Predictors and potentiators of psychedelic-occasioned mystical experiences

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ABSTRACT

Mystical experiences are often described as being among the most profound and meaningful events of a person’s life. Their occurrence, while a normal but uncommon phenomenon, is reliably occasioned by psychedelic substances under the appropriate conditions, although care is needed around the context of usage to help ensure safe and beneficial experiences. The occurrence of mystical experiences in psychedelic sessions is a key mediator of the sustained psychological benefits reported in both healthy and clinical populations. Certain factors including set and setting, drug dosage, trait absorption, drug type, intention and states of surrender and acceptance all predict or influence the occurrence of mystical experiences. Various additional factors may further contribute to the occurrence and intensity of mystical experiences and enhance their long-term benefits, including music, meditation and spiritual practices and nature-based settings. This review examines these factors and considers how they might be optimised to increase the chances of a mystical experience occurring, while also considering factors that are negatively associated with mystical experiences with suggestions on how these might be mitigated where applicable. Finally, potential future research avenues for furthering our knowledge of psychedelic mystical experiences and how their benefits might be enhanced is suggested. Maximising the potential for the occurrence of mystical experiences is an important aspect of the beneficial application of psychedelics.

KEYWORDS

mystical experience, psychedelics, psilocybin, psychological well-being, therapeutic outcomes

INTRODUCTION

Mystical experiences encompass experiential facets of unity, oneness and interconnectedness, transcendence of time and space, deeply felt positive mood (joy, peace and love), a sense of sacredness, reverence or awe, ineffability and a noetic quality – an intuitive belief that what is being revealed has authenticity and validity (Barrett, Johnson, & Griffiths, 2015; Stace, 1960). They have been described for many centuries (Barrett & Griffiths, 2018, Stace, 1960), and appear to be an endogenous but uncommon phenomenon (Griffiths et al., 2011). They occur in both religious and non-religious individuals (Yaden, Haidt, Hood, Vago, & Newberg, 2017a), with the experiences transcending cultural, geographic and religious categories (Hood, 2006; Stace, 1960). Psychedelics are capable of reliably triggering mystical experiences under carefully orchestrated conditions which appear similar to experiences occurring spontaneously (Griffiths, Richards, McCann, & Jesse, 2006; Stace, 1960) including among individuals who lack a connection to a spiritual practice or religious tradition (Griffiths, Hurwitz, Davis, Johnson, & Jesse, 2019).

Use of the term ‘mystical’ applied to the experiences that psychedelics can occasion has been criticised by some researchers due to the perceived supernatural connotations of the term (Carhart-Harris & Goodwin, 2017; Sanders & Zijlmans, 2021), with ‘peak’ experience having been suggested as a more secular, neutral, psychological term to use (Strassman, 2018). However, ‘mystical experience’ is a well-established term in the scientific literature, being an extensively described phenomenon and subject of serious scientific study (Breексena & van Elk, 2021). The term mystical experience has also been used interchangeably with...
a variety of terms (Johnson, Hendricks, Barrett, & Griffiths, 2019; Yaden, Le Nguyen et al., 2017b) but irrespective of the label applied, these experiences are associated with eliciting ‘quantum change’ (Griffiths et al., 2018; Hendricks, 2018), or change that is sudden, robust, benevolent, deeply meaningful and enduring to personal emotion, cognition and behaviour (Miller, 2004; Miller & C’dé Baca, 2001). One seminal study on psilocybin-occasioned mystical experiences found that 67% of participants stated it to be either the single most meaningful experience of their lives, or among the top five, and of equivalent impact to the birth of a child or death of a parent (Griffiths et al., 2006). Mystical experiences have been associated with a deepened appreciation for life, prosocial feelings for others, a greater sense of life meaning and purpose, greater self-acceptance and spirituality and increased concern with social and planetary values, with intensity of experience associated with greater overall change (Schneebberger, 2010). Mystical and spiritual states associated with psychedelic usage have long been recognised, sought and utilised by various indigenous groups (Dobkin de Ríos, 1984; Rätsch, 2005; Winkelman, 2010), although cultures vary in their interpretation of the experience (Ataria, 2016; Wallace, 1959), and there is a lack of research examining to what degree indigenous people have mystical experiences as defined by Western researchers when psychedics are used in traditional contexts. Whether occurring spontaneously or through other means, the occurrence of mystical experiences is often associated with subsequent psychological health benefits (Griffiths et al., 2006; Ludwig, 1985; Russ & Elliott, 2017; Schneebberger, 2010; Snell & Simmonds, 2015; Yaden, Le Nguyen et al., 2017b). Such experiences are key determinants of the sustained therapeutic outcomes or psychological benefits associated with psychedelic usage. They have been found to act as important mediators of clinical outcomes, including existential anxiety (Griffiths et al., 2016; Kurland, Grof, Pahnke, & Goodman, 1972; Pahnke, Kurland, Goodman, & Richards, 1969; Richards, Rhead, Dileo, Yensen, & Kurland, 1977; Ross et al., 2016), addiction (Bogenschutz et al., 2015; Garcia-Romeu, Johnson, & Griffiths, 2014; Johnson, Garcia-Romeu, & Griffiths, 2017; O’Reilly & Funk, 1964), depression (Davis, Barrett, & Griffiths, 2020; Davis, So, Lancelotta, Barsuglia, & Griffiths, 2019; Roseman, Nutt, & Carhart-Harris, 2018; Sarris et al., 2021; van Oorsouw, Toennes, & Ramaekers, 2022) and anxiety (Davis et al., 2019, 2020; Sarris et al., 2021). Importantly, together with emotional breakthrough experiences (Roseman et al., 2019), the occurrence of mystical experiences in psilocybin sessions has been found to reliably predict long-term positive psychological changes when compared to other acute psychedelic experience measures or overall intensity of the experience (Barrett et al., 2015; Griffiths, Richards, Johnson, McCann, & Jesse, 2008; Griffiths et al., 2016; Haijen et al., 2018; Roseman et al., 2018; Ross et al., 2016; Schmid & Liechti, 2018), with intensity of the mystical experience positively influencing clinical outcomes (Griffiths et al., 2016; Roseman et al., 2018; Ross et al., 2016). The importance of the mystical experience in mediating clinical outcomes is highlighted by a study reporting that mystical-type experiences associated with ketamine administration (not typically considered a classical psychedelic and working via distinct brain mechanisms) were significantly associated with improvements in alcohol use disorder (Rothberg, Azhari, Haug, & Dakwar, 2021).

Mystical experiences occurring in healthy populations of psychedelic users are also associated with enduring benefits, including enhanced psychological well-being, life satisfaction and life meaning/purpose in addition to positive changes in attitudes, moods and behaviour (Griffiths et al., 2006, 2008, 2011, 2018; Haijen et al., 2018; MacLean, Johnson, & Griffiths, 2011; Nicholas et al., 2018; Uthaug et al., 2019). These shifts are sustained for at least 14 months post experience and can be elicited by a single experience (Griffiths et al., 2008). Mystical experiences have also been associated with enduring self-reported positive changes in creativity, and in relationships with self and with nature (Kangaslampi, Hausen, & Rauteenmaa, 2020) in addition to sustained shifts in personality traits, including increased openness (MacLean et al., 2011) and decreased neuroticism (Netzband, Ruffell, Linton, Tsang, & Wolff, 2020). This in turn could have positive implications for cognition (DeYoung, Peterson, & Higgins, 2005; Schretlen, van der Hulst, Pearlson, & Gordon, 2010; Rammstedt, Danner, & Martin, 2016), cognitive ageing (Franchow, Suchy, Thorgusen, & Williams, 2013; Williams, Suchy & Kraybil, 2013) and general mental and physical health (Lahey, 2009; Jeronimus, Kotov,RIese, & Ormel, 2016; Widiger & Oltmanns, 2017).

Concerns

Psychedelics are known to enhance suggestibility (Carhart-Harris et al., 2015; Lemerçier & Terhune, 2018), and care must be taken to avoid the potential for directive priming or integration pre or post psychedelic experience in a clinical context. Clinicians should seek to create an open, trusting and supportive environment and allow the person undergoing the psychedelic session to find their own meaning from their experience. Concerns have been raised about the potential of priming through the use of scales used to assess features of mystical experiences prior to psychedelic sessions (Love, 2021; Sanders & Zijlmans, 2021), or their potential incompatibility with individuals lacking any spiritual or religious inclination (Nicholas et al., 2018). In addition, the potential for biased clinical interpretations of the mystical experience has been argued by others (Allman, de la Rocha, Elkins, & Weathers, 1992; Cornelle & Luke, 2021; Strassman, 2018). Researchers or clinicians should be mindful not to impose their own personal spiritual or religious beliefs on people undergoing psychedelic sessions (Strassman, 2018), and while individuals can be encouraged to bring a few objects of personal value to the session if they wish (Watts, 2021), clinicians should be wary of using religious icons in the session room, which may act to prime and alienate some people (Johnson, 2021). However, interpretation of mystical experiences from a purportedly neutral and purely secular and reductionist standpoint may also have limitations. It has
been argued that this may diminish the effectiveness of psychedelic psychotherapy (Miceli McMillan, 2021), and be ill-suited in helping people process the ontological shock that may be associated with such experiences (Love, 2021). More diverse and nuanced perspectives and holistic approaches that encompass multiple narrative frameworks may be beneficial (Virdi, 2021). One alternative option is an inclusive client-centered interfaith approach centered on self-reflection and ethical meaning making, emphasising transparency of the therapist regarding their own views. Such an approach places emphasis on positionality (the notion that one’s understanding of the world is influenced by one’s relative social, cultural and political location and personal values and views) of the patient and therapist (López, 2021; Love, 2021).

Frequent, repeated spiritual or mystical experiences with a lack of subsequent integration could also potentially result in spiritual narcissism, with emphasis placed on the context of the acute experience, with a lack of evidence for positive or transformative change. This can potentially result in spiritual bypass, where people avoid engaging with other areas of their lives (Masters, 2010; Welwood, 1984). Tumultuous mystical experiences may pose challenges due to their potentially disruptive nature (Cornelie & Luke, 2021) and on occasion may be associated with spiritual emergency or transpersonal crises (Lukoff, Lu, & Turner, 1998). These can take a range of forms (Goretzki, Thalbourne, & Storm, 2013; Grof & Grof, 2017), and are associated with an intense and abrupt transformation that leaves little time for understanding, interpretation or adaptation (Taylor, 2017), potentially disrupting the sense of self resulting in crisis (Collins, 2007). A trusted rapport between a therapist and an individual undergoing a spiritual emergency, accompanied by sensitive and respectful therapeutic support may assist individuals in processing the experience, and the reinforcement of the internal nature of the experience to the individual may be helpful. Facilitating situations (such as through meditation and music-accompanied reflection) in everyday life whereby individuals can confront emerging material along with recommendations of relevant literature have been suggested as ways of helping people process such experiences, with the potential for transformative and therapeutic effects (Grof & Grof, 2017; Viggiano & Krippner, 2010).

The various factors that may act to predict and potentiate the occurrence and intensity of psychedelic mystical experiences shall now be examined to explore ways in which these might be optimised to maximise chances of their occurrence in a psychedelic session. In addition, factors that may be negatively associated with the occurrence of these experiences will be examined and potential means of mitigating these suggested where applicable.

**PREDICTORS OF PSYCHEDELIC MYSTICAL EXPERIENCES**

**Set and setting**

It can be considered that ingestion of a psychedelic substance is not the cause of the mystical experience but rather a catalyst that occasions it (Griffiths et al., 2006; Huxley, 1958) and the context framing psychedelic usage, including the set (immediate and extended psychological context) and setting (extended sociocultural and immediate environmental context) determines experiential outcomes including the occurrence of mystical experiences (Carhart-Harris et al., 2018; Griffiths et al., 2006; Johnson, Richards, & Griffiths, 2008; Leary, Litwin, & Metzner, 1963). While the concept of set and setting gained widespread recognition in the 1960’s (Hartogsohn, 2017), it is important to acknowledge that psychedelic-using indigenous groups have long recognised the importance of the context surrounding psychedelic usage, tending to use them in structured ceremonial settings and often following preparation for the experience (Beyer, 2010; Metzner, 1998; Winkelman, 2014). In a modern psychotherapeutic context, great care is taken to ensure a comfortable and secure setting, with interpersonal support provided in the session, in addition to interpersonal preparation and integration prior to the session and following it. During the psychedelic session, participants are encouraged to recline on a sofa or bed and close their eyes while wearing eyeshades and listen to a carefully selected accompanying musical playlist through headphones, with the suggestion that they focus their attention inwards for the duration of the session. However it should be noted that very little research has yet been conducted which systematically explores these factors for their efficacy. It has been reported that exposure to language is negatively associated with the occurrence of psychedelic mystical experiences (Russ et al., 2019a, 2019b), so verbal interaction and music with recognisable lyrics may be best avoided or minimised during the acute experience. If a participant reports significant anxiety or fear, guides provide reassurance either verbally or physically (Griffiths et al., 2006; Johnson et al., 2008). Having guides present who can relate to and interact with the participant on spiritual issues may help support the potential for the occurrence of mystical experiences (Johnson et al., 2008). The integral importance of context in determining outcomes is highlighted by comparing two studies, one using LSD, where complete mystical experiences were reported in 12.5% of participants (Liechti, Dolder, & Schmid, 2017), and another where 61% of participants reported complete mystical experiences under psilocybin, with 11% reporting complete mystical experiences under the active placebo methylphenidate. A mystical experience was considered complete if it achieved a minimum of 60% of the total possible score on each core dimension of the MEQ (Griffiths et al., 2006).

While further research is required to explore the pharmacodynamic differences between psychedelics and how this might influence the occurrence of mystical experiences, these profound differences in outcomes are likely influenced by the substantial differences in context that distinguishes these latter studies. In the Johns Hopkins studies the set and setting were optimised to support the occurrence of mystical experiences. Spiritually active or interested volunteers were selectively recruited and the drug was administered in the soothing and supportive context outlined previously (Barrett et al., 2015; Griffiths et al., 2006; Johnson et al., 2008). In the
LSD study, the drug was administered to paid volunteers in a standard hospital patient room setting with optional music listening and no use of eyeshades, with no preparation bar a screening visit and a psychiatric interview, and participants were not recruited on the basis of being spiritually active or interested (Liecchi et al., 2017). Another small study using psilocybin reported mystical experiences in 36% of cases, but notably in contrast to the Johns Hopkins study samples, several participants reported a lack of spiritual interest or activity or religious belief (Nicholas et al., 2018).

One seminal study by Pahnke comprised an important early study on psychedelics and mystical experiences. 20 divinity students were administered either 30 mg of psilocybin or a placebo in a chapel setting. 30–40% of participants who received the psilocybin reported mystical experiences, while none of those receiving the placebo reported the latter experience (Pahnke, 1963). A follow up survey was conducted among participants 24–27 years following their participation in the study and little change in retrospective measures of mystical experience were found, with a range of enduring positive effects attributed to the experience (Doblin, 1991). Interestingly, despite the religious ‘set’ of the divinity students participating in the study (which may have influenced the long-term outcomes; see Neitzke-Spruill & Glasser, 2018) and the religious chapel setting, similar levels of occasioned mystical experiences have been reported in studies examining psychedelic usage in a much more varied naturalistic context (e.g. Agin-Liebes et al., 2021; Garcia-Romeu et al., 2020; Pallavicini et al., 2021). However, the occurrence of complete mystical experiences in the latter studies was much lower than reported in the studies by Griffiths et al. (2006, 2008, 2011, 2018). Various factors likely influenced these different outcomes, with the greater volunteer preparation prior to the sessions and a more controlled and comfortable setting more conducive to an undisturbed inner journey likely among the more important (Barrett & Griffiths, 2018).

A supportive context framing usage is all the more important when it comes to the administration of 5-MeO-DMT, considered one of the most powerful psychedelic substances known (Weil & Davis, 1994). One study found that a supportive context was associated with the occurrence of complete mystical experiences in 83% of cases, while a non-supportive context was associated with such experiences in 54% of cases. A supportive context comprised a co-created calm and comfortable group setting overseen by experienced facilitators, a health screening, preparatory and post-session discussions, intent by participants to help ensure the well-being of others, and administration of a specific individualised dosage (Sepeda et al., 2020). Another study found that the use of benefit enhancement strategies (including meditating prior to a session, using ceremonial or shamanic techniques, having a clear intention and having a facilitator present) was also found to predict mystical experiences of greater intensity, while at the same time being associated with less intense challenging experiences (Lancelotta & Davis, 2020).

A calm, accepting, unburdened and positive mindset going into a psychedelic experience is supportive of mystical experiences (Aday, Davis, Mitzkovitz, Bloesch, & Davoli, 2021). One double-blind placebo-controlled study found that optimistic attitudes towards life and having experienced few psychological problems in past weeks was predictive of oceanic boundlessness, a state associated with feelings of unity and transcendence of time and space (Smigieliski et al., 2019). A pooled analysis of 23 studies involving 409 psilocybin sessions with 261 healthy volunteers found that state-level measures of general psychological distress were negatively correlated with oceanic boundlessness (Studerus, Gamma, Kometer, & Vollenweider, 2012). Oceanic boundlessness is tied to the core unitive aspect of the mystical experience which is considered a fundamental aspect of the latter experience (Hood, 1975; Stace, 1960), in addition to predicting long-term therapeutic outcomes (Roseman et al., 2018; Uthaug et al., 2019).

Drug Dosage

Dosage of psychedelic substance is a key predictor of mystical experiences, with ascending dosage more commonly associated with their occurrence, although beyond optimal dosage, higher dosages are more likely to trigger adverse reactions (Barrett & Griffiths, 2018; Carbonaro, Johnson, Hurwitz, & Griffiths, 2018; Carhart-Harris et al., 2018; Griffiths et al., 2011; Hajen et al., 2018; Hirschfeld & Schmidt, 2021; Kangaslampi et al., 2020; Lerner & Lyvers, 2006; Lyvers & Meester, 2012; Reckweg et al., 2021; Studerus et al., 2012). The positive outcomes associated with mystical experiences have also been found to increase as a function of psilocybin dose (Barrett & Griffiths, 2018). Dosage is also strongly associated with ego dissolution experiences, which have been defined as a “disruption of ego-boundaries, which results in a blurring of the distinction between self-representation and object-representation” (Nour, Evans, Nutt, & Carhart-Harris, 2016), these being considered a key aspect of the mystical experience (Barrett & Griffiths, 2018). According to obtained estimates from the previous studies, a dosage of 350 μg kg⁻¹ bodyweight (or an absolute dose of 24.5 mg/70 kg) of psilocybin and above is more likely to reliably yield ‘complete’ mystical experiences (Hirschfeld & Schmidt, 2021). While psilocybin content of mushrooms can be highly variable (Beug & Bigwood, 1982; Bigwood & Beug, 1982), this is approximately equivalent to a dosage of 4 g dried *Psilocybe cubensis* mushrooms (Bigwood & Beug, 1982; Carbonaro et al., 2016). 61% of people in the seminal Griffiths et al. study on psilocybin and mystical experiences underwent complete mystical experiences where people were administered 30 mg/70 kg of psilocybin (Griffiths et al., 2006). A follow up study using a range of dosages reported that dosages of 20 mg/70 kg were associated with complete mystical experiences in 44.4% of participants, while a dosage of 30 mg/70 kg was associated with such experiences in 55.6% of participants. While mystical experience scores were higher at 30 mg/70 kg of psilocybin, adverse reactions such as extreme fear, delusions or paranoid reactions were much more common at this dosage than at 20 mg/70 kg. An ascending sequence of psilocybin dose exposure was also positively associated with
increased likelihood of catalysing mystical experiences and sustained positive change (Griffiths et al., 2011).

Dosages of 25 mg psilocybin are commonly used in modern clinical studies. The latter dosage appears to be a good compromise between maximising the chances of a mystical experience, while minimising potential for adverse reactions. 25 mg appears suitable as a standalone dosage, with a lack of evidence to show that bodyweight is an important predictor of subjective reaction to psilocybin (Garcia-Romeu, Barrett, Carbonaro, Johnson, & Griffiths, 2021). However it should be noted that with some psychedelics such as 5-MeO-DMT, the required dose needed to elicit mystical experiences may vary markedly between individuals, making individualised dose escalation beneficial (Reckweg et al., 2021).

**Absorption**

Together with set and setting and drug dosage, level of trait absorption is one of the most important predictors of mystical experiences in psychedelic sessions (Haijen et al., 2018; Russ, Carhart-Harris, Maruyama, & Elliott, 2019a, 2019b; Studerus et al., 2012). Trait absorption is the propensity to become fully immersed or engaged in sensory and imaginative experiences, having been defined as a “disposition for having episodes of ‘total’ attention that fully engage one’s representational (i.e., perceptual, enactive, imaginative, and ideational) resources” (Tellegen & Atkinson, 1974, p. 268). Absorption appears to play a central role in predicting the occurrence of mystical and spiritual experiences (Cornelle & Luke, 2021; Lifshitz, van Elk, & Luhrmann, 2019) and is strongly correlated with personality trait openness to experience (Radjke & Stam, 1991), which is also predictive of the occurrence of mystical experiences under psilocybin (Russ et al., 2019b; Smigielski et al., 2019).

Absorption can also be conceptualised as a state, with absorption found to be enhanced in an acute context by encouraging participants to fully immerse themselves in an external stimulus which in turn provoked stronger feelings of awe (van Elk, Karinen, Specker, Stamkou, & Baas, 2016). Comfortable settings have been proposed to facilitate enhanced state absorption (Kreutz, Ott, Teichmann, Osawa, & Vaitl, 2007) and immersive settings (Ben-Soussan et al., 2019), flow states (Nakamura & Csikszentmihalyi, 2014), hypnagogic states (Mavromatis, 2010), hypnosis (Rainville & Price, 2003; Spiegel & Spiegel, 2004) and music listening (Herbert, 2011; Hall, Schubert, & Wilson, 2016) have all been associated with enhancing state absorption or potential for absorptive experiencing. Given that mindfulness meditation emphases a sustained attention on present-moment experience (Keng, Smoski, & Robins, 2011), it may help promote absorption. It has been proposed that practices conducted in a ceremonial and ritualistic fashion may elevate absorption in a religious context (Bronkhorst, 2016; Luhrmann, Nusbaum, & Thisted, 2010), and this may also apply to a context of psychedelic usage, with psychedelic-using indigenous groups almost invariably using them in this manner (Beyer, 2010; Dobkin de Rios, 1996; Metzner, 1998; Smith, 2000; Wolff, 2020). Trait absorption has been found to be higher in psychedelic microdosing groups compared to non-microdosing controls (Bright, Gringart, Blatchford, & Bettinson, 2021; Polito & Stevenson, 2019) and a single experience with a 25 mg/70 kg dose of psilocybin has been found to increase trait absorption for a minimum of a month following usage (Barrett, Doss, Sepeda, Pekar, & Griffiths, 2020).

These findings suggest that absorption is malleable to change through experience, training and context in both its state and trait form (Hall et al., 2016; Spiegel & Spiegel, 2004), and enhancing absorption prior to a psychedelic session could be beneficial (Hendricks, 2018), potentially increasing the likelihood of a mystical experience occurring. In a psychedelic-assisted psychotherapy session, people tend to be situated in a comfortable setting, lying supine on a couch or bed, wearing eyeshades and listening to music through headphones, it being the main external stimulus (Johnson et al., 2008). These conditions maximise the capacity for absorptive experiencing, reducing the potential for disturbances and distractions and promoting an inner journey.

**Drug type**

While mystical experiences are broadly associated with usage of a range of classical psychedelics (Griffiths et al., 2019; Yaden, Le Nguyen, et al., 2017b), the consistency by which these various substances occasion mystical-type experiences may vary. One study of naturalistic mescaline usage found that complete mystical experiences were reported in 30% of cases (Agin-Liebes et al., 2021), while such experiences were reported in 37% of cases among naturalistic DMT users (Pallavicini et al., 2021) and in 47% of cases among naturalistic psilocybin users (Cummins & Lyke, 2013). This can be contrasted to naturalistic 5-MeO-DMT usage being associated with complete mystical experiences among 57% of people (Davis, Barsuglia, Lancelotta, Grant, & Renn, 2018). While it should be noted that selection bias may be an issue through these internet-based survey studies, this occurrence rate of complete mystical experiences is very similar to that reported in the Johns Hopkins studies using psilocybin, where the setting was primed for the occurrence of mystical experiences (Griffiths et al., 2006, 2008, 2011, 2018), while in naturalistic contexts there is likely to be much wider variation in the study population and the set and setting. When 5-MeO-DMT has been used in a supportive context, mystical experiences were reported among 75% (Barsuglia et al., 2018) and 83% (Sepeda et al., 2020) of people.

One observational study of participants on a four-day psychospiritual retreat programme reported that 5-MeO-DMT usage was associated with complete mystical experiences in 75% of cases. Each participant was administered 50 mg of vapourised *Inciulus alvarius* bufotoxin, which was estimated to contain 5–7 mg of 5-MeO-DMT, with therapeutic preparation, education and integration and a secure and comfortable setting provided (Barsuglia et al., 2018). This estimated dosage of 5-MeO-DMT in the bufotoxin is considered to be among the lower dosage
range (Davis et al., 2019). In spite of this it occasioned mystical experiences with a statistical equivalence of 30 mg/70 kg psilocybin and significantly higher than a moderate/high dosage of 20 mg/70 kg psilocybin (Griffiths et al., 2011; Barsuglia et al., 2018). However, levels of 5-MeO-DMT in bufotoxin are variable: 50 mg of bufotoxin could potentially yield a dosage of up to 12.5–15 mg 5-MeO-DMT (Uthaug et al., 2019). Still, taken together these findings are suggestive that 5-MeO-DMT may occasion mystical experiences more consistently than other psychedelics when used in a supportive context.

### Intention

Having clear intentions prior to a psychedelic session so an individual feels prepared for the experience is also predictive of mystical experiences (Carhart-Harris et al., 2018; Haijen et al., 2018; Lancelotta & Davis, 2020). Psychedelics are not used frivolously by indigenous groups, with intention comprising a key aspect of their usage (Metzner, 1998). Of a range of different motivations behind psychedelic usage, approaching the experience with an emotional intent or with a spiritual motivation have been associated with greater likelihood of mystical-type experiences and well-being scores (Haijen et al., 2018; Russ et al., 2019a).

### Surrender state

The ability to let go and surrender (i.e. volitional release of goals, constructs, preferences and habits) at the beginning of a psilocybin session has been found to be an important predictor of mystical experiences occurring within a session whereas a state of mental apprehension has been found to be negatively predictive of mystical experiences (Russ et al., 2019a, b). “Trust, let go, be open” was the mantra central to the therapeutic approach used by psychedelic therapists overseeing psychedelic sessions at Johns Hopkins (MacLean, 2014), and this central focus has been adopted by other research groups elsewhere. Achieving the disposition to mentally let go and surrender to the experience, or what has been termed the “surrender state” (Richards, 2015) is partly dependent on setting factors, with feelings of safety and trust an important aspect of surrender (Holley, 2007). This latter prerequisite feeling of trust can be fostered through developing rapport with any therapists present prior to the session (Millière, Carhart-Harris, Roseman, Trautwein, & Berkovich-Ohana, 2018), and having the experience in a safe, secure and soothing setting (Johnson et al., 2008). In modern psychedelic therapy sessions, participants are also encouraged to allow the experience to unfold as it will, and to trust that their body will continue to function properly regardless of any sensations they may experience, and that their usual state of consciousness will return with the waning of the drug’s effects (Eisner, 1997). A state of surrender has also been found to be a key predictor of the occurrence of mystical experiences at the start of participation in an intensive meditation retreat (Russ & Elliott, 2017). Practices such as Holotrophic Breathwork place an emphasis on surrendering to the experience (Grof, 2014), and use of such a practice prior to a psychedelic session may assist people in learning to surrender and let go prior to having a psychedelic experience.

### Acceptance

Acceptance is related to a non-judgemental, accepting and appreciative attitude to oneself and one’s experiences, having been defined as “the ability to allow events to unfold without attempting to control them” (Wolff et al., 2020) and it has been found to be predictive of mystical experiences under psilocybin (Smigielski et al., 2019). Acceptance is a key aspect of mindfulness (Baer, 2003) and has been found to be enhanced by mindfulness practice (Tang, Hölzel, & Posner, 2015; Walsh, Saab, & Farb, 2019). An emphasis is placed on cultivating a state of acceptance by a number of different therapeutic approaches that have been used as part of psychedelic therapy including the ACT (Acceptance and Commitment Therapy; Hayes, Luoma, Bond, Masuda, & Lillis, 2006) and ACE (Accept, Connect, Embody; Watts & Luoma, 2020) models. Entering into an experience with a perspective of acceptance may help reduce mental barriers, or the tendency to reject phenomena having no rational explanation, the latter being negatively associated with the occurrence of mystical experiences (Russ et al., 2019b).

### POSSIBLE POTENTIATORS OF PSYCHEDELIC MYSTICAL EXPERIENCES

#### Music

Music has been associated with eliciting mystical-type experiences outside the context of psychedelic usage (Gabrielsson, Whaley, & Sloboda, 2009; Lowis, 2002; Nicholson, 2015). In a psychedelic psychotherapy context, music has been referred to as the “hidden therapist” given the central role it plays in psychedelic sessions, and it has been associated with the occurrence of mystical experiences (Kaelen et al., 2018). It can enhance feelings of wonder and transcendence under a psychedelic (Kaelen et al., 2015), with these latter qualities comprising core facets of the mystical experience (Griffiths et al., 2006; Maslow, 1964, 1971). While further research is required to better elucidate the link between music and the occurrence of mystical experiences, this provides tentative and indirect support for the important role music plays in psychedelic sessions.

One study surveyed individuals with extensive experience of administering psilocybin or psilocybin containing mushrooms (on a minimum of 50 occasions) in a research or therapeutic context in order to identify features of music supportive of the occurrence of mystical experiences within a psilocybin session. Music with “regular, predictable, formulaic phrase structure, and orchestration, a feeling of continuous movement and forward motion that slowly builds over time, and lower perceptual brightness when compared to pre peak music” was found to be conducive to the occurrence of mystical experiences under psilocybin (Barrett, Robbins, Smooke, Brown, & Griffiths, 2017).
Types of music may differ in their capacity to elicit mystical experiences. One small study noted that overtone-based music (emphasising instruments with a particularly strong overtone signature, such as Tibetan singing bowls, gongs, didgeridoo, chimes, bells, sitar, human voice overtone singing) was associated with greater mystical experiences than compositions dominated by Western classical music. However, the inferences that can be made from this small study are limited – the results were not significant, with the study having a sample size of 10 and no control group (Strickland, Garcia-Romeu, & Johnson, 2021). However, given that until very recently, psychedelic playlists have been dominated by Western classical compositions (Strickland et al., 2021), this study highlights the importance of investigating other forms of music in greater depth, to assess how they might influence the occurrence of mystical experiences.

Meditation and spiritual practices

Disciplined contemplative practices such as meditation have been associated with the occurrence of mystical experiences on occasion (Austin, 1999; Reavley & Pallant, 2009), although such experiences are more likely to occur following intensive or sustained long-term practice (Austin, 2006; Coleman et al., 2020; Kundi, 2013; Russ & Elliott, 2017). A number of practices such as meditation, yoga and prayer have been associated with the occurrence of mystical experiences, but the association may be stronger for meditation practice (de Castro, 2015). The occurrence of mystical experiences as part of meditation practice has been linked to some of the positive emotional outcomes associated with it (Russ & Elliott, 2017).

One double-blind, placebo-controlled study was conducted during a five-day mindfulness meditation group retreat setting in the Swiss Alps among a population of experienced Zen Buddhist meditation practitioners where a psilocybin dosage of 315 μg kg⁻¹ of bodyweight (or an absolute dose of 21.76 ± 3.8 mg psilocybin) or placebo was administered. 95% of participants (19 of 20) receiving the psilocybin reported a complete mystical experience (Smigielski et al., 2019). Complete mystical experiences occurred at over double the rate than reported in another study conducted by Griffiths et al. which employed a similar dosage of 20 mg/70 kg psilocybin (Griffiths et al., 2011). This hints at a profound potentiating effect of in-depth meditation experience and practice in eliciting mystical experiences alongside psychedelic administration, although the pristine alpine retreat setting may have also had an influence on outcomes. Mystical experiences were positively associated with baseline levels of meditation depth, and in-session magnitude of self-dissolution as assessed via measures of oceanic boundlessness. These predicted positive changes in psychological functioning and attitudes and behaviours at 4-month follow-up, including higher ratings of self-acceptance, life meaning and appreciation for life and death (Smigielski et al., 2019).

Even shorter-term meditation practice prior to a psilocybin experience can yield beneficial effects. One double-blind study examined the effects of spiritual practices in a high-support group including meditation (10–30 min a day); a daily awareness practice (including use of a mantra and one-pointed attention in daily activities); and a daily self-reflective journaling practice, with participants encouraged to engage in activities personally judged to facilitate spiritual growth. Engagement with spiritual practices commenced 1–2 months prior to psilocybin or placebo sessions and was kept up for 6–8 months. This group was compared to two others, one high and one very low dose psilocybin plus standard-support with the spiritual practices. The mystical experience scores (as assessed via the Mysticism Scale) were significantly higher in the high support group, and there were significant differences in a range of longitudinal psychological measures at 6 month follow-up. 96% of people in the high support group rated one or both of their psilocybin experiences as among the top five most spiritually significant experiences of their lives (Griffiths et al., 2018). This indicates that the spiritual practices enhanced the spiritual significance of the experience and the attribution of enhanced spirituality to it following it.

Prior meditation practice to a psilocybin session has been associated with greater levels of oceanic boundlessness in a psilocybin session (Griffiths et al., 2018; Smigielski et al., 2019) and deep meditative states are associated with boundary dissolution, with the capacity for passive “letting go” driving the depth of the dissolution (Nave et al., 2021). Meditation practice and ego-dissolution experiences under a psychedelic also appear to have a reciprocal and reinforcing relationship, with meditation practice associated with greater occurrence of ego-dissolution experiences while under a psychedelic, while the latter experience was perceived positively in reference to meditation, motivating practice, reducing perceived barriers and associated with finding meditation more effective (Simonsen & Goldberg, 2022). Meditation practice has been associated with enhanced openness (Barner & Barner, 2011; Pokorski & Suchorzynska, 2017; van den Hurk et al., 2011) which may serve to increase propensity to mystical experiences occurring during a psychedelic session, while also helping to sustain gains in openness following it. Meditation (Berko-vich-Ohana & Glicksohn, 2017; Davidson, Golemm, & Schwartz, 1976; Hölzel & Ott, 2006) and yoga practice (Bright et al., 2021) have been associated with higher levels of trait absorption in practitioners when compared to non-practicing controls. Absorption (Laidlaw, Dwivedi, Naito, & Gruzelier, 2005) and openness (De Fruyt, Van De Wiele, & Van Heerening, 2000) also have a strong relationship with the trait of self-transcendence, which involves the expansion of personal boundaries to encompass that which is greater than the self (De Fruyt et al., 2000). It has been linked to mystical experiences (Yaden, Haidt, et al., 2017a), and both meditation (Levenson, Jennings, Aldwin, & Shiraishi, 2005; Lynch, 2016) and yoga practice (Dagar, Pandey, & Navare, 2020) are positively associated with self-transcendence. It seems plausible that the positive association between trait absorption and meditation practice is bidirectional, with a training effect of meditation experience fostering an increase in trait absorption (Ott, 2003).
Taken together, these findings suggest a positive synergy between meditative practice and psychedelic usage, with such practice likely to contribute to the occurrence and intensity of mystical experiences, in addition to enhancing the long-term psychological benefits associated with them.

**Nature-based settings**

Immersion in natural settings can elicit spiritual feelings and mystical experiences (Ashley, 2007; Bethelmy & Corraliza, 2019; Doblin, 1991; Frederickson & Anderson, 1999; Harrild & Luke, 2020; Heintzman, 2012; Hood, 1977; Marshall, 2005; McDonald, Wearing, & Ponting, 2009; Naor & Maysel, 2020; Snell & Simmonds, 2012, 2015; Stringer & McAvoy, 1992; Terhaar, 2009; Williams & Harvey, 2001; Zylstra, 2014). It is notable that LSD inventor and discoverer Albert Hofmann described mystical experiences in nature in his younger days, punctuated by blissful feelings of oneness and unity (Hofmann, 1980, p. 3), which he would credit with his decision to pursue a career in chemistry (Hofmann & Ott, 1996).

In his words:

> “I had profound and visionary encounters with nature, and this was long before I conducted my initial experiments with LSD. Indeed, my first experiences with LSD were very reminiscent of these early mystical encounters I had had as a child in nature. So, you see that it is even possible to have these experiences without drugs.” (Grob & Hofmann, 1998)

Nature-based settings may provide a number of benefits that may potentiate the occurrence of mystical experiences. Such settings can support meditative, reflective mind states (Aspinall, Coyne, & Roe, 2015; Naor & Maysel, 2020), increase mindfulness (Hamann & Ivtzan, 2016; Richardson & Hallam, 2013; Van Gorden, Shonin, & Richardson, 2018) and promote states of absorption (Ballew & Omoto, 2018).

Nature can be considered a prototypical inducer of awe (Bethelmy & Corraliza, 2019; Keltner & Haidt, 2003; Shiota, Keltner, & Mossman, 2007), and nature-based settings appear to trigger awe more reliably than built environments (Ballew & Omoto, 2018). Awe is associated with spiritual experiences and feelings (Hu, Yang, Jing, & Nguyen, 2018; Kearns & Tyler, 2020; Preston & Shin, 2017; Van Cappellen & Saroglou, 2012) and a state of profound awe has been associated with the mystical experiences occasioned by psychedelics (Hendricks, 2018). Feelings of interconnectedness are another core facet of the mystical experience (Barrett & Griffiths, 2018; MacLean et al., 2011). A particularly direct perspective of this interconnectedness is recognition of our place in the web of life which may be more evident in nature-based rather than indoor settings (Ashley, 2007; Cooley, Jones, Kurtz, & Robertson, 2020; Unsworth, Palicki, & Lustig, 2016; Van Gordon et al., 2018). Feelings of awe and interconnectedness elicited during a psychedelic session can persist beyond the acute experience (Noorani, Garcia-Romeu, Swift, Griffiths, & Johnson, 2018), so contact with nature may help enhance the long-term benefits of mystical experiences.

Using psychedelics with the intent to connect with nature has been associated with greater likelihood of mystical experiences and greater well-being scores in comparison to a number of other motivations behind usage (Hajien et al., 2018). Mystical experiences occurring in nature-based rather than human-built settings appear more likely to elicit increases in pro-environmental behaviour (Snell & Simmonds, 2015), the latter being associated with psychological well-being (Corral-Verdugo et al., 2013; Kaida & Kaida, 2016; Netuveli & Watts, 2020; Prati, Albanesi, & Pietrantoni, 2017), while also sharing a mutually enhancing interrelationship with prosocial behaviour (Neaman, Otto, & Vinkur, 2018). These various aspects of nature-based settings suggest that incorporation of more nature-based practices, content and settings into psychedelic therapy models could be beneficial (for additional suggestions, see Gandy et al., 2020). As long as safety is assured, the application of psychedelics in nature immersion or nature-based mindfulness retreat contexts may increase likelihood of the occurrence of mystical experiences.

**Future research avenues**

Future research studies should seek to recruit more heterogeneous study samples and more thoroughly investigate the various factors predictive of mystical experiences and how these may vary between individuals. Mystical experiences may take different forms (Smith & Tart, 1998), and while scales such as the MEQ and MS are useful tools allowing for comparative research between populations, they are limited in the resolution they provide on aspects of mystical experiences and variation between them (Taves, 2020). They may also have limitations when applied to the assessment of mystical experiences associated with more intense and short-acting psychedelics such as 5-MeO-DMT (Reckweg et al., 2021). Despite mystical experiences being described as ineffable in some instances (Stace, 1960), people can meaningfully communicate their experiences when asked to do so (Yaden et al., 2016). Micro-phenomenological interviews have been used to study the experience of meditation (Petitmengin, van Beek, Bitbol, Nissou, & Roepstorff, 2019) and as part of neurophenomenological research into the effects of DMT (Timmermann et al., 2019). Such an approach could be usefully applied to provide a fine-grained assessment of the various facets that make up psychedelic mystical experiences. While much arguably mystico-centric attention has been given the capacity of psychedelics to induce mystical experiences (Strassman, 2018), the therapeutic potential of other forms of exceptional human experience (associated with and without psychedelic usage) to foster well-being has received far less research attention, and this may present a rich avenue to explore.

With the apparent synergy between meditation, spiritual practices and psychedelic mystical experiences (Griffiths et al., 2018; Smigielski et al., 2019), future research could attempt to delineate differences between various awareness practices and how they might influence outcomes. In addition, inclusion of nature-based settings into psychedelic
therapy models could be assessed to evaluate the degree to which they might synergise with the latter to elicit mystical experiences. Given the strong effect absorption has on predicting the likelihood of mystical experiences coupled with tentative evidence to suggest it may be malleable in both its state and trait forms, investigating potential means of enhancing it, both immediately prior to drug administration or over a longer time span, may be beneficial. Other practices and modalities such as rhythmic chanting (Perry, Polito, & Thompson, 2021) and virtual reality (Glowacki et al., 2020) have been associated with eliciting mystical experiences and may prove fruitful avenues to investigate alongside psychedelic administration.

A deeper understanding of psychedelic mystical experiences and their psychological aftereffects may allow for the development of novel therapeutic interventions to help enhance the positive changes associated with them. For example, mindfulness training (Aspy & Proeve, 2017; Keng et al., 2011) and practices or interventions designed to boost gratitude (see Wood, Froh, & Geraghty, 2010) or positive emotions (Aspy & Proeve, 2017; Kok et al., 2013) may enhance long-term outcomes. Psychedelic mystical experiences (coupled with psychological insight) can enhance psychological flexibility which appears to be an important component of their therapeutic effect (Davis et al., 2020). Application and investigation of psychological flexibility models such as the ACT (Hayes et al., 2006) and ACE (Watts & Luoma, 2020) models as part of psychedelic therapy may prove fruitful in a clinical context, these being centered on psychological flexibility processes. The practice of ‘engaged living’ centered on social integration through being of service to others, and an absorptive immersion in activities has been found to increase life satisfaction, prosocial attitudes, feelings of gratitude and positive affect in adolescents (Froh et al., 2010). This may be a beneficial practice to promote to an older audience, helping mirror and augment these qualities which are all associated with the afterglow of a psychedelic mystical experience (Griffiths et al., 2006, 2008, 2011, 2018). Furthermore, given that an enduring positive shift in people’s relationship with nature is commonly associated with psychedelic mystical experiences (Kangaslampi et al., 2020), the field of ecotherapy (Buzzell & Chalquist, 2009; Summers & Vivian, 2018) may provide opportunities for beneficial practices that are likely to synergise with such a shift.

CONCLUSION

One of the most unique and compelling properties of psychedelic drugs is their capacity to reliably induce mystical experiences under the right conditions. A number of different factors including set and setting, drug dosage, trait absorption, drug type, intention, states of surrender and acceptance, and the use of a psychedelic in a mindfulness meditation retreat context all influence their occurrence in the context of psychedelic administration. In addition, music, meditation and spiritual practices and nature-based settings may contribute to their occurrence or augment their long-term benefits. Psychedelics enhance suggestibility and care must be taken by clinicians to avoid directive priming or integration pre or post psychedelic experience to allow individuals to find their own meaning from their experiences. While mystical experiences catalysed by psychedelics are an important predictor of long-term benefits in healthy and clinical populations, our knowledge of them is still in its infancy, and much work remains to be done to examine how to maximise their occurrence and beneficial integration. Such work is warranted, as denying the relevance and importance of these phenomena will limit scientific progress and could have a detrimental impact on the therapeutic application of psychedelics.

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