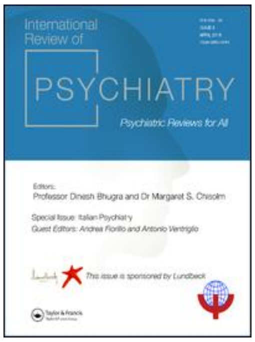

International Review of Psychiatry

ISSN: 0954-0261 (Print) 1369-1627 (Online) Journal homepage: http://www.tandfonline.com/loi/iirp20

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INTERNATIONAL REVIEW OF PSYCHIATRY
https://doi.org/10.1080/09540261.2018.1484342

REVIEW ARTICLE

Psychedelics and music: neuroscience and therapeutic implications

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ABSTRACT
From the beginning of therapeutic research with psychedelics, music listening has been consistently used as a method to guide or support therapeutic experiences during the acute effects of psychedelic drugs. Recent findings point to the potential of music to support meaning-making, emotionality, and mental imagery after the administration of psychedelics, and suggest that music plays an important role in facilitating positive clinical outcomes of psychedelic therapy. This review explores the history of, contemporary research on, and future directions regarding the use of music in psychedelic research and therapy, and argues for more detailed and rigorous investigation of the contribution of music to the treatment of psychiatric disorders within the novel framework of psychedelic therapy.

ARTICLE HISTORY
Received 11 February 2018
Accepted 30 May 2018

KEYWORDS
Psychedelic; hallucinogen; LSD; psilocybin; music; music therapy; music; neuroscience

Introduction

Classic psychedelic drugs[1] are being investigated for the treatment of psychiatric disorders, such as addiction (Bogenschutz et al., 2015; Johnson, Garcia-Romeu, Cosimano, & Griffiths, 2014), end-of-life distress (Griffiths et al., 2016; Grob et al., 2011; Ross et al., 2016), and depression (Carhart-Harris et al., 2016a; Osório et al., 2015; Sanches et al., 2016). Although mood and substance use disorders have a long time-course and uncertain prognosis when treated with currently available methods, psychedelic therapies are showing great promise. Recent studies demonstrate positive behavioural outcomes, including clinically relevant reduction in self-report and clinician-rated disorder severity (Bogenschutz et al., 2015; Carhart-Harris et al., 2016a; Griffiths et al., 2016; Osório et al., 2015; Ross et al., 2016; Sanches et al., 2016), physiological outcomes, including breath carbon monoxide and urine cotinine (Johnson et al., 2014), and, in one case, modulation of potential neurobiological correlates of mood disorders (Carhart-Harris et al., 2017; Roseman, Nutt, & Carhart-Harris, 2018). Given that only one or a small number (i.e. 2) of psychedelic therapy sessions can bring acute and sustained symptom improvements, psychedelic therapies represent a strong departure from the common medical model of chronic, daily pharmacotherapy and/or counselling as treatment.

A central principle in psychedelic therapy is that the quality of subjective experiences during acute drug effects predict (Roseman et al., 2018) and mediate (Griffiths et al., 2016; Ross et al., 2016) clinical outcomes. Music listening during acute drug effects has been a consistent feature of both research and therapeutic administration of psychedelics, as a method to guide or support experiences (Eisner & Cohen, 1958). Although music delivery during psychedelic therapy is not standardized, and methods used to select music for psychedelic therapy are largely untested, there may be some consistency in the features of music that are used to support therapeutic experiences (Barrett, Robbins, Smooke, Brown, & Griffiths, 2017b). Recent findings point to the potential of psychedelics to support meaning-making (Preller et al., 2017), emotion (Carbonaro, Johnson, Hurwitz, & Griffiths, 2018; Kaelen et al., 2015; Kaelen et al., 2017), and mental imagery (Kaelen et al., 2016) during music listening, and suggest that music plays an important role in facilitating positive clinical outcomes of psychedelic therapy (Kaelen et al.,

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2018). In this review, we will explore the history of, contemporary research on, and future directions regarding the use of music in psychedelic research and therapy, and argue for more detailed and rigorous investigation of the contribution of music to the treatment of psychiatric disorders within the novel framework of psychedelic therapy.

The history of music and psychedelic therapies

Music is ubiquitous in society and throughout known history. The earliest known musical instrument, a sophisticated bone flute, dates back at least 35 000 years (Conard, Malina, & Münzel, 2009), but recorded music history begins much more recently (Burkholder, Grout, & Palisca, 2010). The earliest records in music history document the use of music in religious worship, such as plainchant (including Gregorian Chant), and later in maintaining local and cultural histories, as in the medieval troubadours and trouveres (Burkholder et al., 2010). Theories of the origins of music suggest that music evolved to support emotional communication (Juslin & Vastfjall, 2008; Snowdon, Zimmermann, & Altenmüller, 2015), and may even have developed before more formal spoken language (Brandt, Slevc, & Gebrian, 2012; Panksepp, 2009). Theories that associate the co-evolution of language and music gain traction when we consider that the preponderance of brain regions that track syntactic components (Koelsch, 2011) and time-varying structures (Janata et al., 2002) in music are also brain regions critical for language processing (Levitin & Menon, 2003; Patel, 2008; Schön et al., 2010).

Alternative evolutionary theories focus on social functions of music or view music as a product of sexual selection (Hauser & McDermott, 2003). Although a consensus on biological origins of music is yet to be found, an increasing number of empirical studies illustrate a diverse significance of music in human development and culture. Research with infants indicates biological predispositions for melody-perception (Trehub, 2001), which likely serves an important social function (Mehr, Song, & Spelke, 2016), and cross-cultural studies show a universal singing of lullabies by mothers (Trehub & Trainor, 1998). Cross-cultural studies have also provided evidence that emotional content can be universally perceived as being associated with acoustic properties of music (Fritz et al., 2009; Laukka, Eerola, Thingujam, Yamasaki, & Beller, 2013). Emotional responses to music occur reliably in young children (Dalla Bella, Peretz, Rousseau, & Gosselin, 2001; Mote, 2011) and occur continuously in daily life (Juslin, Liljestrom, Vastfjall, Barradas, & Silva, 2008). Across the globe, music is an important element of diverse aspects of life, ranging from work, entertainment, and social settings to medicine and spirituality (Hargreaves & North, 1999; Merriam, 1964; Nettl, 1956).

For the present discussion, the medicinal and spiritual usage of music is particularly relevant. Although the use of music may be diverse, traditionally cultures often place a special emphasis on music's capacity to facilitate altered states of consciousness, and historically music-making has been a respected role reserved for priests or medicine-men (Nettl, 1956). Contemporary research on music listening has begun to address music's capacity to engender or support altered states, including emotionally intense peak experiences (Gabrielsson, 2011), absorption (Sandstrom & Russo, 2013), groove and flow states (Csíkszentmihályi, 1990; Janata, Tomic, & Haberman, 2012), trance (Hove et al., 2016; Rouget, 1985), and states of religious ecstasy (Penman & Becker, 2009).

Similar to the use of music, archeology suggests ancient roots for the use of psychedelics. Cave art depicting mushrooms in Algeria (Lajoux, 1964; Samorini, 1992) and Spain (Akers, Ruiz, Piper, & Ruck, 2011) are dated to be 7000–9000 years old; 4000–5600 year old specimens of psychedelic plants and seeds are found across North, Central, and South America (Bruhn, De Smet, El-Seedi, & Beck, 2002; El-Seedi, De Smet, Beck, Possnert, & Bruhn, 2005; Torres, 1998), and 2000–3000 year old mushroom-shaped stones were uncovered in Guatemala (de Borhegyi, 1963; Guerra-Doce, 2015). Many traditional societies preserved their use of psychedelics until today in a medicinal and spiritual context (Schultes, Hofmann, & Rätsch, 2001), and modern research has demonstrated psychedelics can reliably facilitate spiritual-type experiences (Bogenschutz & Johnson, 2016; Carhart-Harris et al., 2017; Garcia-Romeu, Griffiths, & Johnson, 2015; Griffiths, Richards, McCann, & Jesse, 2006; Griffiths et al., 2011, 2016; Roseman et al., 2018; Ross et al., 2016).

Traditional medicinal and spiritual practice with psychedelics was most likely combined with music (Nettl, 1956). Icaros, or ritual songs, are a universal component of traditional ayahuasca ceremonies, and are considered to be necessary to facilitate both physical and spiritual healing (Dobkin de Rios, 1984). Music is also a central component within mushroom ceremonies of the Mazatec Indians (Estrada, 1981), the peyote ceremonies of Native Americans (Maroukis, 2005), and the ibogaine rituals of Bwiti in west-central Africa (Fernandez, 1982; Schultes et al., 2001). In Europe's antiquity, music was also speculated to play a critical role in the Rites of Eleusis, which involved imbibing a psychedelic mixture (Wasson, Hofmann, & Ruck, 1978).

The synthesis of LSD (Hofmann, 1983) spurred a large wave of psychiatric and neuroscience research with psychedelics in the 1950s and 1960s. The therapeutic potential of psychedelics was heavily explored (Busch & Johnson, 1950), and music was early on identified as a factor that can potentiate and influence drug experiences significantly (Eagle, 1972; Eisner & Cohen, 1958; Gaston & Eagle, 1970). Soon, music was recognized as an important element of the setting to support the therapeutic process (Chandler & Hartman, 1960; Eisner, 1997; Eisner & Cohen, 1958; Hoffer, 1965; Holzinger, 1964). Emphasis was given to view music as a therapeutic aid (Hoffer, 1965), and that, due to music's 'profound' influence (Bonny & Pahnke, 1972), great care and responsibility must be practiced in selecting the music for patient's individual therapeutic needs (Bonny & Pahnke, 1972; Hoffer, 1965).

Studies reported profound alterations in a patient's perception of and response to music, and suggested this underlies the usefulness of music as an adjunct to psychedelic therapy. For example, Hoffer (1965) noted:

> Very often, sounds which normally have no particular aesthetic appeal, were heard in a most unusual manner. Subjects who were indifferent to music, were enthralled by it. […] This property of the experience is very useful in bringing out the psychedelic reaction. Carefully selected music can be very powerful in altering the subject's mood and associations. (p. 204)

Studies investigating the effect of psychedelics on auditory processing reported altered sensitivity and tolerance to sound after the intake of LSD (Silverman, 1971), and have shown that, after the administration of psilocybin, participants listening to music described an intensive, exhilarating sound experience (Weber, 1967). One participant reported that she was for the first time able to fully 'surrender to the music', while at the same time she could not capture the structure of the piece (Weber, 1967).

Subsequent early research on the therapeutic effects of psychedelics included music listening as a consistent feature during acute drug effects (Grof, 1980; Grof, Goodman, Richards, & Kurland, 1973; Kurland, 1985; Kurland, Unger, Shaffer, & Savage, 1967; Pahnke, Kurland, Goodman, & Richards, 1969; Richards, 1979; Richards, Rhead, DiLeo, Yensen, & Kurland, 1977). Guidelines for the use of music in clinical settings were developed (Bonny & Pahnke, 1972), and clinical opinion suggested the use of specific musical pieces (Eisner, 1997), or styles of music (Bonny & Pahnke, 1972) to support specific phases of psychedelic experience (e.g. 'onset of effects', 'peak intensity of drug action', and 'return to normal consciousness') (Bonny & Pahnke, 1972). Consequently, modern guidelines for safe use of psychedelics in research recommend the use of music listening as a critical element of the therapeutic setting (Johnson, Richards, & Griffiths, 2008). The use of music to support specific experiences during psychedelic therapy has been typically framed and characterized in terms of supporting specific emotional experiences, such as peak or mystical experiences[2] or emotional catharsis (Bonny & Pahnke, 1972).

Contemporary research on the neuropsychobiology of music and psychedelics

Music listening has been shown to engage a wide range of domain-general brain areas, including those associated with reward, emotion, and memory processing (Barrett & Janata, 2016; Blood & Zatorre, 2001; Salimpoor, Benovoy, Larcher, Dagher, & Zatorre, 2011; Salimpoor et al., 2013). Brain regions recruited during music listening overlap at least partially with brain regions where activity and connectivity are altered after the administration of psychedelics (Carhart-Harris et al., 2012a; Carhart-Harris et al., 2016b; Preller et al., 2017). Psychedelic drugs have notable effects on auditory perception (Hoffer, 1965; Silverman, 1971; Timmermann et al., 2017; Umbricht et al., 2003; Weber, 1967). This follows from the neurobiology of both psychedelic drugs (serotonin 2A, or 5-HT_{2A}, receptor agonists) and the neurobiology of auditory processing. Brainstem serotonergic neurons have been implicated in selective neuronal responses to auditory stimuli (Hall, Rebec, & Hurley, 2010; Hurley & Pollak, 1999), and 5-HT_{2A} signaling has specifically been shown to alter neuronal responses to auditory stimuli from the cochlear nucleus (Tang & Trussell, 2015), through the pre-cortical primary auditory sensory pathway (Hurley, 2006; Hurley & Sullivan, 2012), through to the primary auditory cortex (Riga, Bortolozzi, Campa, Artigas, & Celada, 2016) and auditory cortical neurons (Luo, Hu, Liu, Guo, & Wang, 2016).

Investigating the neurobiological mechanisms underlying psychedelic-induced alterations in auditory processing, modern neuroimaging studies reported a reduced N1 sensory EEG-ERP, suggesting reduced processing of intensity of auditory stimuli under psilocybin (Umbricht et al., 2003), and altered auditory sensitivity measured with MEG under LSD (Timmermann et al., 2017). Empirical studies further investigated music processing after the administration of LSD, while participants underwent functional magnetic resonance imaging (Barrett, Preller, Herdener, Janata, & Vollenweider, 2017a; Kaelen et al., 2016, 2017; Preller et al., 2017). These studies revealed that LSD alters the perception of the acoustic properties of music. In particular, LSD increased the BOLD signal in response to timbral complexity—indicative of the complexity of the music's spectral distribution—in brain networks associated with music perception and emotion, i.e. the auditory cortices, inferior frontal gyrus (IFG), insula, precuneus, striatum, and the supplementary motor area (SMA; Kaelen et al., 2017). Additionally, processing of high timbral complexity was associated with increased coupling of the precuneus with the right superior frontal gyrus and decreased coupling of the precuneus with the right IFG and auditory cortex after LSD administration (Kaelen et al., 2017). LSD was further shown to influence the neural response to the time-varying tonal structure of music—an effect that was predominantly attributable to LSD's agonist activity on the 5-HT_{2A} receptor (Barrett et al., 2017a). LSD enhanced tonality tracking in areas that respond to music and speech, as well as higher cognitive areas such as the superior temporal cortex, the IFG, medial prefrontal brain regions, the angular gyrus, and the amygdala (Barrett et al., 2017a).

Preller et al. (2017) showed enhanced meaningfulness perceived in music under LSD, associated with greater BOLD activations in regions previously linked to music-listening, emotion, and autobiographical memory, including the SMA, putamen, insula, and the PCC. Kaelen et al. (2016) demonstrated that an interaction between LSD and music lead to increased information flow (effective connectivity) from the parahippocampus towards the visual cortex, and this effect correlated with enhanced mental visual imagery and seeing autobiographical scenes (Kaelen et al., 2016). Together, these results indicate that psychedelics significantly modulate the brain's processing of music, and these effects may explain the altered subjective experience of music under psychedelics (Barrett et al., 2017a; Kaelen et al., 2016, 2017; Preller et al., 2017).

How do music and psychedelics interact to promote healing?

Music supports emotional experiences

A prime motivation for many people to listen to music is to modulate emotion (Berlyne, 1971; Schäfer, Sedlmeier, Städtler, & Huron, 2013), and the emotion-arousing properties of music arguably comprise one important motivation for the application of music therapy in the treatment of various psychiatric (Castillo-Pérez, Gómez-Pérez, Velasco, Pérez-Campos, & Mayoral, 2010; Erkkilä et al., 2011; Zhao, Bai, Bo, & Chi, 2016) and neurological diseases (Fakhoury, Wilhelm, Sobota, & Kroustos, 2017; Hohmann, Bradt, Stegemann, & Koelsch, 2017; Leubner & Hinterberger, 2017). Emotionally intense 'chill-inducing' effects of music are common (Panksepp, 1995) and empirically studied (Grewe, Nagel, Kopiez, & Altenmüller, 2005; Harrison & Loui, 2014; Mori & Iwanaga, 2014; Salimpoor, Benovoy, Longo, Cooperstock, & Zatorre, 2009). However, the mechanisms through which music can modulate emotional experience are many and varied.

Different classes of determinants, from acoustic and musical features of individual stimuli (Coutinho & Cangelosi, 2009; Hevner, 1937; Leman, Vermeulen, De Voogdt, Moelants, & Lesaffre, 2005; Maher, 1980), to personal associations people have made with music (Barrett et al., 2010; Janata, Tomic, & Rakowski, 2007), to more abstract concepts such as preference traits and personality (Dollinger, 1993; Rawlings & Ciancarelli, 1997; Rentfrow & Gosling, 2003; Rentfrow, Goldberg, & Levitin, 2011; Zweigenhaft, 2008), have been shown to influence the emotions that are experienced during music listening (see also Juslin & Vastfjall, 2008). 'Liking', in particular (e.g. a person's affinity for a particular piece of music), is shown to influence the emotions experienced with music significantly (Juslin, 2013; Juslin & Vastfjall, 2008; North & Hargreaves, 1997), and it may be the case that liking moderates the effect of musical features and familiarity on music-evoked emotions (North & Hargreaves, 1995). Consistent with previous theoretical perspectives (Berlyne, 1971), liking may act as an index for the emotional utility of a musical stimulus, thus functioning as a 'gatekeeper' or filter for the subsequent effects of the music on the listener's emotional state.

The effects of psychedelics, however, are conceptualized as a relinquishment of the normal filters the 'self' utilizes to regulate its internal milieu (Barrett & Griffiths, 2018; Carhart-Harris et al., 2014). Thereby, psychedelics may diminish the usual regulatory processes of music-evoked emotion and allow a fuller processing of music and the features of the music that evoke emotion. Support for this hypothesis can be found in both psychopharmacological and neuroimaging investigations. In a comparative psychopharmacology study, volunteers reported far greater absorption in music, as well as greater perceived beauty and significance of music, during the acute effects of psilocybin than during placebo or the acute effects of dextromethorphan (an NMDA antagonist and dissociative hallucinogen) (Carbonaro et al., 2018). Kaelen et al. (2017) demonstrated an association between intensified music-evoked emotion and enhanced BOLD activation to music's timbral complexity—timbre (tone colour) being associated with conveying emotional information in music (Eerola, Ferrer, & Alluri, 2012; Hailstone et al., 2009).

Psychedelics indeed have been shown to not only alter the processing of acoustic properties of music, but also the psychological and emotional reaction to it (Kaelen et al., 2015, 2017; Preller et al., 2017). Intensification of emotion and mental imagery by music was a primary motivation for the use of music in psychedelic therapy in the 1950s and 1960s (Bonny & Pahnke, 1972), and has been most frequently reported by patient's undergoing psychedelic therapy (Kaelen et al., 2018). To illustrate, one patient from Kaelen et al. (2018) reported:

> Under the influence of psilocybin the music absolutely takes over. Normally when I hear a piece of sad music, or happy music, I respond through choice, but under psilocybin I felt almost that I had no choice but to go with the music. (p. 10)

(For more insight in patient's experiences of music, see Supplementary materials in Kaelen et al., 2018).

One way the intensifying effects of psychedelics on music-evoked emotion may support the therapy is by contributing to the occurrence of mystical experiences during psychedelic therapy sessions (Barrett & Griffiths, 2018; Kaelen et al., 2018), which have been associated with positive therapeutic outcomes (Barrett & Griffiths, 2018; Johnson & Griffiths, 2017). LSD has been shown to enhance emotional features of mystical-experiences (Kaelen et al. 2015, 2017), and psilocybin has been shown to enhance absorption in and the beauty and significance of music (Carbonaro et al., 2018), and the music-experience of patients in psychedelic therapy has been associated with the occurrence of mystical-experiences (Kaelen et al., 2018). Furthermore, Lebedev et al. (2016) showed that LSD-induced increases in entropic brain dynamics were related with subsequent increases in personality trait openness, only during the music-listening condition, indicating that music may drive brain dynamics important for the occurrence of experiences that have long-lasting beneficial effects (Lebedev et al., 2016).

Finally, music in therapy is effective in reducing stress and anxiety (Chanda & Levitin, 2013), and, consistent with earlier reports (Bonny & Pahnke, 1972), music is reported to provide a sensation of calm, safety, and support for patients in psychedelic therapy (Kaelen et al., 2018). Hence, in addition to evoking strong emotionality, music may play an important role in reducing emotional arousal too, helping the patient to find meaningful resolutions to transient psychological struggles that are not uncommon in psychedelic therapy (Barrett, Bradstreet, Leoutsakos, Johnson, & Griffiths, 2016; Belser et al., 2017; Swift et al., 2017; Watts, Day, Krzanowski, Nutt, & Carhart-Harris, 2017).

Music supports autobiographical meaning-making

Another potential effect through which psychedelics and music interact on the therapeutic process was described by Preller et al. (2017). This study showed that LSD increases the attribution of personal meaning to music, in particular to music pieces which were not particularly meaningful to participants in the placebo condition. This effect was associated with an increased BOLD signal in the cortical midline structures, brain areas which are associated with self-referential processing (Northoff & Bermpohl, 2004; Preller et al., 2017), and was dependent on 5-HT_{2A} receptor stimulation (Preller et al., 2017). These brain regions have been shown to be clinically relevant in psychiatric disorders and might also be involved in the therapeutic response to LSD (Moeller & Goldstein, 2014; Northoff & Bermpohl, 2004). The ability of LSD to increase perceived meaningfulness can contribute to mystical experiences which have been shown to be related to beneficial therapeutic outcome. Furthermore, by altering brain activity in regions important for self-referential processing, as well as at the same time increasing the meaningfulness of the environment, patients may become more accepting and open to changes (Halberstadt, 2017). Therefore, the potential of psychedelics to enhance perceived meaningfulness could contribute to beneficial therapeutic outcomes, particularly in disorders with altered self-referential processing such as depression (Halberstadt, 2017).

A further study by Kaelen et al. (2016) showed that LSD and music interact to increase effective connectivity from the parahippocampal cortex to the visual cortex, and the magnitude of this effect correlated with increased visual mental imagery and ratings for seeing autobiographical scenes from the past (Kaelen et al., 2016). LSD-induced enhancement of autobiographical memories, and associated with this the potential reversal of negative cognitive biases, might be associated with beneficial therapy outcome (Carhart-Harris et al., 2012b; Kraehenmann et al., 2015; Vollenweider & Kometer, 2010). Together, these studies offer a mechanistic explanation on how LSD together with music stimulates autobiographically meaningful processes, and suggests that music could be a tool to facilitate this process during psychedelic therapy.

Implications for psychedelic therapy

The capacity of psychedelic therapy to facilitate acute and sustained therapeutic changes represents a promising direction in mental healthcare, and a significant deviation from conventional treatments, both in terms of administration of the drug and in the underlying theoretical frameworks. Hence, an empirical understanding of the different components of this new paradigm of therapy is critical to offer evidence-based guidelines for researchers and therapists. The present paper focuses on music, as this is one dominant component in the therapeutic model, and this section will discuss how the previously reviewed research on psychedelics and music begins to inform an evidence-based use of music in psychedelic therapies.

Studies reviewed previously indicate an enhanced emotional and psychological responsivity to music under psychedelics. While evidence exists for potential therapeutic effects of psychedelic drugs absent of music listening (Sanches et al., 2016), patients often emphasize the significant influence of music on their experience in psychedelic therapy (Belser et al., 2017; Swift et al., 2017; Watts et al., 2017). It has been demonstrated that the music-experience during psychedelic therapy correlates with the occurrence of mystical experiences and insightfulness during psychedelic therapy, and with reductions in clinical symptoms 1 week after the session, and that calming effects of music are welcome and potentially beneficial during onset, ascent, and return phases of the psychedelic experience (Kaelen et al., 2018). Together, these findings provide a body of evidence that music can be a potent medium to modulate emotion and meaning-making, to facilitate experiences that have strong therapeutic significance.

As the quality of the music experience has been associated with therapy outcomes, and, more specifically, a music-experience characterized by personal 'resonance' (Kaelen et al., 2018), the music-selection requires a thoughtful optimization to the individual patient. Although tailoring the music to the dynamic needs of the individual patient is standard practice in MDMA-assisted psychotherapy (Mithoefer, Wagner, Mithoefer, Jerome, & Doblin, 2011), most studies with classic psychedelics have prioritized a standardized approach, where all patients listen to the same music playlist. Although from a research perspective this may be desirable, this can jeopardize the therapeutic experience of some patients significantly (Kaelen et al., 2018). Standardization of the process that generates patient-specific music, rather than simply standardizing the mere presence of the music, may harmonize research-standards with the human-centred practice inherent in the therapy model, and is likely to optimize patient-experiences and therapy outcomes.

Limitations

While we have attempted to present a thorough review of studies that inform our understanding of the interaction between music and psychedelic experiences, there are several limitations to our review. First, many of the earlier reports of the relationship between psychedelics and music listening lacked the rigour of modern experimental controls (e.g. reviewed in Eisner & Cohen, 1958 and Richards, 1979) or were largely based on observation and clinical opinion (e.g. Bonny & Pahnke, 1972). In addition, many recent reports, especially those involving clinical outcomes, were open-label studies (e.g. Bogenschutz et al., 2015; Carhart-Harris et al., 2016a; Johnson et al., 2014; Osório et al., 2015; Sanches et al., 2016). While a number of recent reports did involve placebo or active control as well as single-blind (e.g. Kaelen et al., 2015, 2017) or double-blind randomized conditions (e.g. Barrett et al., 2017a; Carbonaro et al., 2018; Griffiths et al., 2016; Preller et al., 2017; Ross et al., 2016), some of the reports cited in this review involved multiple analyses of data from the same sample (e.g. Barrett et al., 2017a; Carhart-Harris et al., 2016a, 2017; Preller et al., 2017; Roseman et al., 2018). While we have reviewed the nascent literature on the interaction between music and psychedelic experiences, which is growing, the field has yet to develop a literature sufficient to support a meaningful systematic review, but we hope that this review will stimulate further structured research in this field.

Future directions

The current state of research regarding psychedelics and music presents several limitations and necessities for future research. The studies reviewed were the first to assess the combined effects of music and psychedelics on subjective experience and brain function, and these findings, therefore, implicate the need of their replication and expansion in independent future studies. Future studies that enable a better separation between music- and drug-conditions are also necessary to deepen our understanding of their interactive effects on subjective experience and therapy outcomes. In therapeutic contexts, studies involving one group of patients undergoing psychedelic therapy with music, and one group without any music, will be needed to reveal both the magnitude and the nature of the therapeutic effects of music. With respect to the latter, studies on the nature of the therapeutic effects of music can provide important insights into key therapeutic processes at play, and the different ways these can be best supported, with and without music.

Furthermore, studies are needed that compare the relative contribution of music to the therapeutic experience and outcome to other factors present during therapy sessions, such as interpersonal factors and physical environment. Future studies can help us to better understand the interactions between the psychological context of the patient (mood, attitudes, expectations, personality-traits) and the patient's subjective experience of music, both with and without psychedelics. Future studies must also address how music can be tailored to the time-phase within the drug-experience, and assess whether any music genres, composition features, or acoustic features in particular are suitable for the facilitation of therapeutic experiences. Related to this, the role of an individuals' music-listening history and its relationship to the music-experience under a psychedelic remains to be clarified, and, together with the above, will aid the construction of empirical guidelines for music-selection and playlist design during psychedelic therapy sessions. The choice of music in the reviewed neuroimaging studies may have significantly influenced their findings, and future studies that use different genres or a multitude of musical genres may be positioned to test hypotheses regarding the effects of and appropriateness of different styles of music in the context of psychedelic therapy. Although individual variation in patients' music-experience has been related to therapy outcomes, there is little experimental insight into how music can be adapted to optimize therapy outcomes. Studying this is crucial to help define music-selection protocols that are empirical and scalable, which must include an accurate mapping of music with its experience, given the psychological context of the patient.

Finally, the subjectiveexperiences of music-listening under a psychedelic can be remarkably profound, indicating that their combined study may significantly advance our understanding of human brain mechanisms of music-perception and subjective experiences of music, as well as the neural correlates of subjective experiences that are normally difficult to access under experimental conditions (for example, emotionally intense peak experiences).

Conclusion

Psychedelics and music listening interact to produce profound alterations in emotion, mental imagery, and personal meaning. Research is beginning to unveil underlying brain mechanisms, and to support a central role of music in psychedelic therapy. Music appears to influence the efficacy of therapy significantly, through modulating emotion, including the facilitating of mystical experiences, and through supporting autobiographical processes. Acknowledging the significance of music and the importance of rigorous future empirical investigations in this young field of research is key to improving our understanding of psychedelic therapies, and key to improving the efficacy of psychedelic therapies.

Disclosure statement

MK is a founder and shareholder in Wavepath Ltd. FSB and KHP report no conflicts of interest. The authors alone are responsible for the content and writing of the paper. FSB was supported in part by NIH grants R03DA042336 and a grant from the Heffter Research Institute. KHP was supported by the SNSF grant P2ZHP1_161626.

Notes

1. 'Classic' psychedelics produce a range of idiosyncratic and often profound subjective effects via agonist actions on the serotonin 2A receptor. Examples of classic psychedelics include lysergic acid diethylamide

or LSD, psilocybin, found in hundreds of species of psychoactive mushrooms, dimethyltryptamine or DMT, found in the *Psychotria viridis* and *Diplopterys cabrerana* plants used to brew ayahuasca, and mescaline, found in some psychoactive cacti. The term psychedelic is derived from merging the Greek word *psyche*, meaning mind or soul, with *delos*, meaning to unveil or make visible effects.

2. Peak experiences with psychedelic drugs were first defined by Pahnke et al. (Pahnke, 1963; Pahnke et al., 1969) as sharing common features with non-drug mystical experiences. Peak/mystical experiences are characterized by an experience of unity (with one's self, one's surroundings, some or all people, or all that exists), loss of one's usual sense of space and time, deeply felt positive mood, the felt sense that the experience involves some fundamental truth (noetic quality), difficulty putting the experience into words (ineffability), a felt sense of sacredness, transiency, and paradoxicality (simultaneously containing contradictory feelings, thoughts, experiences, or characteristics).

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