i.e. uncertainty or disorder) in brain activity. The hypothesis is that psychedelics prevent the mechanisms which ordinarily suppress ‘entropy’, thus enabling broadened patterns of functional connectivity (Carhart-Harris et al, 2014; Swanson 2018). This neurophysiological occurrence is proposed to map onto the phenomenological experience of ‘ego-dissolution’ through enabling an uncertain entropic state whereby the constraints of the ego are lifted. This is proposed to hold therapeutic value through dismantling the brain activity relating to habitual patterns of distressing thoughts and actions, allowing for novel perspectives and insights (Carhart Harris et al, 2014). Indeed, evidence suggests that the experience of psilocybin or LSD induced ego-dissolution appears related to increases in entropy in the brain and global functional connectivity (Milliere, 2017).

Early hypotheses continue to be relevant, with support from modern day cognitive neuroscience, and though no one unifying theory exists (and indeed it is suggested that ‘broad frameworks’ instead offer more value), a core feature of psychedelic’s therapeutic potential is suggested to lie in the interference of normal waking-state neurophysiological, and associated psychological, constraints (Swanson, 2018).

Summary of Psychedelic Experiences and Therapeutic Potential

Given the proposed breadth of the potential benefits of psychedelics (e.g. Carhart-Harris et al, 2018; Grob et al, 2011; Sessa & Johnson, 2015), recent scientific studies of psychedelic compounds and their associated outcomes have sought to understand possible change processes in terms of their neurophysiology and associated phenomenology, as in the case of mystical experiences or ego dissolution. Of further interest, then, is an exploration of potential mechanisms at a psychological level. The following section seeks to do this by applying constructs that have traditionally been used to understand change processes during ‘third-wave’ psychological talking therapies, through examining evidence for their relevance to the psychedelic experience and its effects.

Psychedelics and Third-Wave Psychotherapeutic Constructs

Introduction

In the late 1950’s, psychology underwent a cognitive revolution whereby the traditional behavioural accounts of human behaviour and pathology (e.g. Skinner, 1938) were challenged by cognitive models. These sought to enhance existing behavioural principles through the addition of the identification and modification of unhelpful cycles of interconnected thoughts, feelings and behaviours (Beck, 1993). The role of overt behaviour was relied upon less and focus was given to one’s appraisals and interpretations of events, hypothesised to be rooted in biases developed from early experiences. Thus by the late 1970’s, this “second-wave” Cognitive Behavioural Therapy (CBT) became established as a mainstay of contemporary psychotherapy, with a well-established evidence base to support its theory, mechanisms of action, and use in treating a wide range of mental health difficulties (Cuijpers et al, 2013; Hunot et al, 2007; Bernardy et al, 2010; Burns et al, 2014). Indeed, CBT remains today the recommended first-line treatment for mild to moderate depression and generalised anxiety in the UK, as indicated by the National Institute for

Health and Care Excellence (NICE, 2009; 2019). However, by the mid-2000's, a third-wave of CBT had emerged, with approaches and models that focused less upon examining and updating the content of difficult thoughts and emotions, but rather on the process of how one engages with them (Hayes and Hofmann, 2017), with growing evidence for their efficacy (e.g. Piet & Hougaard, 2011; Powers et al, 2009). Of note, is a synergy between Eastern and Western thought, as third-wave approaches integrate CBT with core ideas from spiritual practices. This integration of ideas uniquely highlights the relevance of one's philosophical stance with regard to an understanding of the self and one's existence (Hurley & Callahan, 2008).

As discussed above, current theories of psychedelics propose that they enable greater functional connectivity, which may in turn underpin a dissolution of reinforced and habitual cognitive and behavioural patterns, and pave an opportunity for change. For instance, from a CBT perspective, this may refer to the breaking down of a stuck pattern of distressing thoughts which stem from a 'negative core belief' of the self, which has been strengthened over time through a selective attending to and storage of experiences in support of this belief. By releasing the constraints which hold this pattern steady, for instance the automatic habitual behaviours which ultimately serve to maintain the problem, the psychological mechanisms (discussed below) capable of eliciting change may be enabled.

Whilst empirical evidence suggests an important role for particular types of psychedelic experiences, namely mystical experiences, this alone does not tell us which known psychological functions may be at play. The following section seeks to explore the relevance of constructs pertaining to third-wave psychotherapies. Whilst not an exhaustive list, below is an overview of the constructs which underpin several of the widely used third-wave approaches with established evidence-bases. Of particular focus will be those

constructs proposed to be relevant to the psychedelic experience, i.e. mindfulness, decentring, acceptance and psychological flexibility. The relevance of these third-wave constructs will be considered not only with regard to the acute psychedelic experience, but with regard to sustained effects and the integration of the experience.

Mindfulness & Psychedelics

Mindfulness and Mindfulness-Based Interventions

‘Mindfulness’ is a construct that has gathered increased attention in recent years, not only amongst psychology and psychiatry professionals, but in wider society. With roots in Eastern Buddhist philosophy, numerous secular definitions have been proposed and their use adopted by the Western scientific community. A key figure in popularising modern mindful practices is Jon Kabat-Zinn, who in 1979 pioneered the translation of historically Buddhist principles into a secular stress reduction programme known as ‘Mindfulness-Based Stress Reduction (MBSR)’. Kabat-Zinn (2006) defines mindfulness as “the awareness that emerges through paying attention on purpose, in the present moment, and non-judgmentally to the unfolding experience moment by moment”, and acknowledges it as a fundamental attentional position which underpins Buddhist meditative practice.

Mindfulness is considered to be a meditative practice and attentional stance, and forms a core component of Acceptance and Commitment Therapy (ACT) (explored separately in relation to psychedelics below). Thus, whilst other meditative practices exist, this review will focus on mindfulness both as a stand-alone evidence-based psychotherapeutic technique recommended by the National Institute for Health and Care Excellence (NICE, 2009), and later as a core component of ACT.

Though mindfulness practices vary, many focus on encouraging attention to be directed to internal experiences (e.g. the breath, thoughts) or external aspects of the environment (e.g. sights, sounds, smells). If the mind is noted to wander, it is gently

directed back to the chosen focus of attention. Mindfulness is thus understood to promote a shift from 'doing mode' into 'being mode', taking practitioners out of 'autopilot', thus enabling goal-directed choice rather than automatic reactions. Whilst a range of contemporary psychotherapeutic modalities incorporate mindfulness techniques, two of the most prominent interventions are Mindfulness Based Stress Reduction (MBSR) and Mindfulness Based Cognitive Therapy (MBCT). Both interventions promote the cultivation of mindfulness and a transience of passing experience, encouraging a detached observation of mental events. For Teasdale et al (1995), this space created between a cognitive event and one's response is capable of interrupting escalating patterns of depressive rumination, thus preventing relapse. MBCT borrows from CBT its use of psychoeducation regarding the interrelatedness of thoughts, feelings, behaviour and physical sensations in inducing and maintaining distress. The intervention postulates that by combining this understanding with skills in mindful awareness, individuals are able to interrupt the habitual cognitive processes perpetuating distress and disengage from them (van der Velden et al, 2015), a similar mechanism to that proposed by the neurobiological theories of psychedelics, which argue that it is the opportunity to break free from habitual reinforced tendencies which elicits change (e.g. Carhart-Harris et al, 2014).

The efficacy of both MBSR and MBCT has been demonstrated through studies of their use in the treatment of stress and physical or mental health difficulties (e.g. Piet & Hougaard, 2011; Williams et al, 2006; Kenny & Williams, 2007; Roberts & Surawy, 2002; Janssen et al, 2018; Rush & Sharma, 2017; Anheyer et al, 2017). Of interest, then, is the psychological mechanism of action behind such improvements, to enable a comparison and consideration of the mechanisms behind the improvements seen with psychedelics. Whilst ongoing research is needed, provisional studies have examined the predictors or mediators of MBCT's benefit, with a systematic review of 23 clinical trials (van der Velden et al, 2015) demonstrating that the empirical data tend to support MBCT's underlying theory. Twelve

studies demonstrated that the effect of MBCT on treatment outcome was either associated with, predicted, or mediated by the intervention's proposed theoretical mechanisms, i.e. increases in mindfulness, self-compassion, decentering and meta-awareness, as well as decreases in worry and rumination. 'Decentering' has gained particular attention as a potential mediator of effects, and refers to the ability to relate to one's own thoughts, feelings and sensations as temporary events, characterised by a detached 'observer' perspective (Fresco et al, 2007a; Teasdale et al 2002). The capacity to decenter is deliberately fostered in mindfulness-based interventions (Naragon-Gainey & DeMarree, 2017; Fresco et al, 2007a) and evidence for its mediating role in the relationship between mindfulness interventions and therapeutic outcomes has emerged (Hoge et al, 2016; ; Naragon-Gainey & DeMarree, 2017; Sauer & Baer, 2010; Fresco et al, 2007b).

Mindfulness & Psychedelics

As is evident from the above discussion of mindfulness and mindfulness based interventions (i.e. MBCT, MBSR), the retraining and refocusing of one's attention appears capable of eliciting significant positive behavioural, emotional and physiological change. Emerging evidence suggests that both meditation and high doses of psychedelics are able to induce reversible altered states of consciousness, including a sense of 'self-loss' (Letheby and Gerrans, 2017; Vago & David, 2012). This is commonly referred to amongst the psychedelic literature as 'ego-dissolution' (Nour et al, 2007), and may be understood as comparable to the hypo-egoic self-awareness proposed to arise through mindfulness (Leary et al, 2006), though, it is noted that there is some divergence in the composition of these alterations in awareness according to various dimensions of self-consciousness (Milliere et al, 2018). Indeed, even different meditation styles (of which mindfulness is one) appear to have different neural correlates (Tang et al, 2015). Whilst it is acknowledged that data thus far is insufficient to reliably dismantle the similarities and differences between drug- and meditation-induced alterations in experiences of 'the self', an overlap is recognised not only

in terms of phenomenology but in sustained positive psycho-social effects. With both meditative practices and psychedelic experiences capable of inducing ‘self-transcendence’ or ‘ego-dissolution’ (Letheby and Gerrans, 2017; Vago & David, 2012). With common neurophysiological activity also identified between these meditation- or psychedelic-induced states (Carhart-Harris et al, 2014; Milliere et al, 2018), the role of mindfulness in understanding the psycho-social benefits of psychedelics is of significant interest.

Accordingly, to examine the relevance of mindfulness, one must consider whether psychedelic drug use is indeed associated with improved mindfulness-related capacities. A body of research has very recently begun to emerge examining the therapeutic role of Ayahuasca with regard to mindfulness, with evidence demonstrating that a single intake in a supportive yet non-religious lay setting resulted in significant improvements in several core facets of mindfulness, 24 hours later (Soler et al, 2016). The changes observed were significant shifts in two of five facets assessed by the Five Facets Mindfulness Questionnaire (Baer et al, 2006), namely ‘non-judgement’ (a non-evaluative position regarding inner experiences) and ‘non-reacting’ (allowing inner experiences to arise without becoming bound up in them. Increases were also seen in decentering (the observation of inner experiences as transient mental events) (Fresco et al, 2007a), a proposed mechanism of change regarding mindfulness’ beneficial effects on wellbeing (Gecht et al, 2014). These changes were noted by Soler et al, (2016) to be akin to the desired outcomes of mindfulness-based intervention programmes, with the scores in non-judgement, non-reacting and decentering presented as comparable to those observed following long-standing meditation practice. The non-judgement and non-reacting facets of mindfulness have been considered as measures of acceptance (Baer et al, 2006), and indeed Soler et al (2016) suggest that ‘self-acceptance’ – a key feature of the third-wave psychotherapy ACT - may hold an important role in the benefits of ayahuasca, with this attitudinal change potentially capable of reducing psychopathology. Acceptance and its relation to

mindfulness is explored in detail below, through a discussion of the model underpinning ACT.

A similar pattern of findings to Soler et al (2016) has been demonstrated alongside neural modifications (which persist beyond the acute experience), suggesting that a neurophysiological shift corresponds to the observed improvements in mindfulness following ayahuasca use (Sampedro et al, 2017). Such changes at the level of brain activity and at the subjective level (i.e. changes in mindful state) following an ayahuasca experience, parallel those seen with extended mindfulness meditation practice (Holzel et al, 2011). In support of these findings, a comparison of ayahuasca users with non-users on a questionnaire measure of decentering demonstrated higher levels of decentering amongst users (Franquesa et al, 2018). Notably, however, this greater degree of decentering was only found in those who had consumed ayahuasca greater than 15 times, suggestive of a cumulative benefit. This finding may be considered as consistent with Soler et al's (2016) finding of increased decentering, which was observed in a sample with a relatively large number of lifetime ayahuasca doses (mean=79 doses).

The potential of ayahuasca to increase mindfulness is further highlighted by findings from a study which compared two independent groups: one undertaking four weekly ayahuasca sessions (with no explicit mindfulness training), and the other completing an 8-week MBSR programme (Soler et al, 2018). Results demonstrated that whilst MBSR elicited greater increases in total mindfulness score, as well as increases in the 'MINDSENS' Index (a measure of those aspects of mindfulness deemed most sensitive to change through meditation practice, Soler et al, 2014), the ayahuasca sessions elicited increases in non-judgement comparable to the MBSR sessions. Seemingly, ayahuasca appears capable of inducing meaningful shifts in this domain; encompassing detached 'mindful' awareness, a key position and feature of MBSR/MBCT interventions. Shifts in additional facets of

mindfulness have also been found to persist beyond the acute psychedelic experience. In a study of participants completing measures before and 24 hours after an ayahuasca session, the abilities to observe, describe, act with awareness, and take a non-reactive stance towards internal events were shown to significantly increase after ayahuasca (Murphy-Beiner & Soar, 2020). Decentering ability, as an important mindfulness-related capacity, similarly increased in this group of users. All effects were unrelated to previous ayahuasca use, thus demonstrating equivalent benefits for both naïve and experienced users. However, Murphy-Beiner & Soar (2020) acknowledge that the likely confounding role of previous or concurrent meditation experience was not controlled for, and should be considered in future studies.

A limitation of the above studies is that longer term effects or follow up were not described. With single doses of psychedelics capable of producing therapeutic benefits (e.g. Osorio et al, 2015; Palhano-Fontes et al, 2019), one might expect the post-acute effects of mindfulness to similarly endure. However, whilst a study of attendees of an ayahuasca ceremony demonstrated significant increases in non-judgement, acting with more awareness and observation one day after the experience, a sustained effect was not evident at 4 weeks follow up (Uthaug et al, 2018). The increases in mindfulness significantly correlated with the level of ego-dissolution experienced during the psychedelic experience, in line with above hypotheses relating to mechanisms of change. However, the small yet significant changes in mindfulness were lost at follow up, possibly due to drop-outs and loss of statistical power (Uthaug et al, 2018).

Whilst the above literature describes mindfulness effects as related to Ayahuasca, a small number of studies are emerging which examine mindfulness with regard to other psychedelic substances. The active psychedelic ingredient of DMT occurs naturally in the secretion of certain psychoactive toads, typically used for spiritual reasons and capable of

inducing mystical experiences (Davis et al, 2018). A single inhalation of vapor from this dried toad secretion has been shown to increase mindfulness capacities at four weeks, as well as lowering depression, anxiety and stress (Uthaug et al, 2019). Higher degrees of ego-dissolution correlated with the effects of lower depression and stress. Again, the psychedelic experience, ego-dissolution and mindfulness appear connected, with this study demonstrating the potential for psychedelics to produce enduring effects with regard to mindfulness, persisting beyond the acute and post-acute experience. Similarly, a recent study of psilocybin taken by psychedelic naïve participants in a supportive setting demonstrated significant increases in mindfulness 3 months following the experience, in the absence of any specific mindfulness training, with effect sizes comparable to MBSR programmes (Madsen et al, 2020). Madsen et al (2020) thus highlight a possible core therapeutic role for mindfulness following psilocybin therapy.

The majority of research examining the relationship between psychedelics and mindfulness-related capacities has been conducted in non-clinical samples, however, the relationship between psychedelics and mindfulness has further been explored in specific client groups. Some promising provisional results have been demonstrated, with an addiction and stress programme in combination with two ayahuasca ceremonies demonstrating statistically significant improvements in mindfulness 6 months later (Thomas et al, 2013). However, a study comparing participants with and without 'BPD-like (borderline personality disorder) traits' examined emotion regulation and mindfulness-related capacities 24 hours after an ayahuasca session, finding that whilst emotional regulation improved, mindfulness capacities only improved in those without BPD-like traits (Dominquez-Clave et al, 2019). Thus, future research should seek to understand the role of mindfulness in relation to psychedelic use across varying client groups.

Whilst the above evidence provides a growing foundation of research, which begins to help us understand the relevance and role of mindfulness in explaining the beneficial effects of psychedelics, there is inconsistency amongst findings related to which facets of mindfulness are implicated, and to what extent effects endure. Notably, the preliminary evidence to date hosts important methodological limitations. A lack of control groups (Soler et al, 2016; Sampedro et al, 2017; Murphy-Beiner & Soar, 2020; Uthaug et al, 2018, 2019; Madsen et al, 2020), randomisation and blinding, with few instances of long term follow up, may bias the reported findings (Jungaberle et al, 2018). Further studies with tighter methodological controls would enable researchers to begin to reliably identify the role of mindfulness in psychedelic therapy, as a core variable of interest.

Psychological Flexibility and Psychedelics

Psychological Flexibility & ACT

Despite second-wave CBT having become the dominant modern psychotherapeutic approach, radical behavioural researchers continued examining the role of verbal behaviour and rule-governance and presented Relational Frame Theory (RFT) (Barnes-Holmes & Roche, 2001) as an account of language, cognition and operant behaviour, upon which Acceptance and Commitment Therapy (ACT) is based. ACT presents at the centre of its model of distress that humans are able to attribute meaning to internal or external events, meaning which is then capable of inducing pain and subsequent suffering. This is proposed to occur through a tendency to restrict and limit our lives as an unintentional consequence of attempting to control and eliminate distressing experiences (Boorman et al, 2012).

To alleviate this self-limiting and suffering, ACT holds at its core the intention to increase 'psychological flexibility', a construct which incorporates present moment awareness as a conscious human being, and behaviour directed towards the pursuit of one's values (Hayes et al, 2006). ACT presents six underlying processes which act as barriers

to this, which map directly onto the model's core change processes. Psychological flexibility is conceptualised as the positive consequence of these interrelated practices (See Figure 1)(Hayes et al, 2006).

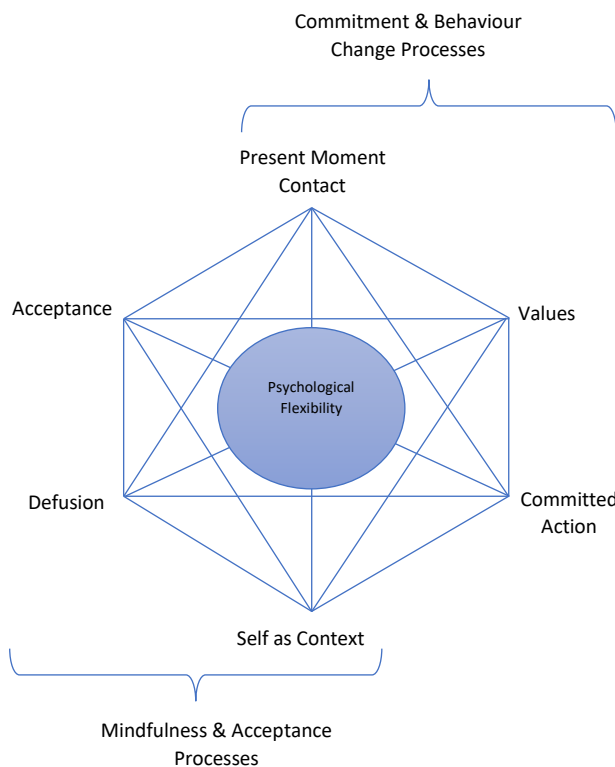


Figure 1: ACT's 'hexaflex' model of the positive psychological processes relating to psychological flexibility (adapted from Hayes et al, 2006).

Similar to the above described construct of decentering – though demonstrated as subtly distinct (Fresco et al, 2007a; Naragon-Gainey & DeMarree, 2017b) - is 'defusion', which focuses not upon changing the content of a thought (as typically in second-wave CBT) but changing ones relationship to and interaction with thoughts. This is done by creating contexts – using a variety of techniques – in which the literal quality and believability of the thought is weakened, and it is related to as what it is (i.e. a thought) rather than in terms of its content. 'Acceptance' refers to the willingness to allow all internal experiences to emerge and exist, including pain and distress, without attempting to modify or eliminate them. The role of acceptance is to set the conditions which enable subsequent value-based

action, as an alternative to the avoidance proposed to perpetuate distress. 'Being present' is encouraged and consists of a non-judgemental stance towards both internal and external experiences as they arise, simply noting them, rather than judging them. The ACT model further describes the idea that the sense of self or 'I' can be understood as a 'perspective' originating from the 'observing self', enabling a spiritual and transcendent experience and providing a 'context' for knowing rather than a focus on any specific content; that is, this perspective enables a distanced position from which to view thinking, feeling or experiencing. This stance is integral to the ACT model and paves the way for the process of defusion and detachment from internal experiences, thus lending itself to mindful awareness and acceptance. The core behaviour change processes of ACT are the conscious identification of ones 'values', and 'committed action' in line with these. Hayes et al (2006) highlight that the above processes do not exist as isolated therapeutic processes, but as conditions for the value-oriented behaviour that provides one with a sense of meaning and purpose.

Whilst the evidence base for ACT continues to grow, it is presently understood that ACT is likely efficacious for a range of physical and mental health difficulties, as compared to non-active (i.e. no intervention/treatment as usual) control conditions (Powers et al, 2009; Graham et al, 2016; Hughes et al, 2017; Byrne et al, 2019). In order to understand the ways in which ACT exerts its therapeutic influence, the core change processes outlined in the model have been examined. Again, it is of interest for this review to examine any overlaps between the mechanisms of change in ACT, and those implicated in psychedelic therapy. A systematic review of ACT mediation studies, i.e. studies which seek to identify mechanisms of change, concluded that whilst further - more methodically stringent - research is needed, the evidence suggests that the model's mechanisms of change appear consistent with the proposed processes relating to psychological flexibility, with 'acceptance' highlighted as a particularly unique or salient mediating component of ACT

(Stockton et al, 2018). Evidence exists for the positive effect of the acceptance, defusion and mindfulness components of the model (Levin et al, 2012), and the individual role of 'self-as-context' - as a flexible observer perspective – is emerging. There is limited preliminary evidence suggesting that this perspective can be taught, and may uniquely improve emotional well-being (Godbee and Kangas, 2019). The complex nature of the 'self-as-context' process itself, which is contingent on and related to other processes and intrinsically linked to mindfulness, highlights the interrelated nature of the ACT model and the overarching construct of psychological flexibility. Indeed, psychological inflexibility has been demonstrated to correlate with rates of mental health difficulty and work-related absence (Bond et al, 2011), with the cultivation of flexibility predictive of positive outcomes (Hayes et al, 2006; Vowles et al, 2014)

Psychological Flexibility, ACT & Psychedelics

Very recently, proponents of the integration of ACT and therapeutic psychedelic use have argued for not only a psychological understanding and formulation of the mechanisms of change, but a psychotherapeutic model to guide and support enduring change. Whilst ACT is primarily a behavioural model of change, it is underpinned by aspects of transcendent and mindful awareness (explored above); aspects which both feature heavily in the psychedelic experience. The altered states of consciousness and patterns of relating to the 'self' which are induced by psychedelics, namely ego-dissolution, can be likened to the distanced, contextual perspective taking 'self' promoted through ACT (Luoma et al, 2020), where other psychotherapeutic approaches may otherwise neglect or even pathologise this position.

ACT is argued to offer an evidence-based theoretical frame from which the positive and negative aspects of the psychedelic experience can be understood (Hayes et al, 2019). Referencing ACT's six core change processes, the sense of insight and 'noetic quality' of

mystical experiences has been discussed through the lens of ACT's 'self-as-context' or 'perspective-taking self', with the transcendent nature of this 'self' considered not dissimilar in essence to the psychedelic-induced phenomenon of ego-dissolution. The occasional intensely frightening experiences under the influence of psychedelics have been considered within the context of ACT's 'experiential acceptance', with the endurance and tolerance of such an experience paving the path for decreased avoidance (a known perpetuator of distress) once returning to ordinary consciousness (Luoma et al, 2019; Hayes et al, 2019). Thus it appears that accepting and tolerating the psychedelic experience may not solely be of benefit in the immediate sense (i.e. to reduce acute distress), but may promote a position of tolerance and acceptance towards distressing internal phenomena beyond the experience itself. Indeed, empirical evidence suggests that increases in acceptance occur following the psychedelic experience (Soler et al, 2016, 2018; Watts et al, 2017), supporting the notion of an important role for acceptance as a mechanism of change. A vital role for acceptance has similarly been highlighted through the broad lens of traditional CBT theory, explaining the benefits of psychedelics through a relaxation of avoidance-related beliefs, exposing one to private events and altering the previously long-standing reinforcement contingences perpetuating distress (Wolff et al, 2020). This may be considered in relation to the neurobiological theories of psychedelics, which propose that psychedelics release the mental constraints associated with rigidity and neuroticism (Swanson, 2018). Such characteristics may be comparable to psychological inflexibility and avoidance, with psychedelics capable of releasing the 'filter' - at a neurobiological level - which maintains avoidance and thus distress.

Overall, relevant features of the ACT model include the mindful, meditative and contemplative practices (which underpin ACT's processes of acceptance, self-as-context, defusion and present moment contact) and their ability to induce experiences likened to the psychedelic-induced dissolution of the 'ego' or familiar sense of 'self' (Hayes et al,

2019). Given the integral role of mindful awareness in the ACT model, the above reviewed evidence relating to the relationship between psychedelics and mindfulness can be considered relevant here also, particularly given emerging empirical evidence regarding psychedelics and the outcome of decentring, which may be understood as conceptually similar to ACT's cognitive defusion.

Whilst the components of ACT appear important, psychological flexibility - positioned as the overarching construct of ACT and comprising of the six core processes - has been implicated as a mediating mechanism of the therapeutic change seen with psychedelic use. A recent cross-sectional online survey study of 985 respondents examined the relationship between acute psychedelic effects and changes in anxiety and depression following a psychedelic experience. Results demonstrated that mystical and insightful experiences predicted increases in psychological flexibility, which in turn predicted decreases in depression and anxiety (Davis et al, 2020). This early evidence of the mediating role of psychological flexibility highlights the need for further studies examining its role, to establish whether it emerges as a reliable mediator of effects.

Psychedelic-Assisted Psychotherapy

ACT's psychological flexibility model (which incorporates mindful awareness) holds theoretical value through helping to provide an understanding of the psychedelic experience and its mechanisms. Psychological flexibility and mindfulness also demonstrate more practical potential, through the use these constructs (or their associated psychotherapeutic approaches) as an adjunct to the psychedelic experience, i.e. applying therapeutic mindfulness/ACT-based ideas prior to, during and/or after a psychedelic session. Both rooted in (or at least consistent with) psychological concepts relevant to contemplative and spiritual traditions, there appear to be shared phenomenological and psychological aspects between third-wave approaches and therapeutic psychedelic use -

notably alterations in self-awareness and self-relating. These alterations seemingly lend themselves to a potentially transformative shift of the self and the mind, through a possible breakdown of neurophysiological constraints and habitual cognitive and behavioural responding. Given the significant overlaps between the proposed mechanisms of change of either approach, third-wave psychotherapies may support the psychedelic experience. Support prior to the experience may cultivate a conducive physiological and cognitive context ('set'; a known contextual determinant of effects), and support following the experience may integrate and maintain benefits through committed practice (Walsh & Thiessen, 2018). Additionally, knowledge of third-wave principles during the experience may support the navigation of painful or difficult experiences encountered, through a detached awareness enabling these experiences to be observed and tolerated, rather than fused with and overwhelmed by (Hayes et al, 2019).

Regarding the psychedelic experience and psychedelic-assisted psychotherapy, the process of preparation is considered key in maximising potential positive outcomes, with integration then supporting the cultivation of long term benefits (Watts & Luoma, 2020). ACT's model of psychological flexibility has been recognised for its potential in supporting these processes (Walsh & Thiessen, 2018; Luoma et al, 2019; Watts & Luoma, 2020; Sloshower et al, 2020) and redeveloped as the Accept, Connect, Embody (ACE) model (Watts & Luoma, 2020), based on a qualitative analysis of participant's perceived change processes following psilocybin (Watts et al, 2017). With 'connection' and 'acceptance' identified by participants as key to their experience of positive change following the psychedelic experience, the ACE model was developed to present the six core processes of ACT's psychological flexibility model under a novel orientation; with an acceptance triad encompassing defusion, present moment focus and willingness, and a connection triad encompassing self-as-context, values and committed action (Watts & Luoma, 2020). Qualitative accounts from participant's undergoing psilocybin treatment for treatment-

resistant depression are provided by Watts & Luoma (2020), illustrating lived-experiences of these processes. Through the use of metaphor, imagery and direction, the ACE model acts as a map to guide the psychedelic experience, both through the acute phase and beyond. The model prompts the acceptance of uncomfortable experiences through letting go and decentering from mental chatter, sensing the body and opening up to feeling emotion. A metaphorical 'pearl' is used to represent hidden feelings and their meaning. To connect with meanings, values and insights, participants are guided to breathe, narrate the 'what' and the 'why' of this pearl, and create intentions which honour this newly uncovered meaning (Watts & Luoma, 2020). For proponents of ACT's psychological flexibility model as a guide for psychedelic-assisted psychotherapy, the combination of an evidence-based psychological practice with the embodied, visceral, unconstrained psychedelic experience provides a profound opportunity for patients to discover and sustain relief from painful, habitual, 'stuck' positions of distress.

Summary of Relevant Psychotherapeutic Constructs

Taken together, the above explored third-wave constructs demonstrate common themes, with mindful attention and detached and non-judgemental awareness arguably underpinning the opportunity to alter the conditioned and habitual responses maintaining distress. Whilst undeniably distinct, of note is that ACT, MBSR and MBCT may even be understood as self-compassion related therapies, with evidence demonstrating their efficacy in reducing psychopathology through the promotion of self-compassion (Wilson et al, 2018). Regardless, it is acknowledged that the hallmark of these third-wave therapeutic interventions is their transdiagnostic focus on underlying mental processes, rooted within the context of the wider human experience of conscious awareness and an ability to relate to internal events. Regarding psychedelics and their effects, parallels are evident between the state of self-awareness and self-relating cultivated by the above summarised therapeutic interventions, and that generated by the acute psychedelic experience. Given

the breadth of mental health difficulties that psychedelic therapy has been implicated in, it too may be considered a transdiagnostic approach, acting upon core underlying processes of the human experience.

Conclusions and Implications for the Present Study

This review describes contemporary third-wave psychotherapies and their core constructs in relation to the psychedelic experience, its proposed benefits and mediating mechanisms. Despite existing as distinct therapeutic interventions, mindfulness-based interventions (MBCT & MBSR) and Acceptance and Commitment Therapy (ACT) all encompass a position of detached, decentred or defused awareness, creating space between stimulus and response and paving an opportunity for change. This theoretical stance is echoed by neurophysiological data, demonstrating shifts in neural connectivity following these practices. Similarly, the acute psychedelic experience is characterised by profound changes in self-relating, with corresponding alterations in brain activity characteristic of a mind unconstrained. With the explored psychological constructs gaining traction amongst the psychedelic research community, further research is indicated to explore a potential pathway of effects.

To begin understanding the relationship between some of these key variables of interest, this study used a cross-sectional internet based survey specifically developed to capture the experiences and characterises of psychedelic drug users. Since research in this area is in its infancy, aspects of the study are necessarily exploratory. With the evidence relating to psychedelics and third-wave constructs still emerging, effect sizes are generally unknown and the meaningful role of these variables not yet established, with some inconsistent evidence demonstrated amongst research thus far. The chosen method of a survey, similar to other exploratory studies of psychedelic experiences and effects (Carbonaro et al, 2016; Hendricks et al, 2015; Nour et al, 2017), was considered an

appropriate method capable of both gathering data on a large number of variables across a large sample of participants, as well as providing a step towards experimental studies. This step may be particularly important given the historical challenges and regulatory barriers faced by those studying therapeutic psychedelic use; the provision of preliminary evidence to demonstrate their relevance for modern psychology may thus support the occurrence of future research.

The aims of the study (detailed in Part 2) were to preliminarily test the relationship between some of the constructs highlighted in the section above, namely mindfulness, decentering, mystical experiences and mental health. It is envisaged that findings will contribute to an understanding of these interrelated phenomena and their patterns of association within a non-clinical population of psychedelic drug users. Due to a cross-sectional non-experimental design, it is acknowledged that this study holds important limitations, with causality or the temporal nature of associations unable to be determined. Despite this, 'dose-response' analysis was used regarding frequency of psychedelic use to ascertain whether the variables of interest increased or decreased as a function of use, a method commonly used to establish linear relationships. Furthermore, attempts were made to control for the effects of likely confounding variables, to compensate for the lack of control inherent in a non-experiment design. The results of the present study are accordingly presented and discussed within their methodological context.

With preliminary evidence outlined within this review, an understanding of the relationship between known beneficial third-wave psychotherapeutic constructs and the psychedelic experience may better equip the design of future research, encouraging the capturing of relevant psychological ideas. It is envisaged that this understanding may both support the ongoing efforts to establish change mechanisms in psychedelic therapy, as well as continue to embed psychedelic therapy within a psychologically informed framework.

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Part 2: Empirical Paper

An exploration of the relationship between psychedelic drug use, mystical experiences, mindfulness,
and depression.

Abstract

Background & Aims: Emerging research suggests that psychedelic drugs hold therapeutic potential in the treatment of psychological disorders, though the psychological mechanisms by which this occurs are not currently fully understood. This study aims to explore the associations and pathways of effects between several key variables already implicated in the therapeutic benefits of psychedelics.

Method: Adult participants (N=1298), with at least one use of psychedelics within their lifetime, completed an online survey with questions relating to; frequency of lifetime psychedelic use; degree of psychedelic-induced mystical experience (MEQ-30; Maclean et al, 2012); trait mindfulness (FFMQ-15; Baer et al, 2006); decentering tendency (EQ; Fresco, Moore, et al, 2007) and meditation practice. Multiple hierarchical regression analyses were used to determine the association between variables and mediation analyses were employed to examine pathways of effects.

Results: Mystical experiences occurring during psychedelic use were predictive of higher trait mindfulness ($\Delta R^2=0.059$, $F(1,1291)=85.953$, $p<.001$) and decentering ($\Delta R^2=.095$, $F(1,1291)=140.678$, $p<.001$). These effects were found after controlling for meditation practice, as well as age, gender and education. A small negative association between mystical experience and depressive symptomology was found ($\Delta R^2=.006$, $F(1,129)=7.339$, $p=.007$), mediated by decentering ability (indirect effect =-.710, BCa 95% CI [-.870, -.571]). A small yet significant association was found between the frequency of lifetime psychedelic use and measures of trait mindfulness ($\Delta R^2=.004$, $F(1,1289)=5.289$, $p=.022$) and decentering ($\Delta R^2=.008$, $F(1,1291)=10.675$, $p=.001$) with the latter mediated by the degree of mystical experience reported (Indirect effect =.0014, BCa 95% CI [.001, .002]).

Conclusion: The quality of the psychedelic experience appears to be an important predictor of mindfulness. Measures of mindfulness-related capacities, i.e. decentering, seem to

mediate the small association between psychedelic-induced mystical experiences and depressive symptomology. Findings are discussed within the context of methodological limitations and suggestions for future research.

Introduction

Following a hiatus spanning several decades, a revival of interest in psychedelic drugs research has been seen in recent years amongst the psychological and psychiatric community, with research investigating their acute and sustained effects demonstrating potential therapeutic value. Classic psychedelic drugs, i.e. hallucinogens with 'serotonergic' neurochemical actions, typically refers to LSD (lysergic acid diethylamide), DMT (commonly prepared as a brew known as 'ayahuasca'), psilocybin (the active ingredient in 'magic mushrooms' and truffles), and mescaline (ingested via the Peyote or San Pedro cacti). These drugs have common subjective effects of profound disturbances in perception, affect and cognition (Dos Santos & Hallak, 2020). In addition to these effects, 'mystical experiences' have been demonstrated to occur under high doses (Griffiths et al, 2006; Johnson et al, 2019), that is, experiences which encompass a profound sense of unity (i.e. with one's surroundings), sacredness, truth and transcendence of time and space (Stace, 1960). These experiences have been understood to incorporate a sense of 'egoless-ness' (commonly termed 'ego-dissolution') or compromised sense of self, which may be experienced as both a positive or feared phenomena (Nour et al, 2016). Such an altered state of self-awareness may be comparable to meditative states of consciousness (Dor-Ziderman et al, 2013), including hypo-egoic self-awareness arising through mindfulness (Leary, Adams & Tate, 2006), or mystical states arising through instances of great awe (Hendricks, 2018).

Beyond these acute effects of psychedelic drugs, emerging studies of their use have demonstrated their potential in alleviating symptoms of OCD (Morena, Wiegand, Taitano et al, 2006), cancer-related anxiety and low mood (Grob et al, 2011; Griffiths, Johnson, Carducci et al, 2016; Ross, Bossis, Guss, 2016), as well as reducing drug dependence (Sessa & Johnson, 2015; Bogenschutz & Pommy, 2012; Pisano, Putman et al, 2017), alcoholism (Bogenschutz, Forcehimes, Pommy et al, 2015) and tobacco addiction (Johnson, Garcia-Romeu, Johnson, Griffiths, 2017; Johnson et al, 2014; Johnson, Garcia-Romeu, Griffiths,

2017). Interest has focused in particular on the relationship between psychedelic use and reductions in symptoms of depression and low mood (Carhart-Harris et al, 2016; Carhart-Harris et al, 2017; Osorio et al, 2015; Palhano-Fontes et al, 2019), with current randomised controlled trials underway internationally to investigate this therapeutic potential with methodological rigour (e.g. ClinicalTrials.gov NCT Number: NCT03181529, NCT03429075, NCT03554174, NCT03380442).

Of interest, then, is an understanding of the mechanisms by which psychedelics may be eliciting their therapeutic benefits. Theories have been proposed to explain their effects, with suggestions that psychedelics alter functional connectivity in such a way that enables a breaking down of habitual (distressing) patterns of thinking and responding, paving the way for change (Swanson, 2018; Carhart Harris et al, 2014). More specifically, studies have investigated the role of mystical experiences, of which ego-dissolution is one aspect, with regard to the therapeutic outcomes of psychedelic use. For instance, adaptive changes in attitudes and behaviour (Griffiths, Richards, McCann et al, 2006; Griffiths, Johnson, Richards et al, 2011), improvements in end-of-life related anxiety and depression in cancer patients (Griffiths et al, Ross et al, 2016), improvements in alcohol and tobacco dependence (Bogenschutz et al, 2015; Garcia-Romeu, Griffiths & Johnson, 2015) as well as attributions of meaningfulness and spiritual significance (Griffiths et al, 2008), have all been associated with the degree of mystical experience reported to occur under psychedelics, suggestive of a potentially mediating role.

Whilst emerging evidence points to the occurrence and degree of a mystical experience as a possible explanatory mechanism, the role of other psychological processes in mediating the effects of psychedelics remain unclear. For clinical psychologists, psychiatrists and other psychotherapists, treatment of psychological disorders with psychedelic drugs may represent an opportunity for an adjunct to known

psychotherapeutic modalities. Recent research has sought to integrate psychedelics with the principles and theory of Acceptance and Commitment Therapy (ACT) - a 'third-wave' Cognitive Behavioural Therapy (CBT) approach promoting 'psychological flexibility' to alleviate distress - given overlaps between ACT's core constructs and the subjective psychedelic experience (Watts & Luoma, 2020). Psychological flexibility refers to the ability to notice and distance oneself from distressing thoughts and emotions, and commit to action in accordance with one's values despite emotional – or even physical – pain (Hayes et al, 2006). The ACT model emphasises 'mindfulness and acceptance' processes, key constructs of which include 'cognitive defusion' (a shifting away from the literal meaning of thoughts) and 'present-moment contact' (a non-judgemental way of relating to arising internal and external experiences, to return focus to the here and now) (Hayes et al, 2006).

'Mindfulness' refers to a meditative practice and attentional stance which encompasses the state of awareness that arises through 'paying attention on purpose, in the present moment, and nonjudgmentally to the unfolding experience moment by moment' (Kabat-Zinn, 2003). High levels of mindfulness are associated with reduced psychological distress (Keng et al, 2011) and mindfulness-based programmes are recommended in clinical guidelines for the treatment of recurrent depression (NICE CG90, 2009). Studies from the past decade have begun to demonstrate an overlap between meditation- and psychedelic-induced 'self-transcendent' or 'ego-less' states at both a neurophysiological and subjective level (Carhart-Harris et al, 2014; Milliere et al, 2018), and there has therefore been interest in the role mindfulness may play in explaining the beneficial effects of psychedelics. In addition to the role of mindfulness as a broad construct, the potential role of related constructs or specific facets of mindfulness have also been highlighted. 'Decentering' refers to the ability to relate to one's own thoughts, feelings and sensations as temporary events, characterised by a detached 'observer' perspective (Fresco, Moore, et al, 2007; Teasdale et al, 2002). Though often considered

overlapping constructs, decentering has been conceptualised as related to but not synonymous with trait mindfulness (Fresco, Moore, et al, 2007). Whilst both encompass the ability to observe mental events as transient, studies and conceptualisations of the association between these constructs propose that decentering may contribute as one aspect of mindfulness ability (Naragon-Gainey & DeMarree, 2017a), though a sequential chain of effects is not necessarily established (Sauer & Baer, 2010), and it is therefore unclear. It is accepted, however, that mindfulness-based interventions explicitly seek to foster the capacity of decentering (Naragon-Gainey & DeMarree, 2017a; Fresco, Moore, et al, 2007), and there are indeed suggestions of its mediating role in the relationship between mindfulness interventions and therapeutic outcomes (Hoge et al, 2016; Naragon-Gainey & DeMarree, 2017b; Sauer & Baer, 2010; Fresco, Segal, et al, 2007a).

Accordingly, recent research has sought to examine the hypothesis that psychedelic use is related to improvements in mindfulness and decentering capacities, with regard to both the post-acute phase of the psychedelic experience as well as sustained effects. A study of 25 ayahuasca users assessed trait mindfulness and decentering both before and 24 hours after an ayahuasca session in a supportive non-religious setting. It was found that the capacities of being non-judgemental and non-reactive to internal experiences, as well as decentering, significantly increased 24 hours post-session (Soler et al, 2016). Such post-acute improvements have been demonstrated to correlate with changes in functional connectivity in an open-label uncontrolled fMRI study of 16 users, following a single dose of ayahuasca (Sampedro et al, 2017). A larger sample of 48 participants completing measures before and 24 hours after ayahuasca similarly demonstrated improvements in various facets of mindfulness (ability to observe, describe, act with awareness and take a non-reactive stance towards thoughts, feelings and sensations) (Beiner & Soar, 2020). Some studies have included measures at follow up to examine sustained effects, with variable findings. A two-month follow up following an ayahuasca ceremony found that only the non-

judgement facet of mindfulness was sustained (Sampedro et al, 2017). Similarly, initial increases in trait mindfulness have been found to be diminished at four week follow-up, though the role of dropout rates and loss of statistical power is acknowledged (Uthaug et al, 2018).

Contrarily, a single inhalation of the dried secretion from the *Bufo alvarius* toad, which contains the DMT analogue 5-MeO-DMT, has been demonstrated to increase mindfulness and decrease depression and stress four weeks after the experience (Uthaug et al, 2019). Similarly sustained effects have been demonstrated with a study of ten psychedelic-naïve participants taking psilocybin in a supportive setting demonstrating improvements in mindfulness at three-month follow up, with an effect size comparable to those produced following mindfulness-based stress reduction (MBSR) programmes (Madsen et al, 2020). Indeed, a direct comparison of four ayahuasca sessions with an eight-week MBSR course demonstrated comparable increases in the mindfulness facet of non-judgement, despite the ayahuasca sessions holding no specific purpose related to mindfulness, indicating a pharmacologically-induced change in mindfulness (Soler et al, 2018).

Regarding a possible pathway of effects, the previously discussed mechanism involving psychedelic-induced mystical experiences has been supported empirically. Increases in mindfulness following ayahuasca have been demonstrated to correlate with the level of ego-dissolution experienced (Uthaug et al, 2018), with ego-dissolution correlating with decreases in depression and stress following inhalation of 5-MeO-DMT (Uthaug et al, 2019), and the degree of mystical experience following psilocybin consumption predictive of decreased depressive symptomology in participants with treatment-resistant depression (Roseman et al, 2018). Taken together, these findings imply a potential pathway of effects of psychedelic-induced mystical experiences eliciting increases in mindfulness, and subsequent decreases in symptoms of depression.

The post-acute and sustained mindfulness effects of psychedelics appear to emerge in psychedelic-naïve participants irrespective of previous experience with these drugs (Beiner & Soar, 2020; Madsen et al, 2020; Uthaug et al, 2018). However, whilst it has been suggested that the frequency of previous experience with psychedelics is not a predictor of outcomes (Mian et al, 2019), questionnaires administered to two separate groups of users (previous use ranging between 1-100 times) and non-users of ayahuasca revealed that only those users with more than 15 experiences of taking ayahuasca scored significantly higher than non-users in the capacity of decentering (Franquesa et al, 2018). This is in accordance with Soler et al's (2016) finding that decentering significantly increased following ayahuasca in a sample with an average of 79 previous uses.

In light of the above summary, this study aims to begin to understand the relationship between several key variables: frequency of lifetime psychedelic use, degree of mystical experience, mindfulness and decentering, and mental health. Specifically, depression was focused on due to its focal role amongst the literature relating to psychedelics, as well as its established association with mindfulness-based interventions. As an exploratory investigation interested in the possible pathways between potential effects, this study seeks to answer the following questions:

1. Is frequency of lifetime psychedelic use positively associated with measures of (a) trait mindfulness and more specifically (b) decentering?
2. Is frequency of lifetime psychedelic use negatively associated with symptoms of depression?
3. Is the degree of psychedelic-induced mystical experience positively associated with measures of (a) trait mindfulness and (b) decentering?
4. Is the degree of psychedelic-induced mystical experience negatively associated with symptoms of depression?

5. Does the degree of mystical experience reported mediate a relationship between lifetime psychedelic use and measures relating to mindfulness (i.e. trait mindfulness, decentering)?
6. Do mindfulness-related capacities mediate a relationship between mystical experiences and symptoms of depression?

Method

This study was granted ethical approval by the UCL Ethics Committee Project ID: 15153/001 (see Appendix 1).

Design

In order to answer the stated research questions, this study adopts a within-subjects cross-sectional correlational design, using an internet-based survey, similar to other studies exploring associations related to psychedelic use (Barrett et al, 2017). To attempt to begin understanding a temporal chain of effects, dose-response analysis was used to infer whether frequency of psychedelic use was linked to the outcomes of trait mindfulness, decentering and depression. Multiple regression analyses were used to examine all predictor/outcome relationships whilst controlling for potentially co-varying or confounding variables. Mediation analyses were used to understand hypothesised pathways between effects.

Participants

Recruitment

Participants were primarily recruited through online advertisements posted across various relevant internet sites. The advertisement, including brief details of the study as well as the survey link, was posted on pages across social media platforms (i.e. Facebook, Twitter, Instagram, Reddit) related to an interest in psychedelic substances. The UK Psychedelic Society disseminated the study advertisement via their social media channels and email newsletter. The Multidisciplinary Association for Psychedelic Substances (MAPS),

based in the USA, similarly posted the study advertisement across their channels and on the 'participate in research' section of their website. Snowball sampling was promoted through social media, with viewers of the advertisement encouraged to share the survey link with their own networks. The advertisement was also shared by email with individuals familiar with or knowledgeable about psychedelic drugs, with a request to share this amongst their networks. The survey link directed potential participants to a set of screening questions to ascertain eligibility. All participants provided full informed consent.

Inclusion Criteria

In order to be eligible to take part in the study, participants were required to confirm that they were (1) at least 18 years old and (2) had taken a psychedelic drug at least once in their lifetime. Participants were asked to endorse any substance they had taken at least once in their lifetime from a predetermined list of psychedelic substances (see Appendix 2), established in consultation with experts by experience. It was acknowledged that this was not an exhaustive list, and an option was provided for participants to endorse and provide details of other psychedelic substances, though it was noted that this did not include drugs like MDMA, Cannabis, Ketamine or nitrous oxide, though they may have some psychedelic effects.

Power Analysis

As this was an exploratory study, power analysis was informed by the expectation of a small effect size using multiple linear regression (effect size $f^2 = 0.02$). Power calculation was carried out using the "G*Power3" computer software (Faul, Erdfelder, Lang & Buchner, 2007), specifying $\alpha = 0.05$, desired power = 0.95, with 6 predictors. The required sample size was determined to be 1050. We recruited slightly beyond this given the uncertainty regarding the true effect size and potential difficulties with missing data.

Procedure

Having arrived at the secure survey site, hosted by the platform Qualtrics, respondents provided answers to two screening questions; indicating whether they are at least 18 years old and have used a psychedelic drug at least once in their lifetime. Regarding this latter criteria, participants chose from a provided list of widely recognised psychedelic drugs (based on expert consensus; see Appendix 2). An 'Other' category was also provided, with participants who endorsed this option required to indicate details of any other psychedelic compounds they have taken which were not already listed, with a caveat noting that this should not include substances like MDMA, Ketamine and Cannabis, though they may have some psychedelic effects. Given the uncertainty regarding which substances participants may list here, we allowed those participants who solely endorsed this option to proceed with the survey to ensure that we did not lose relevant data. These participants were screened for suitability based on whether the indicated substance shared more properties with classic psychedelics than related drugs (e.g. dissociative anaesthetics, e.g. ketamine) prior to analysis.

Participants who met the above eligibility criteria viewed the study's information sheet and informed consent document (see Appendix 3), and were able to download copies of these to their devices. These documents detailed the purpose of the study, relevant data protection information and details of how to withdraw from the study. No personal identifying information was collected in the survey and data remained anonymous.

Materials

This study uses data obtained from a larger study which was developed to gather data for research and analysis beyond the scope of this thesis. As such, a detailed description is only provided for those questions and measures relevant to the present study.

Demographics

We obtained details regarding participant's gender, nationality, ethnicity (categories based on the latest UK census), religion (categories based on the latest UK census) and level of education.

Patterns of Drug Use

Participants provided details regarding their history of drug use, indicating whether they have ever taken each of the following substances at all within their lifetime (yes/no) and if so, on approximately how many days within the past twelve months:

benzodiazepines; alcohol; tobacco; e-cigarettes; amphetamine; methamphetamine; cocaine; ecstasy/MDMA; ketamine poppers; nitrous oxide; opioids (e.g. heroin, morphine, oxycodone); cannabis; synthetic cannabis/cannabinoids; GHB/GBL. This list was developed in collaboration with researchers from the UCL Clinical Psychopharmacology unit with extensive experience regarding drug use and classification. A 'decoy' drug was included amongst the list ("spanglers") to aid in the identification of careless or unreliable responding.

History of Psychedelic Use

Participants were reminded of the psychedelic substances that they endorsed during screening, before being asked a series of follow up questions regarding their experience with these drugs. Participants were asked to provide the age at which they both first and last used a psychedelic drug, as well as the total number of times they have used each endorsed drug both in their lifetime (variable: '[frequency of] lifetime psychedelic use'), and within the past 12 months. Guidance was provided to inform participants that this does not include micro-dosing (with questions specific to this appearing later in the wider survey). An acknowledgement was made that whilst it may be difficult to be precise, an estimate may helpfully be calculated based on first use, last use, and frequency of use within a typical year.

Participants were then required to separately consider the first (or first few) and last (or last few) time(s) they used a psychedelic drug, and rank their top three reasons or intentions for use from the following options: for fun/recreational; for personal growth; to foster creativity; for spiritual or religious reasons; out of curiosity/interest; social reasons (e.g. to connect deeply with others); to connect with nature; to help manage or confront difficult emotions (including to help manage a specific psychological problem (e.g. depression, anxiety, trauma)); to enhance cognitive performance (e.g. to improve attention). A final option allowed an “other reasons” response, followed by a text box allowing participants to enter specific additional reasons for use. Response options were modified from previous research (Haijen et al, 2018), with the addition of ‘enhancing cognitive performance’ in line with observed trends in popular culture use.

Again holding in mind their experience with the endorsed psychedelic substances, participants were asked to respond to a series of questions in line with their most “significant” or “important” psychedelic experience (i.e. the one experience that was the most influential or memorable), indicating which of the endorsed drugs this was elicited by and at which age the experience occurred. Participants then reported on the following set of items, developed and administered in several laboratory studies of the effects of psilocybin (Griffiths et al, 2006; Griffiths et al, 2011), to ascertain their appraisal of the overall impact of the experience. The meaningfulness of their chosen experience was indicated using the following response options: “no more than routine, everyday experiences”, “similar to meaningful experiences that occur on average once or more a week”, “similar to meaningful experiences that occur on average once a month”, “similar meaningful experiences that occur on average once a year”, “similar to meaningful experiences that occur on average once every 5 years”, “among the top 10 most meaningful experiences of my life”, “among the top 5 most meaningful experiences of my life”, and “the single most meaningful experience of my life”. The degree to which the

experience was spiritually significant was indicated using the following scale: “not at all”, “slightly”, “moderately”, “very much”, “among the top 5 most spiritually significant experiences of my life”, and “the single most spiritually significant experience of my life”. Participants also indicated the perceived impact of the experience on their well-being or life satisfaction (“Do you believe that the experience and your contemplation of that experience have led to a change in your current sense of personal well-being or life satisfaction?”) using the following scale: “Increased very much (+3)”, “Increased moderately (+2)”, “Increased slightly (+1)”, “No change (0)”, “Decreased slightly (-1)”, “Decreased moderately (-2)”, “Decreased very much (-3)”.

Mystical Experiences Questionnaire (MEQ-30)

The Mystical Experiences Questionnaire (MEQ30) is a 30-item self-report measure designed to assess the nature and extent of subjective mystical experiences that may occur after use of psychedelics (Maclean et al, 2012). Covering the descriptions of dimensions of mystical experiences (Stace, 1960; Pahnke & Richards, 1966), the MEQ30’s four subscales provide measures of a sense of unity, noetic quality and sacredness (termed ‘*mystical*’); *positive mood*; *transcendence of time/space*; and *ineffability*. The measure also yields a total scale score indicative of the overall intensity of mystical experiences. As in previous studies, the occurrence of a “complete” mystical experience was determined by participants obtaining a score of at least 60% of the maximum possible score across each of the four subscales (Griffiths et al, 2006; Barrett et al, 2015).

Reflecting on their chosen psychedelic experience, participants were asked to respond to each of the MEQ30’s items using a 6-point scale ranging from “0 -None; not at all” to “5 - Extreme (more than any other time in my life and stronger than 4)”. Example items include “Experience of fusion of your personal self into a larger whole”(‘*mystical*’ subscale); “Sense of being ‘outside of’ time, beyond past and future” (‘*transcendence of time/space*’ subscale); “sense of awe or awesomeness” (‘*positive mood*’ subscale); and

“Feeling that you could not do justice to your experience by describing it in words” (‘ineffability’ subscale). Subscale scores are computed by calculating the average response to relevant items, with a full scale score computed by taking the average response to all items. The MEQ-30’s full scale score was used in all analyses for this study to represent the variable: ‘[degree of] mystical experience’, associated with participations chosen most important or significant experience. The measure has demonstrated good reliability and validity in studies of psychedelic drug users (Full Scale: Cronbach’s alpha = .97) (MacLean et al, 2012; Barrett et al, 2015).

Mindfulness-Related Capacities

Two measures were included to capture both the breadth of the construct of mindfulness, as well as more specific detail regarding the construct of decentring. The below measures were selected due to their use in previous research relating to mindfulness-related capacities and psychedelics, demonstrating their sensitivity to psychedelic use.

Trait Mindfulness - Five Factors Mindfulness Questionnaire (FFMQ-15). The Five Facet Mindfulness Questionnaire (Baer et al. 2006) is a 15-item measure yielding a full-scale score indicating overall trait mindfulness, as well as five different subscale scores; *observe*: noticing external and internal experiences, e.g., body sensations, thoughts, or emotions; *describe*: putting words to, or labelling the internal experience; *acting with awareness*: focusing on the present activity instead of behaving mechanically; *non-judging the inner experience*: taking a nonevaluative stance towards the present experience, thoughts, or emotions; and *non-reacting to the inner experience*: allowing thoughts and feelings to come, without getting caught up in, or carried away, by them. Participants were asked to respond to each item using a 5-point scale ranging from 1 (never or very rarely true) to 5 (very often or always true). Example items include: “I pay attention to sensations, such as

the wind in my hair or sun on my face” (*observe* subscale); “I’m good at finding words to describe my feelings (*describe* subscale); “I find myself doing things without paying attention” (*acting with awareness* subscale); “I tell myself I shouldn’t be feeling the way I’m feeling (*non-judging* subscale) and “When I have distressing thoughts or images I just notice them and let them go” (*non-reacting* subscale).

Scores are computed by summing subscale items (or all items for the full scale score), after reverse scoring relevant items. Whilst previous research has demonstrated that particular facets of the FFMQ may be specifically related to psychedelic use, there are inconsistencies amongst results. In keeping with the exploratory nature of this study, the FFMQ-15’s full scale score was used for analyses, in order to capture the breadth of this construct. The psychometric properties of the FFMQ-15 have been tested and its factor structure confirmed with adequate internal consistency, (Full Scale: Cronbach’s alpha = .80 to .85)(Baer et al, 2006, Baer et al, 2012, Gu et al, 2016).

Decentering - Experiences Questionnaire (EQ). The Experiences Questionnaire (EQ) comprises 11 items and measures the construct of *decentering*, understood as the capacity to observe one’s thoughts and emotions as temporary events of the mind rather than fundamental truths relating to the self (Fresco, Moore, et al, 2007). Participants responded to each item based on their ‘general experiences’ using a five-point scale, ranging from ‘1 - Never’ to ‘5 – All the time’. All items are summed or averaged to compute the scale score, with a higher score indicating greater levels of decentering. Example items include “I can observe unpleasant feelings without being drawn into them” and “I can slow my thinking at times of stress”. The EQ demonstrates convergent and discriminant validity, strong internal consistency and good temporal stability and has been demonstrated to be sensitive to treatment changes across a range of psychological disorders (Cronbach’s alpha = .83 to .90) (Fresco, Moore, et al, 2007; Naragon-Gainey et al, *in press*).

Depression

Depression, Anxiety and Stress Scale (DASS-21) – Depression Subscale. Data regarding symptoms of depression was gathered through use of the DASS-21's 'depression' subscale, assessing this negative mood state over the previous week. The subscale comprises of seven items (e.g. "I felt that I had nothing to look forward to"), scored using a four-point scale (0 = "these statements did not apply to me at all," 1 = "applied to me some of the time," 2 = "applied to me a good part of the time," and 3 = "applied to me most of the time") (Lovibond & Lovibond, 1995). A score for the subscale is calculated by summing the scores for each item. As a dimensional rather than categorical conception of psychological distress, a higher score indicates a higher degrees of the emotional state of depression. The DASS-21 demonstrates good construct validity and internal consistency, is widely regarded as a reliable tool and used in research (Depression Scale: Cronbach's alpha = .88) (Henry & Crawford, 2005; Lovibond & Lovibond, 1995).

Meditation

Participants were asked whether or not they practice any form of meditation. Given the lack of consensus regarding a definition of meditation, the following broad guidance was provided:

"'Meditation' can mean different things to different people. Here we mean a practice in which you deliberately set time aside to use techniques to rest the mind and body by suspending the tendency to analyse or judge your experience. Many techniques can be used in meditation: focusing on an object, sound, experience or on the breath; using a mantra or chanting; special breathing practices (pranayama). It can involve sitting or lying still, or deliberate movement; it can be practiced alone or in groups, with or without an instructor. Some examples of types of meditation are: Vipassana, Zen meditation, Anapana Sati,

mindfulness, transcendental meditation, yoga/yogic breathing, Qigong. There are many other types.”.

Those endorsing meditation practice were asked to indicate the age at which they started meditating, as well as the frequency at which they meditate (providing details of, generally speaking, how many days each month, and for how many minutes per day on these days). In line with the previously provided response options regarding intentions for psychedelic use (see above ‘History of Psychedelic Use’), participants were asked to rank their top 3 most important reasons or intentions for meditating.

Statistical Analysis

Descriptive statistics (mean, standard deviations, frequency and percentages) were used to describe the sample, using participant’s responses to those questions relating to demographics and sample characteristics. All analyses were conducted using SPSS version 26 (IBM Corp, New York, NY, USA). To analyse the relationships between key variables pertaining to the specified research questions, hierarchical multiple regression analyses were conducted. Baseline covariates (i.e. age, gender and level of education) were entered into Block 1 of the regression analyses and hypothesis-led predictor(s) entered into Block 2. Covariates were selected based on similar previous research (Mian et al, 2019; Hendricks et al, 2015). For all analyses, a significance level of $p < .05$ was used. The regression analyses were conducted for several associations of interest, outlined in further detail below as per the stated research questions, between the following key constructs: *trait mindfulness* (FFMQ Full Scale Score), *decentering* (EQ Total Score), *depression* (DASS-21 Subscale), *lifetime psychedelic use*, expressed as ‘number of uses’, and degree of *mystical experience* associated with the most significant psychedelic experience (MEQ30 Full Scale Score). For regression analyses with trait mindfulness (FFMQ Score) or decentering (EQ Score) as the outcome variable, *meditation practice* was included as an additional dummy coded

predictor due to its strong potential for covariance (Beiner & Soar, 2020).¹ *Gender* was dummy coded due to the 3 possible response options (male/female/other), with *female* (as compared to a reference category including male and other) and *other* (as compared to a reference category including male and female) entered into each model as covariates. *Male* was not entered as a separate variable due to collinearity, as this was already accounted for by the inclusion of the *female* and *other* variables. Regression analyses were thus conducted, corresponding to the research questions previously stated, as follows:

1. *Lifetime psychedelic use* was used to predict the outcome of *trait mindfulness* and, separately, *decentering*, whilst controlling for age, gender, level of education, and meditation practice.
2. *Lifetime psychedelic use* was used to predict the outcome of *depression*, controlling for age, gender and level of education.
3. *Mystical experience* was used to predict the outcome of *trait mindfulness* and, separately, *decentering*, whilst controlling for age, gender, level of education, and meditation practice.
4. *Mystical experience* was used to predict the outcome of *depression*, controlling for age, gender and level of education.

All regression models were tested to determine whether assumptions for the general linear model were met. Tests for influential cases (Cook's distances), non-multicollinearity, homoskedasticity and normality of residuals were conducted and no serious issues were detected, thus the reported models were considered to be acceptable.

Mediation analyses were conducted using the PROCESS plug-in for SPSS (Hayes, 2017). The significance of mediation effects was determined by interpreting bias corrected

¹ Whilst data was available relating to participant's frequency of meditation (i.e. 'minutes per month'), this data was largely skewed towards zero given that 33% of the sample did not endorse having a meditation practise. As such, meditation was controlled for in analyses as a binary variable.

bootstrapped confidence intervals (CIs) based on 1000 samples regarding the indirect effect of the predictor on the outcome via the mediator, with a CI range that does not include '0' indicative of a significant indirect effect and mediation (Field, 2013). The following mediation analyses were planned regarding the final two research questions:

5. In the case of a significant positive association between the predictor of *lifetime psychedelic use* and the outcome(s) of mindfulness-related capacities (i.e. *trait mindfulness, decentering*), mediation analysis was planned with *mystical experience* as mediator. As per the regression analyses, age, gender, level of education and meditation practice were included as covariates.
6. In the case of a significant negative association between *mystical experience* and *depression*, mediation analysis was planned with measures of mindfulness-related capacities (i.e. *trait mindfulness, decentering*, considered separately) as mediator. As per the regression analyses, age, gender and level of education were included as covariates.

Results

Survey completion

A total of n=3172 followed the link to the survey's screening questions. Of this, n=258 did not confirm meeting the inclusion criteria (n=9 were below the age of 18, n=258 did not endorse any lifetime psychedelic drug use, n=2 did not complete the screening questions). A further n=1005 did not then provide informed consent to continue to the survey, thus participation ceased for these individuals. Of the remaining n=1909, n=13 were excluded because they endorsed only 'other' as their lifetime psychedelic drug use and examination of text details demonstrated an ineligible substance; n=593 were excluded as they did not complete the survey in its entirety (median progress of 52% upon discontinuing); and a further n=5 were excluded because they endorsed a decoy fictional

drug indicating unreliable responding. Accordingly, N=1298 participants provided useable data and constituted the final sample upon which analysis was completed. Data reported refers to this full sample of participants unless otherwise stated.²

Sample Characteristics

Demographics

The majority of respondents were male (57%), of white European, North American or other white ethnicity (82%), non-religious (70%), with a mean age of 33 years old (range 18-79), educated with at least a Bachelors university degree (67%) and of primarily American (37%) and British (22%) nationality (likely as a result of distribution through the UK Psychedelic Society and US MAPS organisations). For details regarding the demographic characteristics of the sample see Table 1.1.

History of Drug Use

Participants reported having consumed a variety of non-psychedelic drugs in their lifetime and the 12 months prior to completing the survey, with alcohol (96%, n=1246), cannabis (95%, n=1227), ecstasy/MDMA (70%, n=904), tobacco (69%, n=897) and cocaine (62%, n=806) the most frequently reported substances (see Table 1.2 for full details of reported substance use).

² Despite the sample completing the survey in its entirety, several questions – for practical reasons – were not ‘forced response’, that is, they did not require participants to provide a response before continuing. In cases where responses were not provided, these data points were coded as missing.

Table 1.1: *Sample by Gender, Ethnicity, Religion and Education Level (Frequency and Percentage).*

| | N | % | |
|-----------------|-------------------------|------|----|
| Gender | Male | 734 | 57 |
| | Female | 523 | 40 |
| | Other | 41 | 3 |
| Ethnicity | White | 1061 | 82 |
| | Mixed Heritage | 120 | 9 |
| | Asian | 43 | 3 |
| | Black | 11 | 1 |
| | Hispanic/Latin American | 26 | 2 |
| | Other | 32 | 3 |
| Religion | No Religion | 912 | 70 |
| | Christian | 116 | 9 |
| | Buddhist | 60 | 5 |
| | Hindu | 16 | 1 |
| | Jewish | 28 | 2 |
| | Muslim | 4 | 0 |
| | Spiritual | 39 | 3 |
| | Other | 123 | 10 |
| Education Level | GCSE/Equivalent | 40 | 3 |
| | A-Level/Equivalent | 381 | 29 |
| | Bachelors Degree | 535 | 41 |
| | Masters Degree | 264 | 20 |
| | Doctoral Degree | 78 | 6 |

Table 1.2: Lifetime use and previous 12 month frequency of use for licit and illicit substances
(*n*=1296).

| | Lifetime Use Endorsed | | Past 12 Months Frequency | |
|------------------------|-----------------------|----|--------------------------|-----------|
| | <i>n</i> | % | <i>Mean</i> | <i>SD</i> |
| Benzodiazepines | 511 | 40 | 6.89 | 37.52 |
| Alcohol | 1246 | 96 | 72.12 | 89.56 |
| Tobacco | 897 | 69 | 74.45 | 128.04 |
| E-Cigarettes | 456 | 35 | 33.80 | 92.69 |
| Amphetamine | 464 | 36 | 6.30 | 37.28 |
| Methamphetamine | 186 | 14 | 1.33 | 17.93 |
| Cocaine | 806 | 62 | 3.75 | 15.03 |
| Ecstasy/MDMA | 904 | 70 | 2.94 | 11.90 |
| Ketamine | 492 | 38 | 2.85 | 12.73 |
| Poppers | 289 | 22 | 0.59 | 4.99 |
| Nitrous Oxide | 483 | 37 | 2.15 | 11.91 |
| Opioids | 381 | 29 | 4.89 | 35.32 |
| Cannabis | 1227 | 95 | 133.63 | 144.45 |
| Synthetic Cannabinoids | 166 | 13 | 1.76 | 17.50 |
| GHB/GBL | 111 | 9 | 0.20 | 3.08 |

Frequency of Previous Psychedelic Drug Use

Participant's reported having used psychedelics for the first time an average of 11.5 years ago (Mean(M)=11.48, SD=11.63), with most recent use an average of 1.5 years ago (M=1.57, SD=5.23). Across all psychedelic substances, the average frequency of lifetime use was 54 times (M=53.75, SD=163.4), and 7 times (M=7.49,SD=24.6) in the past 12 months. See Table 1.3 for more details regarding the lifetime and the previous 12 month's frequency of use for each psychedelic drug.

Table 1.3: *Lifetime and 12 Month frequency of psychedelic drug use (Mean and Standard Deviation).*

| | Lifetime Frequency | | Past 12 Months Frequency | |
|--------------------------|--------------------|-----------|--------------------------|-----------|
| | <i>Mean</i> | <i>SD</i> | <i>Mean</i> | <i>SD</i> |
| LSD (n=1071) | 32.58 | 126.82 | 3.28 | 7.60 |
| Psilocybin (n=1144) | 18.52 | 56.01 | 2.63 | 4.72 |
| Ayahuasca/Yage (n=226) | 9.57 | 28.71 | 2.48 | 6.29 |
| DMT/Changa (n=445) | 13.82 | 56.29 | 4.14 | 33.59 |
| Mescaline (204) | 4.27 | 11.14 | 0.62 | 1.42 |
| Psychoactive Toad (n=62) | 3.23 | 5.22 | 1.13 | 2.41 |
| Iboga (n=15) | 2.19 | 3.02 | 0.47 | 0.52 |
| Salvia Divinorum (n=303) | 7.41 | 56.36 | 1.30 | 17.28 |
| NBOMe(n=95) | 5.15 | 6.14 | 0.43 | 1.67 |

Intentions for Psychedelic Drug Use

Regarding motivations for using psychedelic drugs, the majority of participant's reported 'fun/recreational' reasons (35%) and 'out of curiosity/interest' (33%) the first or first few times they used psychedelics, and for 'personal growth' (31%) and 'fun/recreational' reasons (23%) the last or last few times. See Figure 1.2 for details regarding participant's intentions for using psychedelics across their first and last few uses.

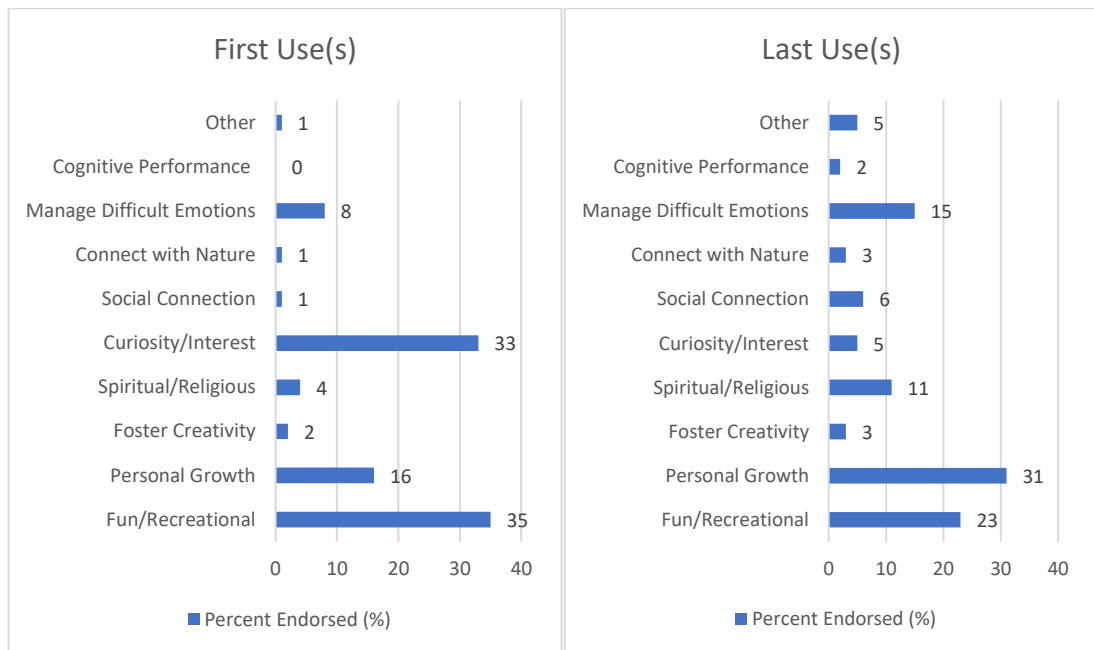


Figure 1.2: Intentions for first (or first few) and last (or last few) uses of psychedelics (% endorsed).

Characteristics of Most Significant Psychedelic Experience

Reporting on their most significant or important psychedelic experience, the majority of participants attributed this experience to LSD (40%), psilocybin (37%) and DMT (ayahuasca/yage) (10%), with the chosen experience occurring an average of 5.97 years ago (SD=9.11). The majority of participants ranked this experience amongst at least: the five most meaningful experiences of their lives (60%), the five most spiritually significant experiences of their lives (63%), and believed that their experience had led to increases in their personal wellbeing or life satisfaction (93%). Almost two thirds of participants (59%) demonstrated having had a ‘complete mystical experience’ during their chosen experience (according to Griffiths et al’s (2011) criteria of a score of >60% of the maximum possible score across all four subscales of the MEQ-30). This is consistent with findings of studies from the John Hopkins laboratory, as discussed by Johnson et al (2019), who have demonstrated complete mystical experience occurring in 61% of participants taking a high dose of psilocybin.

Meditation Experience

Two thirds of the sample endorsed having a meditation practice (67%), with the two main reasons for this highlighted as being for personal growth (35%) or to help with difficult emotions or a specific psychological difficulty (31%). Other reasons identified are detailed in Figure 1.3. Meditators reported meditating on an average of 9.50 days per month (SD=10.27), for 19.24 (SD=26.42) minutes per day.

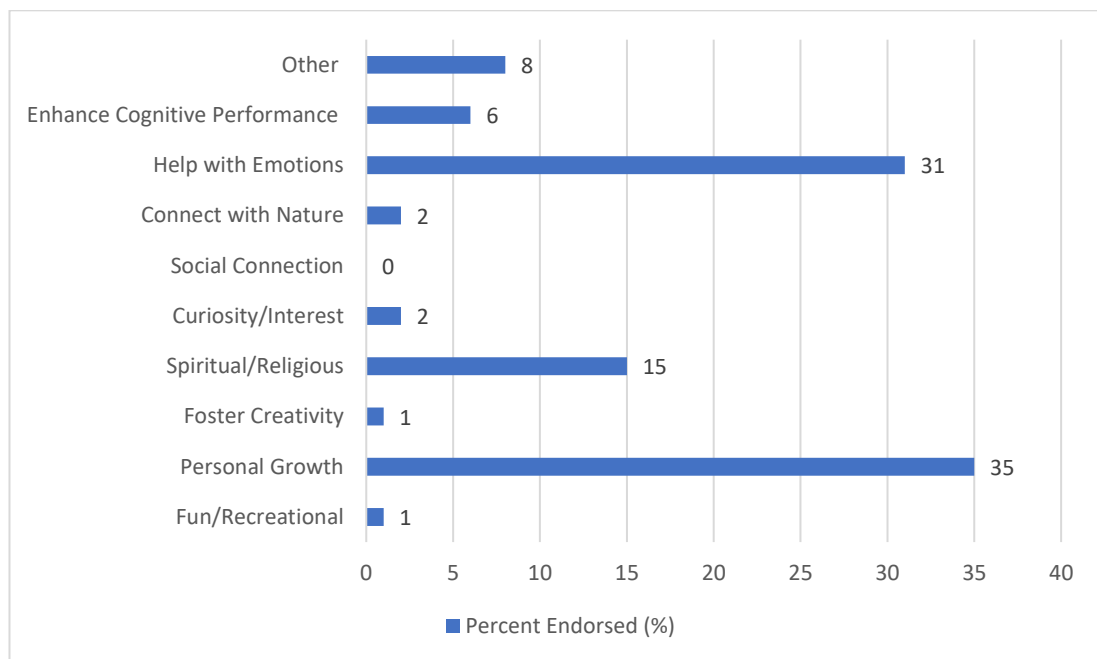


Figure 1.3: *Main reason/intention for having a meditation practice (% endorsed).*

Influence of Lifetime Psychedelic Use on Trait Mindfulness and Decentering

Trait Mindfulness – FFMQ

To examine the association between lifetime psychedelic use and mindfulness, hierarchal multiple regression analysis was conducted to predict trait mindfulness (FFMQ Full Scale Score), based on lifetime psychedelic drug use, controlling for the influence of age, gender, education level and previous meditation practice. Whilst statistically significant, only 0.4% of the variance in trait mindfulness was specifically accounted for by lifetime psychedelic use ($\Delta R^2=.004$, $F(1,1289)=5.289$, $p=.022$), with a small positive association demonstrated (see Table 2.1).

Table 2.1: Hierarchal multiple regression analysis results for the influence of Lifetime Psychedelic Use on Trait Mindfulness (n=1296).

| | <i>B</i> | SE <i>B</i> | β | <i>t</i> | <i>p</i> | <i>R</i> ² |
|--------------------------|----------|-------------|---------|----------|----------|-----------------------|
| Step 1 | | | | | | |
| Constant | 48.984 | 0.863 | | | | |
| Age | 0.103 | 0.019 | 0.154 | 5.564 | <.001 | |
| Gender – Female | -0.049 | 0.435 | -0.003 | -0.112 | .911 | |
| Gender – Other | -0.405 | 1.205 | -0.009 | -0.336 | .737 | |
| Education Level | 0.001 | 0.234 | 0.000 | 0.004 | .997 | |
| Meditation Endorsed | 3.102 | 0.447 | 0.189 | 6.945 | <.001 | .064*** |
| Step 2 | | | | | | |
| Constant | 48.906 | 0.862 | | | | |
| Age | 0.095 | 0.019 | 0.142 | 5.067 | <.001 | |
| Gender – Female | 0.053 | 0.436 | 0.003 | 0.121 | .904 | |
| Gender – Other | -0.289 | 1.204 | -0.007 | -0.240 | .810 | |
| Education Level | 0.054 | 0.235 | 0.006 | 0.229 | .819 | |
| Meditation Endorsed | 3.077 | 0.446 | 0.188 | 6.899 | <.001 | |
| Lifetime Psychedelic Use | 0.003 | 0.001 | 0.063 | 2.300 | .022 | .068* |

Note. *R*² change (ΔR^2) significant at **p*<.05; ***p*<.01; ****p*<.001.

Reported *B* and β values refer to unstandardised and standardised betas, respectively.

Dependant Variable: Trait Mindfulness (FFMQ Full Scale Score).

Decentering – EQ

Decentering (EQ score), was predicted based on lifetime psychedelic drug use, controlling for the influence of age, gender, education level and meditation practice. Lifetime psychedelic use again only accounted for a very small proportion (0.8%) of additional variance in decentering ($\Delta R^2=.008$, $F(1,1291)=10.675$ *p*=.001), beyond the influence of controls, which together accounted for 3.2% of the variance.

Table 2.2: Hierarchical multiple regression analysis results for the association between Lifetime Psychedelic Use and Decentering (n=1296).

| | B | SE B | B | t | p | R ² |
|--------------------------|--------|-------|--------|--------|-------|----------------|
| Step 1 | | | | | | |
| Constant | 40.417 | 0.761 | | | | |
| Age | -0.001 | 0.016 | -0.002 | -0.063 | .950 | |
| Gender – Female | -1.079 | 0.383 | -0.079 | -2.815 | .005 | |
| Gender – Other | -2.798 | 1.063 | -0.073 | -2.633 | .009 | |
| Education Level | -0.113 | 0.206 | -0.016 | -0.547 | .585 | |
| Meditation Endorsed | 2.254 | 0.394 | 0.158 | 5.723 | <.001 | .032*** |
| Step 2 | | | | | | |
| Constant | 40.308 | 0.759 | | | | |
| Age | -0.011 | 0.017 | -0.019 | -0.652 | .514 | |
| Gender – Female | -0.953 | 0.384 | -0.070 | -2.481 | .013 | |
| Gender – Other | -2.653 | 1.060 | -0.069 | -2.504 | .012 | |
| Education Level | -0.047 | 0.207 | -0.006 | -0.227 | .812 | |
| Meditation Endorsed | 2.224 | 0.393 | 0.156 | 5.665 | <.001 | |
| Lifetime Psychedelic Use | 0.004 | 0.001 | 0.091 | 3.267 | .001 | 0.40** |

Note. R² change (ΔR^2) significant at * $p < .05$; ** $p < .01$; *** $p < .001$.

Reported B and β values refer to unstandardised and standardised betas, respectively.

Dependent Variable: Decentering (EQ Total Score)

Influence of Lifetime Psychedelic Use on Depression

Depression - DASS-21 Subscale

Analysis was conducted to examine whether a negative association exists between lifetime psychedelic use and depression (DASS-21 subscale). Examination of R² change and coefficients revealed that the addition of lifetime psychedelic use to the covariates of age, gender and education did not significantly add to the variance explained in depression

scores ($\Delta R^2 = <0.001$, $F(1,1290) = .568$, $p = .451$), nor did lifetime psychedelic use independently predict depression (see Table 3.1).

Table 3.1: Hierarchical multiple regression analysis results for the association between Lifetime Psychedelic Use and Depression ($n=1296$).

| | <i>b</i> | SE B | β | <i>t</i> | <i>p</i> | R^2 |
|--------------------------|----------|-------|---------|----------|----------|---------|
| Step 1 | | | | | | |
| Constant | 6.569 | 0.475 | | | | |
| Age | -0.045 | 0.010 | -0.121 | -4.302 | <.001 | |
| Gender - Female | 0.062 | 0.246 | 0.007 | 0.252 | .801 | |
| Gender - Other | 2.425 | 0.680 | 0.099 | 3.568 | <.001 | |
| Education Level | -0.305 | 0.132 | -0.066 | -2.309 | .021 | .032*** |
| Step 2 | | | | | | |
| Constant | 6.587 | 0.476 | | | | |
| Age | -0.044 | 0.011 | -0.117 | -4.092 | <.001 | |
| Gender - Female | 0.043 | 0.247 | 0.005 | 0.175 | .861 | |
| Gender - Other | 2.405 | 0.680 | 0.098 | 3.534 | <.001 | |
| Education | -0.314 | 0.133 | -0.068 | -2.370 | .018 | |
| Lifetime Psychedelic Use | -0.001 | 0.001 | -0.021 | -0.754 | .451 | .033 |

Note: Note. R^2 change (ΔR^2) significant at * $p < .05$; ** $p < .01$; *** $p < .001$.

Reported B and β values refer to unstandardised and standardised betas, respectively.

Dependent Variable: Depression (DASS-21 Subscale)

Influence of Mystical Experiences on Trait Mindfulness & Decentering

Trait Mindfulness - FFMQ

Regression analysis revealed that degree of mystical experience (MEQ30 Full Scale Score) significantly predicted trait mindfulness (FFMQ Full Scale Score), with mystical experience accounting for an additional 5.9% of the variance in mindfulness ($\Delta R^2 = 0.059$,

$F(1,1291)=85.953, p<.001$) after controlling for the influence of age, gender, education level and meditation practice (see table 4.1).

Table 4.1: Hierarchal multiple regression analysis results for the association between Mystical Experience and Trait Mindfulness ($n=1298$).

| | <i>b</i> | SE B | β | <i>t</i> | <i>p</i> | R ² |
|---------------------|----------|-------|---------|----------|----------|----------------|
| Step 1 | | | | | | |
| Constant | 48.903 | 0.861 | | | | |
| Age | 0.105 | 0.019 | 0.156 | 5.638 | <.001 | |
| Gender – Female | -0.083 | 0.434 | -0.005 | -0.192 | .848 | |
| Gender - Other | -0.420 | 1.206 | -0.010 | -0.348 | .728 | |
| Education | 0.028 | 0.234 | 0.003 | 0.118 | .906 | |
| Meditation Practice | 3.083 | 0.446 | 0.188 | 6.911 | <.001 | .064*** |
| Step 2 | | | | | | |
| Constant | 41.746 | 1.137 | | | | |
| Age | 0.102 | 0.018 | 0.152 | 5.677 | <.001 | |
| Gender - Female | -0.101 | 0.421 | -0.003 | -0.240 | .810 | |
| Gender - Other | -0.692 | 1.168 | -0.016 | -0.592 | .554 | |
| Education Level | 0.158 | 0.227 | 0.019 | 0.697 | .486 | |
| Meditation Practice | 2.482 | 0.437 | 0.151 | 5.679 | <.001 | |
| Mystical Experience | 1.949 | 0.210 | 0.245 | 9.271 | <.001 | .123*** |

Note. R² change (ΔR^2) significant at * $p<.05$; ** $p<.01$; *** $p<.001$.

Reported B and β values refer to unstandardised and standardised betas, respectively.

Dependent Variable: Trait Mindfulness (FFMQ-15 Full Scale Score)

Decentering – EQ

The outcome of decentering was similarly examined to ascertain the predictive value of mystical experiences on this construct (EQ Total Score). Degree of mystical experience was positively associated with decentering and significantly accounted for an additional

9.5% of variance after controlling for the influence of age, gender and meditation practice ($\Delta R^2=.095$, $F(1,1291)=140.678$, $p<.001$) (see table 4.2).

Table 4.2: Hierarchical multiple regression analysis results for the association between Mystical Experience and Decentring ($n=1298$).

| | <i>b</i> | SE B | β | <i>t</i> | <i>p</i> | R ² |
|---------------------|----------|-------|---------|----------|----------|----------------|
| Step 1 | | | | | | |
| Constant | 40.363 | 0.759 | | | | |
| Age | -0.000 | 0.016 | 0.000 | -0.006 | .995 | |
| Gender – Female | -1.099 | 0.383 | -0.080 | -2.869 | .004 | |
| Gender – Other | -2.810 | 1.063 | -0.073 | -2.643 | .008 | |
| Education Level | -0.091 | 0.206 | -0.013 | -0.439 | .661 | |
| Meditation Endorsed | 2.219 | 0.393 | 0.156 | 5.640 | <.001 | .032*** |
| Step 2 | | | | | | |
| Constant | 32.443 | 0.983 | | | | |
| Age | -0.003 | 0.016 | -0.005 | -0.189 | .850 | |
| Gender - Female | -1.119 | 0.364 | -0.082 | -3.074 | .002 | |
| Gender – Other | -3.111 | 1.010 | -0.081 | -3.079 | .002 | |
| Education Level | 0.054 | 0.196 | 0.007 | 0.274 | .784 | |
| Meditation Endorsed | 1.554 | 0.378 | 0.109 | 4.111 | <.001 | |
| Mystical Experience | 2.156 | 0.182 | 0.312 | 11.861 | <.001 | .127*** |

Note. R² change (ΔR^2) significant at * $p<.05$; ** $p<.01$; *** $p<.001$.

Reported B and β values refer to unstandardised and standardised betas, respectively.

Dependent Variable: Decentring (EQ Total Score)

Influence of Mystical Experiences on Depression

Depression - DASS-21 Subscale

Whilst depression was not significantly associated with lifetime psychedelic use, analysis revealed that mystical experiences made a small yet significant negative

independent contribution to the outcome of depression, accounting for an additional 0.6% of the variance ($\Delta R^2=.006$, $F(1,129)=7.339$, $p=.007$) after controlling for the influence of age, gender and education.

Table 5.1 Hierarchal multiple regression analysis results for the association between Mystical Experience and Depression.

| | <i>b</i> | SE B | β | <i>t</i> | <i>p</i> | R^2 |
|---------------------|----------|-------|---------|----------|----------|---------|
| Step 1 | | | | | | |
| Constant | 6.580 | 0.474 | | | | |
| Age | -0.045 | 0.010 | -0.121 | -4.320 | <.001 | |
| Gender - Female | 0.065 | 0.245 | 0.007 | 0.264 | .792 | |
| Gender - Other | 2.429 | 0.679 | 0.099 | 3.576 | <.001 | |
| Education Level | -0.308 | 0.132 | -0.067 | -2.344 | .019 | .032*** |
| Step 2 | | | | | | |
| Constant | 7.828 | 0.660 | | | | |
| Age | -0.044 | 0.010 | -0.120 | -4.265 | <.001 | |
| Gender - Female | 0.072 | 0.245 | 0.008 | 0.296 | .768 | |
| Gender - Other | 2.494 | 0.678 | 0.102 | 3.678 | <.001 | |
| Education | -0.326 | 0.131 | -0.070 | -2.482 | .013 | |
| Mystical Experience | -0.328 | 0.121 | -0.074 | -2.709 | .007 | .038** |

Note. R^2 change (ΔR^2) significant at * $p<.05$; ** $p<.01$; *** $p<.001$.

Reported B and β values refer to unstandardised and standardised betas, respectively.

Dependent Variable: Depression (DASS-21 Subscale)

Mystical Experience as a Mediator of the Association between Lifetime Psychedelic Use and Mindfulness

An aim of this study was to assess whether the degree of mystical experience reported for participant's chosen most significant experience mediates the relationship

between lifetime psychedelic use and measures of mindfulness related capacities (see Figure 2.1). Given the exploratory nature of the study, mediation analysis was conducted separately for both trait mindfulness and decentering. For brevity, mediation analysis using only the measure of decentering (EQ Total Score) is reported. Decentering was selected for inclusion on statistical grounds, given the stronger positive correlation between the lifetime psychedelic use and decentering, and the greater amount of variance explained by the predictor.

As in the case of the above regression analyses with the outcome of decentering, age, gender, education and meditation practice were included as covariates. Analysis revealed a significant positive indirect effect of lifetime psychedelic use on decentering via the degree of mystical experience reported (Indirect effect = .0014, 95% CI [.001, .002]).³

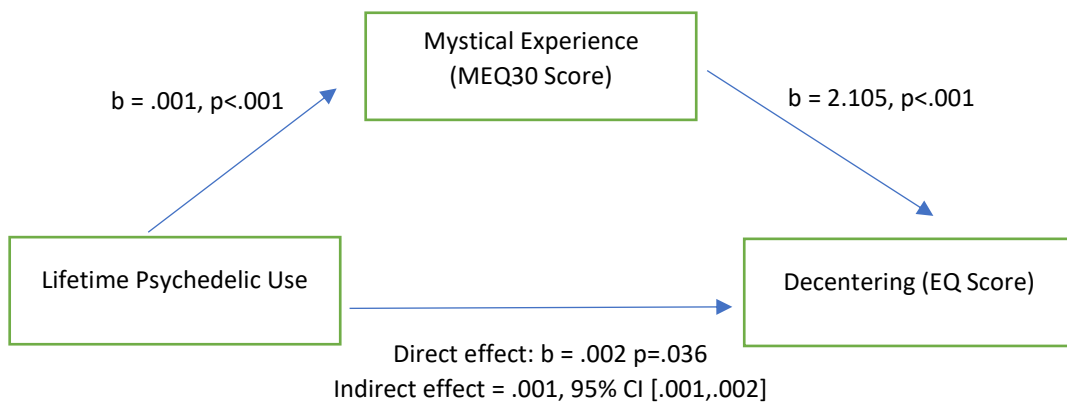


Figure 2.1: Mediation model of lifetime psychedelic drug use as a predictor of decentering, mediated by degree of mystical experience ($n=1296$).

³ Following conventions for reporting mediation (Field, 2013; Hayes, 2017) each mediation analysis is reported with an indirect effect using bias-corrected bootstrapped 95% confidence intervals based on 1000 samples, with regression coefficients and associated p values reported for all other paths of the mediation model.

Mindfulness as a Mediator of the Association between Mystical Experience and Depression

Mediation analysis was conducted to establish whether mindfulness mediates the relationship between greater mystical experiences and lower depression scores (see Figure 3.1). Again for brevity, mediation analysis using only the mindfulness-related capacity of decentering as a mediator is reported. Decentering was selected as mediator over the FFMQ-15 on a statistical basis, given the stronger positive correlation between mystical experience and decentering, and the greater amount of variance explained in decentering (EQ Score) by mystical experience compared to trait mindfulness (FFMQ-15 Score) (see Tables 2.1 and 2.2).

Consistent with the above regression analyses for the outcome of depression, age, gender and education were included as covariates. Mediation analysis revealed a significant negative indirect effect of mystical experience use on depression via decentering (indirect effect = $-.710$, 95% CI [$-.870$, $-.571$]).

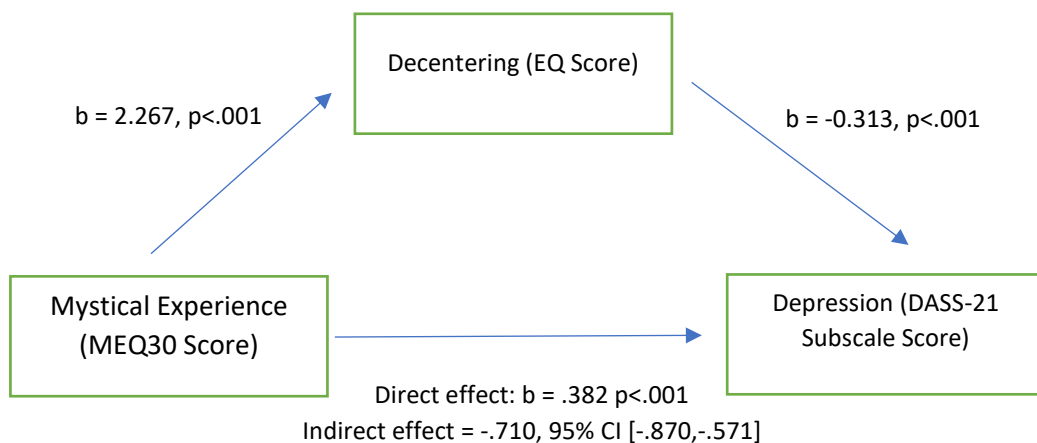


Figure 3.1 Model of an increased mystical experience as a predictor of lower depression scores, mediated by decentering capacity ($n=1298$).

Discussion

The present study aimed to explore the association between frequency of lifetime psychedelic drug use, mystical experiences, trait mindfulness, decentering ability and depression. Previous research has demonstrated both post-acute and sustained increases in mindfulness and decentering following a psychedelic experience (e.g. Soler et al, 2016; Uthaug et al, 2018; Madsen et al, 2020); with suggestions of an important role for mystical experiences proposed by the wider body of research examining positive outcomes following psychedelic use (e.g. Roseman et al, 2018; Griffiths et al, 2011; Ross et al, 2016). Furthermore, mindfulness has been shown to be predictive of reduced depression severity in ayahuasca users (Mian et al, 2019), in accordance with the substantial body of evidence demonstrating the value of mindfulness-based interventions in the treatment of recurrent depression (Hoffman et al, 2010).

Through use of an internet-based survey, this study collected data from 1298 psychedelic drug users, with an average of 54 lifetime uses. Results from the survey demonstrated that lifetime psychedelic use predicted higher trait mindfulness and decentering scores, although these associations were small. The relationship between lifetime use and decentering was mediated by the degree of mystical experience associated with participant's chosen most significant psychedelic experience. This mystical experience was significantly predictive of higher trait mindfulness and decentering, as well as lower depression scores. The relationship between mystical experiences and depression scores was mediated by degree of decentering ability. These associations are discussed in more detail below, alongside limitations of the present study and suggestions for future research.

Participants were predominantly white, male and university educated; a similar demographic composition to other survey studies of psychedelic users (Johansen & Krebs 2015; Hendricks et al, 2015; Hendricks et al, 2018). The psychedelic drugs most frequently

endorsed as having been used at least once were psilocybin and LSD, in line with previous findings (Hendricks et al, 2015; Johnsen & Krebs, 2015). With regard to the participant's lifetime use of other illicit substances, similar rates of cannabis and cocaine use were reported compared to previous samples of psychedelic users (Johnsen & Krebs, 2015; Hendricks et al, 2015; Hendricks et al, 2018), however the present study appears to present a higher incidence of MDMA/ecstasy use amongst participants. Participant's predominantly reported using psychedelics initially for fun/recreational reasons or out of curiosity/interest. However, regarding later uses, a greater spread of provided reasons is observed, with almost half of the sample having most recently used psychedelics with the intention to manage difficult emotions or promote personal growth. The below discussed results with regard to depression may be considered within this context, with previous research demonstrating the importance of intention setting in determining outcomes (Haijen et al, 2018).

A small, yet significant, positive association was found between lifetime psychedelic drug use and both trait mindfulness and decentering, independently accounting for just 0.4% and 0.8% of the variance in each outcome, respectively. Ongoing meditation practice was a stronger significant predictor of both mindfulness and decentering, in accordance with research highlighting the role of meditation and mindfulness-based interventions (Hoffman et al, 2010; Blanck et al, 2018). The small size of the association between lifetime use and mindfulness-related capacities may best be understood both within the context of previous research findings, as well as methodological considerations relating to the present study. First, it may be the case that although the finding is a true positive and is statistically significant, it is unlikely to be clinically important and its detection was likely a simple consequence of a large sample size and hence, high power to detect very small effects. There is a discrepancy within the literature as to whether frequency of use is related to the mindfulness-related outcomes in question, with most suggesting no significant relationship

(e.g. Beiner & Soar, 2020; Madsen et al, 2020; Uthaug et al, 2018; Mian et al, 2019), although one study has demonstrated an association (Franquesa et al, 2018). The current study tends to favour the conclusions reached in the former studies.

The results of this study may be interpreted as indicating that whilst a small association between lifetime psychedelic use and mindfulness may exist, this may likely not be cumulative or increase meaningfully as a function of *quantity* of uses, but rather may be related to the *quality* of psychedelic experiences. In support of this notion are studies of psychedelics which emphasise the role of ‘context’ in determining the nature of the experience, highlighting the impact of ‘set’ (i.e. one’s personality, expectations and assumptions) and ‘setting’ (i.e. the external environment of the experience, including the atmosphere and people present). Such considerations have been shown to be capable of predicting the occurrence of mystical experience, a proposed determinant of positive therapeutic outcomes (e.g. Ross et al, 2016; Garcia-Romeu et al, 2014).

Indeed the results of the present study demonstrate a mediating role for mystical experiences, with the small association between frequency of lifetime use and decentering explained – at least in part - by the degree of mystical experience related to participants’ most significant psychedelic experience. This finding is supportive of the notion that it may be a single experience, characterised by the phenomena of a mystical experience, that drives the association with decentering. This is in accordance with studies of a single session with a psychedelic drug demonstrating significant positive therapeutic outcomes (Osorio et al, 2015; Palhano-Fontes et al, 2019). The increased opportunity for this type of psychedelic experience to occur may be brought on by repeated use of psychedelics, potentially underpinning the small significant predictive value of lifetime use on mindfulness and decentering. Another consideration, in keeping with the above described and known importance of ‘set’ and ‘setting’, is the lack of control of these contextual

determinants within this study. Whilst a measure of frequency of uses was obtained, the setting and experience of these uses remains unknown – with the exception of participations chosen most significant experience. A psychedelic drug consumed within a supportive ceremonial context (such as an ayahuasca ceremony) represents a distinct setting from consumption for recreational reasons (such as the use of LSD as part of ‘party’ culture), with psychedelics considered highly sensitive to the influence of context (Carhart-Harris et al, 2018). The present study was unable to capture this nuance and its potential effect on outcomes, indeed it may be the case that the predictive power of frequency of use changes when contextual determinants across participant’s breadth of experiences are accounted for.

The lack of association between frequency of lifetime psychedelic use and depression scores may be understood through several lenses. It may be the case that the frequency of uses indeed has no bearing on depressive symptomology. Similar to the above discussion, the therapeutic effects of psychedelics on depression may be determined by the presence of a supportive environment (Carhart-Harris et al, 2018) intention setting (Haijen et al, 2018), and be unrelated to the frequency of uses but rather associated with the context and nature of a single high-dose session. However, it may additionally be relevant to examine the recency of participant’s most significant experience, to ascertain whether time elapsed has any bearing on therapeutic effects, given the previously discussed evidence suggesting significant post-acute effects on depression, mindfulness, and decentering.

In support of existing literature positing an important therapeutic role for psychedelic-induced mystical experiences (e.g. Roseman et al, 2018; Griffiths et al, 2011; Ross et al, 2016), the present study demonstrated that the degree of mystical experience (reported for participant’s chosen most significant psychedelic experience) significantly

predicted higher trait mindfulness, higher decentering, and lower depression scores. Though all findings represent small associations (variance explained by mystical experience in: trait mindfulness = 5.9%, depression = 0.6%), the largest proportion of variance explained by mystical experience was for decentering, at 9.5%. Regarding the outcome of trait mindfulness, the finding of this study supports the previously demonstrated effect of ego-dissolution – understood as an aspect of the broader mystical experience - positively correlating with increases in mindfulness following ayahuasca (Uthaug et al, 2018). The finding of the present study that mystical experiences accounted for more of the variance in decentering than in trait mindfulness may be in accordance with the notion that decentering presents an important related but distinct facet of mindfulness that is specifically predictive of therapeutic outcomes in mindfulness-based interventions (e.g. Naragon-Gainey & DeMarree, 2017a; 2017b). Indeed, the mediating role of decentering is demonstrated by the present study with regard to the association between degree of mystical experience and lower depression scores, with higher levels of decentering found to mediate this small yet significant relationship. Given the phenomenological and neurophysiological overlaps noted between mystical experiences and meditative states of consciousness (Letheby and Gerrans, 2017; Vago & Silbersweig, 2012), and the proposed core role of decentering in mindfulness-based interventions (Naragon-Gainey & Demarree 2017b; Sauer & Baer, 2010; Hoge et al, 2016), the present study suggests that decentering may exist as a shared psychological mechanism.

Previous research has demonstrated that psychedelic-induced mystical experiences are associated with significant decreases in depressive symptomology (Roseman et al, 2018). The relatively small size of the association between degree of mystical experience and depression in the present study may be understood again through several means, including a consideration of methodological constraints and exploratory aims (as opposed to a formal treatment setting with strict inclusion criteria), as well as the inherent

challenges of capturing the nuanced subjective effects of the psychedelic experience (Garcia-Romeu et al, 2016). First, due to this study's cross-sectional design and concern for burden on participants, several important determinants of depressive symptomology were not measured as part of this study, and given the complexity of mental health it was not possible to control for all potential covariates. For instance, the influence of pre-existing (i.e. prior to the mystical experience) mental health difficulties or significant life events were not able to be captured nor accounted for. Second, mystical experiences represent a broad experience encompassing numerous phenomena, as expressed – in part – through the six scales of the MEQ-30 (Maclean et al, 2012). It had been suggested that ego-dissolution represents an aspect of the mystical experience which drives psychedelic's therapeutic effects (Nour et al, 2007), with the 8-item Ego Dissolution Inventory (Nour et al, 2007) recently developed as a tool for measuring this construct. The present study sought to examine the broad constructs implicated in the therapeutic potential of psychedelics, thus using a well-established full scale measure of mystical experiences for examination in analyses. Should a particular aspect of the psychedelic-induced mystical experience, such as ego-dissolution, indeed be more predictive of effects, the measurement tool and variable used in the present study may not have sufficiently captured nor represented this, due to interference from other potentially less important aspects of the experience obfuscating precise relationships.

The present study has several important limitations, and all above discussed findings should be considered within this context. Due to the cross-sectional correlational design of this study, inferences regarding the temporal nature of the found associations cannot be reliably determined, nor causality established. To help with causal reasoning, the use of adapted scales which query *change* in mindfulness and depression relative to prior to the reported mystical experience could have been of benefit. Though, a limitation of this would of course have been the issue of recall bias. Whilst data collected from participants

was gathered retrospectively through self-report, opening up the possibility of memory or other biases, survey studies of psychedelic-induced mystical experiences using the MEQ-30 have not specified a limit on time elapsed since the event (e.g. Maclean et al, 2012). The design of the present study meant that there was limited control over covarying variables for which data was not available, including the important contextual determinants of set and setting (Carhart-Harris et al, 2018; Haijen et al 2018), as well as pre-existing characteristics of the sample. Collection of such data was either omitted in order to reduce burden on participants, or unable to be reliably obtained without bias due to a cross-sectional design. Though, notably, the study did control for meditation practice in all analyses relating to outcomes of mindfulness-related capacities, suggestive of an association with psychedelics irrespective of any specific intention to affect such abilities. Future research may helpfully employ more rigorous methodology to not only ascertain the temporal nature of associations, but include longitudinal follow up to enable an understanding of the extent to which relationships are sustained. Studies investigating the role of contextual factors, including intention setting, supportive environments, concurrent meditation practice or post-psychedelic integration sessions, with regard to outcomes relating to mindfulness, mystical experiences and mental health, will enable a more detailed understanding of these seemingly interrelated constructs.

A further limitation relates to the generalisability of the sample, as participants were primarily white, male and highly educated. Additionally, participants who responded to advertising through the UK Psychedelic Society and MAPS may have contributed to bias within the sample, with followers of these organisations likely already aligning with a view that psychedelic drugs may hold some benefit. An investigation of the effects of psychedelics amongst more demographically diverse and representative user groups, with both positive and exclusively negative experience(s) with psychedelics, would thus be of benefit.

Despite its limitations, this study suggests a significant role for both mystical experiences and mindfulness-related capacities in understanding the therapeutic benefits of psychedelic drugs. This work corroborates findings from previous research which posits that mindfulness and decentering are related to psychedelic use, and suggests a potential pathway of effects from psychedelic-induced mystical experiences to decentering and depression. Given the interest in integrating psychedelic therapy with known psychotherapeutic modalities which seek to foster mindfulness-related capacities, such as ACT (Watts & Luoma, 2020), an enhancement of decentering through existing interventions related to similar constructs (i.e. the cultivation of cognitive defusion in ACT) may amplify the degree to which either approach provides therapeutic gains, and the extent to which these are sustained.

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Part 3: Critical Appraisal

Introduction

This critical appraisal reflects on my experience of developing and conducting the study described in Part 2 of the thesis, exploring the challenges which arose with regard to five areas. First, I describe my experience of researching a historically, and to some extent presently, controversial subject area, as well as one which is in its infancy. Second, the establishing of a direction for the project is considered within the context of my role as a psychologist. Third, the development of the study's materials, i.e. the survey, is discussed, including the processes relating to decision making. The fourth section comprises a reflection on recruitment and the challenges faced, before finally, a brief consideration is offered of several learning points which, with hindsight, have prompted me to consider those aspects of the study which may have been done differently.

Reflections on Project Selection and Subject Area

Conducting a study within the field of psychedelic drug use and the potential for psychedelic therapy proved itself to be an insightful and fascinating experience, though inherently challenging. I selected this project due to an interest in its broad and transdiagnostic implications, drawing attention to processes of the mind and the overarching features of distress. Whilst psychedelic drugs have demonstrated benefits in clinical populations, research into their effects has seemingly considered these substances with regard to mental health in terms of wellness and positive psychology, as opposed to a focus solely on pathology. This breadth and positioning aligned with my own perception and understanding of mental health, and arguably with the stance of third-wave approaches, as explored within this study. The overlap between psychedelic theory and therapy, and those psychotherapies with which my own theoretical orientation aligned, peaked my interest in exploring this field further. As a trainee psychologist, this allowed me to broaden my understanding of 'bottom-up' processes in psychology, as well as accessing

literature which considers the experiential role of spirituality and connection with regard to meaning-making and mental health.

Whilst intrigued by the ideas presented amongst the literature, I was aware of the contentious nature of the subject, and the historical controversy surrounding the therapeutic use of psychedelics, as well as their illegality and the social discourses regarding psychedelics as illicit substances. With the field in infancy, and evidence only just emerging and not yet established, I reminded myself to adopt a necessary curious yet critical approach. Reading of the promising research findings demonstrated with regard to psychedelic therapy, it became important to remain rooted in science as I explored the literature, applying my knowledge of research methodology to ensure critical evaluation of findings and ideas. Given the enthusiasm developing in the field, I was cautious to not quickly view psychedelic therapy as a panacea for mental health difficulties, and remain curious from a psychologically-informed position.

Given the rapidly growing nature of the field, with highly relevant research findings emerging as my study progressed, it was both challenging and vital to remain on top of the literature, with the focus of the study informed and refined by some of the most novel evidence-based ideas in the field. During the study's conception, the direction of the project was shaped by this ongoing emergence. For instance, a number of those studies investigating the specific outcome of mindfulness emerged in the midst of project development, and thus guided the focus of the project.

Establishing Research Questions from a Psychological Perspective

Given the developing nature of the field of psychedelic research, and the existing hypotheses, theories and evidence, I was encouraged to consider my role as a psychologist and position myself and the project from this stance. This positioning was extremely helpful throughout the process of establishing and refining research questions. This enabled me to

consider the unique and important contribution that psychology can make to understanding mechanisms and effects, given an existing understanding of psychological constructs already established amongst the psychotherapeutic literature. Having encountered, practiced and pursued third-wave cognitive behaviour approaches throughout training as a psychologist, as well as holding a strong interest in compassion and meditative practices, I hold a belief in the value of mindfulness and related capacities, and an altering of one's relationship to the self and to distress. With an already well established evidence based for interventions such as Mindfulness Based Cognitive Therapy (MBCT), and growing traction for Acceptance and Commitment Therapy (ACT) and compassion-based therapies such as Compassion Focused Therapy (CFT), drawing attention to the parallels between the psychedelic experience and such approaches appeared an important step towards the embedding of psychedelic therapy within a psychologically informed frame, and growing an evidence base for its psychological mechanisms. Indeed, the very recent work of Watts & Luoma (2020) highlights the efforts already made amongst the research community to integrate ACT with psychedelic use, given their conceptual similarities, to support and potentially enhance therapeutic benefits. With psychologists already highlighting and incorporating psychotherapeutic ideas into clinical trials of psychedelic therapy (Watts & Luoma, 2020), I considered the role of this project and the value of supporting such endeavours through the provision of evidence relating to the associations between psychedelic use and already implicated psychological constructs.

Reflections on Survey Development

Having established research questions and study design, it was necessary to develop the study materials. With the survey developed 'from scratch', for the purposes of this study, I was required to carefully consider issues relating to measurement, not only in terms of psychometric properties, but with regard to factors such as completion time, participant fatigue, usability and understandability. Establishing a balance between

gathering necessary data and tightening controls within the study (i.e. by capturing covariates), and keeping the load on participants to a minimum to ensure completion, was paramount. For instance, whilst uncontrolled for in studies of psychedelics and mindfulness to date, it was considered imperative from the onset of this study's development to obtain details regarding meditative practice, as a covariate of mindfulness. Questions relating to meditation practice were kept brief, and followed an almost identical and therefore familiar format to previous questions relating to psychedelic use (i.e. onset, frequency) and intentions, to reduce burden.

It was necessary throughout the process of survey development to carefully consider the inclusion of questions and selection of measures, based on a critical understanding of research methodology, as well as a consideration of the study's priorities. For those variables not gathered using validated questionnaire measures, such as those relating to history/patterns of drug use, it was considered important to capture this data as informed by the existing literature as well as by 'experts-by-experience'. Accordingly, a discussion was held between myself and a knowledgeable and experienced contact from the UK Psychedelic Society, the purpose of which was to cement the project in lived experience and face validity. This discussion proved invaluable, and I extend my thanks to this individual for kindly volunteering their time and expertise. For instance, one aspect of the conversation focused upon the decision of which substances to include in the provided list of psychedelic drugs, which to accept as listed as 'other', and what language to use to describe these drugs based on lay terminology (i.e. through their active ingredient (e.g. 'DMT') or preparation (e.g. 'ayahuasca')). Ultimately, this question was informed by both this discussion and the academic literature, taking into account the listed drugs' chemical nature and subjective effects.

Selecting measures for each of the key variables within this study, namely trait mindfulness, decentering, mystical experiences and depression, required a consideration of psychotherapeutic literature more broadly, as well as psychedelic research more specifically. Whilst psychological researchers have already examined all but mystical experiences to a great extent in studies of psychological therapies, few studies had begun to examine these in relation to the psychedelic experience. As such, selection of measures was made based on a consideration of reliability, validity, and evidence of use in psychedelic research and thus sensitivity to shifts in psychedelic users. For instance, whilst other measures of trait mindfulness exist, the Five Factors Mindfulness Questionnaire (Baer et al, 2006) has been the measure of choice in almost all studies of psychedelics and mindfulness, and its use in this study would enable direct comparison of results and support the aggregating of findings in future meta-analytic studies for instance.

Through an examination of the literature it was evident that psychedelic experiences represent a complex phenomenon, contingent upon contextual determinants (Carhart-Harris et al, 2018). Given this study's methodology and design, it was acknowledged from the onset that the vast array of such determinants could not be ensured nor sufficiently captured. Unable to determine participant's pre-existing 'set' prior to psychedelic use, nor the breadth of settings in which prior use has occurred, it was decided that rather than burden participants with repetitive questions regarding the details of their – possibly many – psychedelic experiences, to acknowledge this as a limitation of the study. Rather, participants intentions – a known determinant of outcomes (Carhart Harris et al, 2018; Haijen et al, 2018) – across first and last uses were captured to provide descriptive data characterising the sample, contextualising findings and enabling them to be viewed through this lens of understanding the variation in intentions amongst the sample.

The Process of Recruitment

Once the survey had been piloted and finalised, the process of online recruitment began. With the aim of a large sample size (final sample N=1298), accessing those who met the inclusion criteria required deliberate and dedicated recruitment efforts. Bespoke pages on all of the main social media platforms were created, to promote the advert for the survey and provide the link to its completion. This enabled the project to relay a consistent message across different channels, with cohesive messaging and clear branding. The importance of professionalism was considered and adhered to, being careful to root the study within science and academia rather than a cultural movement. This was particularly important given the contentious subject area of the research, and the stringent policies of social media platforms in place to protect against harm online. Branding and advertising was carefully developed to not 'promote' nor 'glorify' drug use, but rather attract existing users who wished to contribute to a scientific understanding of psychedelic substances and their psychological effects. I was aware throughout recruitment of the possibly deeply personal experiences and opinions participant's may have had with regard to psychedelic drugs, given their potential to be both transformative and/or extremely difficult. I was aware of a felt pressure to do justice to the profound meaningful experiences of some users, whilst holding with similar regard the challenges others may have experienced. As such, and as is characteristic of scientific research, the study materials were carefully positioned as neutral, neither 'pro' nor 'anti' psychedelic drugs.

The sample was obtained entirely through online advertisement, shares amongst family, friends and known individuals with a network of interested others, as well as promotion through two large organisations with a membership of psychedelic users (The UK Psychedelic Society, and the US' Multidisciplinary Association for Psychedelic Studies (MAPS). With great thanks to advertisements by these organisations, I was able fulfil the study's required sample size. As noted however, in the discussion of Part 2, is that whilst

this enabled access to a large sample of users, bias may have been introduced into the sample. Participants obtained through these channels were likely those who have already aligned themselves with a belief in support of psychedelic drugs, and may indeed be those who have had particularly meaningful or transformative experiences. Whilst not all participants were recruited through these means, it is acknowledged that a sample characterised by diverse experiences of psychedelics (including solely negative) would result in a potentially less biased (i.e. in favour of psychedelics) sample.

Reflections on Limitations

As discussed in Part 2, this study holds some important methodological limitations. Whilst these will not be repeated in detail here, there are several decisions that may have been made differently were I to conduct this research again. Retrospectively, it may have been helpful to adopt a between-groups design, comparing psychedelic users with non-users, with correlational analyses (as described in Part 2) carried out for the user group. This design would enable an understanding of effects not only in terms of their relationship to frequency of use (i.e. the dose-response analyses conducted in this study) but a comparison of outcomes between those who have and have not used psychedelics. Whilst this design was considered during the study's conception, a decision was made against this primarily due to issues relating to recruitment and obtaining sufficiently large sample sizes for each group, in the context of the thesis' time constraints.

As is evident from the literature relating to psychedelic drug use, there are important contextual determinants of the experience and its outcomes (Carhart-Harris et al, 2018; Haijen et al, 2018). Whilst it is acknowledged that compromises were necessarily made in this study regarding what to measure (given the length of the survey, demand on participants, and a need for a large sample size of survey completers within a constrained time frame), it would have been useful to obtain more details relating to 'set' and 'setting'

(as described in detail in Part 1). Given the potential for the environment in which one uses to determine the effects of psychedelics and their outcomes, it may have been helpful to gather data relating to the context of participant's chosen most significant psychedelic experience, on which they reported. This would allow analyses to determine whether the demonstrated effects between this experience, decentering and depression, are influenced by, for example, consumption within a ceremonial versus recreational context.

Conclusion

Overall, undertaking research with regard to psychedelic drug use and psychotherapeutic constructs has required a curious, critical position and a necessary cautious and exploratory approach. I found the project to be thought provoking and insightful, peaking my interest in the breadth of psychology and the mysterious and yet to be fully understood nature of human consciousness. It has taught me of the value and potential that researchers hold in driving forward novel ideas, challenging social and political discourses, and holding at the core of the work the pursuit of unbiased and rigorous scientific evidence.

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Appendices

Appendix 1: UCL Ethical Approval Letter and Email Confirmation of Amendment.

10th September 2019

Dr Sunjeev Kamboj
Department of Clinical, Educational and Health Psychology
UCL

Cc: Kiana Azmoodeh

Dear Dr Kamboj

Notification of Ethics Approval with Provisos

Project ID/Title: 15153/001: Examining the relationship between psychedelic drug use, mystical experiences, mental health and well-being

Further to your satisfactory responses to the Committee's comments, I am pleased to confirm in my capacity as Chair of the UCL Research Ethics Committee (REC) that your study has been ethically approved by the UCL REC until **31st July 2022**. Ethical approval is granted on condition that "email addresses will remain within Qualtrics until the study is complete (either 31/07/2022 or until 1000 responses are achieved, whichever is earlier)" is declared in the Information Sheet and Consent Form. Otherwise a participant could assume that upon completing the survey their email address is discarded.

Ethical approval is also granted subject to the following conditions:

Notification of Amendments to the Research

You must seek Chair's approval for proposed amendments (to include extensions to the duration of the project) to the research for which this approval has been given. Each research project is reviewed separately and if there are significant changes to the research protocol you should seek confirmation of continued ethical approval by completing an 'Amendment Approval Request Form'
<http://ethics.grad.ucl.ac.uk/responsibilities.php>

Adverse Event Reporting – Serious and Non-Serious

It is your responsibility to report to the Committee any unanticipated problems or adverse events involving risks to participants or others. The Ethics Committee should be notified of all serious adverse events via the Ethics Committee Administrator (ethics@ucl.ac.uk) immediately the incident occurs. Where the adverse incident is unexpected and serious, the Joint Chairs will decide whether the study should be terminated pending the opinion of an independent expert. For non-serious adverse events the Joint Chairs of the Ethics Committee should again be notified via the Ethics Committee Administrator within ten days of the incident occurring and provide a full written report that should include any amendments to the participant information sheet and study protocol. The Joint Chairs will confirm that the incident is non-serious and report to the Committee at the next meeting. The final view of the Committee will be communicated to you.

Final Report

At the end of the data collection element of your research we ask that you submit a very brief report (1-2 paragraphs will suffice) which includes in particular issues relating to the ethical implications of the research i.e. issues obtaining consent, participants withdrawing from the research, confidentiality, protection of participants from physical and mental harm etc.

In addition, please:

- ensure that you follow all relevant guidance as laid out in UCL's Code of Conduct for Research: <https://www.ucl.ac.uk/srs/file/579>
- note that you are required to adhere to all research data/records management and storage procedures agreed as part of your application. This will be expected even after completion of the study.

With best wishes for the research.

Yours sincerely



Professor Lynn Ang
Joint Chair, UCL Research Ethics Committee

Dear Kiana,

The REC Chair has approved your attached amendment request. Please take this email as confirmation of that approval.

IMPORTANT: For projects collecting personal data only

If you are collecting personal data and your project is registered with the UCL Data Protection Officer and the parameters of the processing of your research data have changed significantly (or you wish to extend your study for an additional period) from your original application for Data Protection registration you will need to advise the UCL Data Protection Office forthwith: data-protection@ucl.ac.uk

With best wishes, Helen

Helen Dougal
UCL Research Ethics Co-ordinator
Office of the Vice-Provost (Research)
University College London
2 Taviton Street, London, WC1H 0BT
Email: ethics@ucl.ac.uk

Appendix 2: List of Psychedelic Substances Provided to Participants.

- LSD/ Acid (and analogues) [*LSD, or 1P-LSD, AL-LAD*]
- ‘Magic’ mushrooms and truffles (not including Amanita) [*Psilocybin, psilocin*]
- Ayahuasca, yage [*DMT+MAOIs (in a brew)*]
- DMT and Changa [*DMT (inhaled/smoked)*]
- Peyoté, San Pedro (and other cacti) [*Mescaline*]
- Psychoactive toad [*5-MeO-DMT, Bufotenin*]
- Iboga [*Ibogaine*]
- Salvia Divinorum
- NBOMe (*25I-NBOMe, N-Bomb*)
- Other: If you have used a psychedelic drug(s) that is not listed, please provide

details: *(Please note: we do not include non-psychedelic drugs like MDMA, Cannabis, Ketamine or nitrous oxide/NOS though they may have some psychedelic effects)*

Appendix 3: Participant Information Sheet and Consent Form.

Participant Information Sheet

UCL Research Ethics Committee Approval ID Number: 15153/001

PLEASE SAVE A COPY OF THIS INFORMATION SHEET

Title of Study: Examining the relationship between psychedelic drug use, mystical experiences, mental health and wellbeing.

Department: UCL Department of Clinical, Educational and Health Psychology

Name and Contact Details of the Researcher(s): Kiana Azmoodeh

Email: k.azmoodeh.17@ucl.ac.uk

Name and Contact Details of the Principal Researcher: Professor Sunjeev Kamboj

E: Sunjeev.kamboj@ucl.ac.uk

Please Note: All data for this project will comply with the current data protection legislation (General Data Protection Regulation). Your data will be collected and stored anonymously and you will not be able to be identified from your data.

Invitation Paragraph

You are being invited to take part in a research project which is being conducted by University College London (UCL) as part of the researcher's doctoral thesis. Before you decide to continue, it is important that you understand why it is being done and what taking part will involve. Please take some time to read the following information carefully and discuss it with others if you wish. Please contact us using the above email

addresses if there is anything that is not clear or if you would like more information.

Take time to decide whether or not you wish to take part, and be aware that your participation is completely voluntary.

What is the project's purpose?

The purpose of the study is to understand the relationship between psychedelic experiences, and characteristics of people who have used them at least once. We are firstly interested to learn about both the 'mystical' and challenging experiences which can occur. We are also interested in psychedelic drug use in people who do and do not meditate, and finally in whether psychedelic use is related to mental health.

Why have I been chosen?

We are looking to investigate the effects of psychedelic drug use and therefore, we are collecting data from anybody who meets the criteria below:

Participants must be over 18 years old
Participants must have at least one experience of psychedelic drug use;

- This can be current or previous drug use,
- This can be of any psychedelic drug in any amount.

Your responses to our screening questions indicate that you meet these 2 criteria and therefore you can complete the survey and be involved in the study.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part we advise that you save a copy of this information sheet to keep, and you will be asked to electronically 'sign' a consent form which confirms for us that you agree to take part in the study and understand what this means. You can withdraw from the study at any time without giving a reason.

If you do not complete the survey in one sitting, or if you would like to no longer continue with the survey, you can exit the survey by closing your browser. If you exit the survey, your data that you have submitted up until that point will be saved. Your incomplete data may still be used in our analysis, to avoid your efforts being wasted.

If you would like to withdraw your data, you can contact us within 1 month of completing the survey (either partially or fully) and we will delete your data. At the start of the survey you will be asked to provide the last 4 digits of your mobile phone number to form your ID number. As we are not collecting any identifying information from you, you can quote this 4-digit ID number to us to request that we remove your data.

Withdrawing from the survey will not involve any penalty or loss of benefits that you are otherwise entitled to.

What will happen to me if I take part?

In order to try and answer our questions about psychedelic drug use, we have devised an online survey consisting of various questionnaires which measure the areas we are interested in. The survey should take no longer than 30 minutes, and should be

completed in one sitting. Please ensure that you are comfortable with sufficient time before commencing the survey.

All participants will answer questionnaires relating to:

- demographic details, i.e. your age, gender, ethnicity, etc.;
- your previous drug use, giving details of which drugs you have taken and an estimate of how frequently;
- any current or previous meditation practice;
- mindfulness, acceptance and openness;
- depression, anxiety and stress symptoms.

If you indicate that you have taken psychedelic drugs at least once in your lifetime, you will be asked further questions relating to this experience, including any adverse experiences. We will also ask if you have had any experience of meditating (e.g. mindfulness meditation).

What are the possible disadvantages and risks of taking part?

We will ask you questions about your mental health and historical drug use. It is possible that questions about these sensitive subjects can be experienced as upsetting for some. As this is an online survey we are unable to provide support to people who are experiencing current mental health difficulties. If you are likely to find such questions especially distressing, you should not take part in the study. It is important for you to contact your GP if you have any concerns about your mental health.

What are the possible benefits of taking part?

Whilst there are no immediate benefits for those people participating in the project, it is hoped that you will leave with the knowledge that you have contributed to our understanding of the effects of psychedelic drug use, which could eventually inform future research in clinical psychopharmacology and the development of treatments for mental health difficulties.

What if something goes wrong?

If you wish to raise a complaint then please contact Dr Sunjeev Kamboj (the Principal Investigator for the study) at sunjeev.kamboj@ucl.ac.uk. If you feel that your complaint has not been handled to your satisfaction, you can contact the Chair of the UCL Research Ethics Committee at ethics@ucl.ac.uk.

Will my taking part in this project be kept confidential?

All the information that we collect about you during the course of the research will be kept strictly confidential. The data collected will be anonymous and collected through Qualtrics which complies with current data protection legislation (GDPR). Your anonymous data will then also be stored within a password-protected document on the secure UCL network.

There will be no way to identify you from the anonymised survey data and no participants will be able to be identified in any ensuing reports or publications.

What will happen to the results of the research project?

The results will be presented as scientific papers in peer reviewed journals, at conferences, and in student dissertations. You will not be able to be identified in any reports, publications, talks or media. The findings will be published on the UCL Clinical Psychopharmacology Unit's website.

The data collected during the course of the project might be made openly available and used for additional or subsequent research, this data will be fully anonymised and you will not be identifiable. Any personal data you provide (e.g. age, gender, socioeconomic status, ethnicity, country of residence) will be collected as broad categories (e.g. collecting age as a number rather than date of birth) to ensure that you cannot be identified by the details you provide.

Local Data Protection Privacy Notice

The data controller for this project will be University College London (UCL). The UCL Data Protection Officer provides oversight of UCL activities involving the processing of personal data, and can be contacted at data-protection@ucl.ac.uk

This 'local' privacy notice sets out the information that applies to this particular study. Further information on how UCL uses participant information can be found in our 'general' privacy notice.

- For the general privacy notice click [here](#).

The information that is required to be provided to participants under data protection legislation (GDPR and DPA 2018) is provided across both the 'local' and 'general' privacy notices.

For this study, the categories of personal data collected will be as follows: Gender; Age; Ethnicity; Mental Health and Drug Use information. The lawful basis for processing your personal data is the performance of a task in the public interest, and for scientific and historical research or statistical purposes. You can provide your consent for the use of your personal data in this project by completing the consent form on the next page.

Your personal data will be processed so long as it is required for the research project. Where we are able to anonymise or pseudo-anonymise the personal data you provide we will undertake this, as outlined above, and will endeavour to minimise the processing of personal data wherever possible.

If you are concerned about how your personal data is being processed, or if you would like to contact us about your rights, please contact UCL in the first instance at data-protection@ucl.ac.uk.

Contact for further information

The study is being conducted by researchers from the Department of Clinical, Educational and Health Psychology at University College London.

Kiana Azmoodeh

k.azmoodeh.17@ucl.ac.uk

Professor Sunjeev Kamboj

+44 (0) 20 7679

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sunjeev.kamboj@ucl.ac.uk

If you would like more information or if anything is unclear, please contact the researchers using the contact details above. If you decide to take part, please save a copy of this information sheet as well as your completed consent form (to be completed on the next page).

Thank you for reading this information sheet and for considering to take part in this research study.

Consent Form.

Title of Study: Examining the relationship between psychedelic drug use, mystical experiences, mental health and wellbeing.

Department: Department of Clinical, Educational, and Health Psychology, UCL

Name and Contact Details of the Researcher: Kiana Azmoodeh,

k.azmoodeh.17@ucl.ac.uk

Name and Contact Details of the Principal Researcher: Professor. Sunjeev Kamboj,

sunjeev.kamboj@ucl.ac.uk

Name and Contact Details of the UCL Data Protection Officer: [data-](mailto:data-protection@ucl.ac.uk)

protection@ucl.ac.uk

This study has been approved by the UCL Research Ethics Committee: Project ID

number: 15153/001

Thank you for considering taking part in this research. The person organising the research must explain the project to you before you agree to take part. If you have any questions arising from the Information Sheet, please contact the researcher to ask them before you decide whether to join in. You are advised to save a copy of this Consent Form to keep and refer to at any time.

I confirm that I understand that by ticking each box below I am consenting to this element of the study.

I understand that it will be assumed that unticked boxes means that I DO NOT consent to that part of the study.

I understand that by not giving consent for any one element that I will be deemed ineligible for the study.

I confirm that I have read and understood the Information Sheet for the above study. I have had an opportunity to consider the information and what will be expected of me. I have also had the opportunity to ask questions, and where relevant these have been answered to my satisfaction and I would like to take part in the survey.

I consent to participate in the study. I understand that my personal information, i.e. gender, age, ethnicity, mental health and drug use information, will be used solely for the purposes explained to me. I understand that according to data protection legislation, 'public task' will be the lawful basis for processing.

I understand that all personal information will remain confidential and anonymous, so that I cannot be identified. I understand that my data gathered in this study will be collected and stored securely. I understand that it will not be possible to identify me in any publications.

I understand that my information may be subject to review by responsible individuals from the University for monitoring and audit purposes.

I understand that my participation is voluntary and that I am free to withdraw at any time without giving a reason. If I decide to withdraw, any data I have provided up to that point will be submitted anonymously and stored.

I understand that I can withdraw my data (either partially or fully) within 1 month of completing the survey by emailing the researchers and quoting my 4-digit ID number with a request to withdraw.

I understand that though the potential risks of participating are low, that some questionnaires refer to potentially sensitive subjects such as mental health and drug use.

I understand that no promise or guarantee of benefits have been made to encourage me to participate.

I understand that the data will not be made available to any commercial organisations but is solely the responsibility of the researcher(s) undertaking this study.

I understand that I will not benefit financially from this study or from any possible outcome it may result in in the future.

I agree that my anonymised research data may be used by others for future research. [No one will be able to identify you if this data is shared.]

I understand that the information I have submitted will be published as a report and that upon publication, a version of the report will be made available on the university website.

I hereby confirm that I understand the inclusion criteria as detailed in the Information Sheet.

I am aware of who I should contact if I wish to lodge a complaint.

I voluntarily agree to take part in this study.

I understand that my data will be stored securely and anonymously.

I would be happy for the anonymous data that I have provided to be archived at UCL and I understand that others may have access to the anonymised survey data.