



UvA-DARE (Digital Academic Repository)

Psychedelic drug use in healthy individuals

A review of benefits, costs, and implications for drug policy

Elsey, J.W.B.

Published in:
Drug Science, Policy and Law

DOI:
[10.1177/2050324517723232](https://doi.org/10.1177/2050324517723232)

[Link to publication](#)

Creative Commons License (see <https://creativecommons.org/use-remix/cc-licenses/>):
CC BY-NC

Citation for published version (APA):
Elsey, J. W. B. (2017). Psychedelic drug use in healthy individuals: A review of benefits, costs, and implications for drug policy. *Drug Science, Policy and Law*, 3. <https://doi.org/10.1177/2050324517723232>

General rights

It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations

If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: <https://uba.uva.nl/en/contact>, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

UvA-DARE is a service provided by the library of the University of Amsterdam (<http://dare.uva.nl>)

Psychedelic drug use in healthy individuals: A review of benefits, costs, and implications for drug policy

James W.B. Elsey

Drug Science, Policy and Law

Volume 3: 1–11

© The Author(s) 2017



Reprints and permissions:

sagepub.co.uk/journalsPermissions.nav

DOI: 10.1177/2050324517723232

journals.sagepub.com/home/dsp

Abstract

The potential of psychedelic drugs in the treatment of mental health problems is increasingly being recognized. However, relatively little thrust has been given to the suggestion that individuals without any mental health problems may benefit from using psychedelic drugs, and that they may have a right to do so. This review considers contemporary research into the use of psychedelic drugs in healthy individuals, including neurobiological and subjective effects. In line with findings suggesting positive effects in the treatment of mental health problems, such research highlights the potential of psychedelic drugs for the enhancement of wellbeing even in healthy individuals. The relatively low risk associated with usage does not appear to align with stringent drug laws that impose heavy penalties for their use. Some policy implications, and suggestions for future research, are considered.

Keywords

Psychedelics, ayahuasca, psilocybin, DMT, LSD, drug policy, drug use, healthy participants

Researchers and clinicians are becoming increasingly open to the possibility that psychedelic drugs might prove useful in the treatment of mental health problems. Studies conducted primarily in the 1950s and 1960s furnished a wealth of (methodologically imperfect) clinical findings to suggest beneficial effects of psychedelic drugs in the treatment of mood, anxiety, and addictive disorders (Grinspoon and Bakalar, 1979; Sessa, 2005). However, due to highly restrictive drug laws that effectively foreclosed research into psychedelic drugs in the 1960s, their possible benefits have been widely overlooked (Nutt et al., 2013). More recent studies have begun to corroborate the suggestion that treatments involving psychedelic drugs may be effective in the alleviation of a range of mental health problems (see Vollenweider and Kometer, 2010 for a review). In light of such findings, several authors have argued for changes in drug policy in order to facilitate basic research and treatment innovation regarding psychedelics (Gross, 2013; Nutt et al., 2013).

However, relatively little thrust has been given to the argument that even healthy individuals can experience

considerable benefits from consuming psychedelics, and that they may have a right to experience these (Walsh, 2016). Bioethical discussion of the use of drugs in the healthy population to improve wellbeing has typically focused on the use of pharmaceuticals such as selective serotonin reuptake inhibitors (SSRIs) and other antidepressants as a means of improving mood (Kramer, 1993; Schermer, 2015). Either through the true lack of effects or due to inadequate research designs, evidence for strong mood enhancing effects of such substances in healthy individuals is scarce (Ilieva, 2015; Repantis et al., 2009). Without evidence for clear effects, and with the necessity for relatively long-term, daily usage before any such effects are likely to be apparent (Harmer, 2008), coupled with the possibility of unpleasant side effects further deterring usage, it seems unlikely

Roeterseilandcampus – gebouw G, the Netherlands

Corresponding author:

James W.B. Elsey, Roeterseiland Campus, Building G, 129 Nieuwe Achtergracht, Amsterdam, Postbus 15933, Noord Holland, 1001 NK, the Netherlands.

Email: j.w.b.elsey@uva.nl

that a large number of otherwise healthy individuals would seek to use these pharmaceuticals for the purpose of improving their lives. In contrast, over 30 million people in the United States are estimated to have experimented with psychedelic drugs (Krebs and Johansen, 2013a), and with new research garnering considerable attention and suggesting positive effects, it seems possible that more individuals may seek out psychedelic experiences. Use of psychedelic drugs in this way may prompt not only bioethical, but legal discussions. It is essential that such discussions proceed in a way that takes current scientific research into account.

The purpose of this review is to provide an up to date overview of current knowledge regarding psychedelic drug effects in healthy individuals, with the hope of grounding future discussion of psychedelics in the existing evidence base. I first describe the psychedelic state and present research on its neurobiological underpinnings. I then review contemporary research on the effects of psychedelic drugs in healthy individuals. This is followed by consideration of possible adverse effects. Finally, I consider some implications of such research for drug policy.

Psychedelic drugs and the psychedelic state

Psychedelics are a type of drug capable of reliably bringing about states of altered perception, thought, and feeling that are not usually experienced, besides in dreams or during religious exaltation (Jaffe, 1990), and have been used for their mind-altering properties for thousands of years (Bruhn et al., 2002; Schultes and Hofmann, 1979; Strassman, 1984). Classic psychedelics include dimethyltryptamine (DMT—found in ayahuasca), lysergic acid diethylamide (LSD), mescaline (found in peyote), and psilocybin (found in “magic mushrooms”). Psychedelic researchers have delineated three broad stages of psychedelic drug effects (Majić et al., 2015).

Firstly, shortly after drug administration, a short-term (lasting from minutes to hours) acute psychedelic state is induced. This phase is characterized by a significant alteration of conscious experience, and in some cases may result in a ‘complete mystical experience’, also known as a psychedelic peak experience (Majić et al., 2015). Complete mystical experiences include a sense of unity (e.g. merging with the universe, the sense that all things are one), ineffability (being unable to fully describe the experience in words), a deep positive mood, a sense of sacredness or awe, transcendence of time and space, and a noetic quality (a feeling of revelation or intuitive understanding) (Pahnke, 1969). Secondly, it has been reported that following the acute drug phase, a ‘psychedelic afterglow’ state may

be produced, in which the recipient of the drug may have an elevated mood and feel less burdened by previous worries (Pahnke, 1969). This phase typically subsides after approximately 2–4 weeks (Majić et al., 2015; Pahnke, 1969). Finally, as discussed in more detail below, over the long term there may be lasting psychological changes precipitated either by general drug effects or the subjective psychedelic/mystical experience itself.

Neurobiology of psychedelic drugs

Neuroscience research has recently begun to investigate the acute effects of psychedelic drugs on the human brain. Brain imaging has been performed on participants in the acute drug state for LSD (e.g. Carhart-Harris et al., 2016; Tagliazucchi et al., 2016), psilocybin (e.g. Carhart-Harris et al., 2012), and ayahuasca/DMT (e.g. Palhano-Fontes et al., 2015), enabling researchers to piece together a possible model for the effects of these substances.

Studies of the psychedelic state typically show changes in the connectivity and activity of brain regions constituting the “default mode network” (DMN), particularly regions that are usually highly active, such as the posterior cingulate cortex (PCC) and medial prefrontal cortex (mPFC) (Carhart-Harris et al., 2014; Raichle et al., 2001). The DMN is a network of brain regions that is typically engaged when the mind wanders, and is often thought to support metacognitive processes such as self-reflection, thinking about others, and thinking about one’s past and future (Carhart-Harris et al., 2014; Raichle and Snyder, 2007).

Although the connectivity of brain regions comprising the DMN appears integral to sustaining normal waking consciousness, it has also been pointed out that this may come at the price of restricting other possible brain states and thus limiting conscious experience (Carhart-Harris et al., 2014). Indeed, while the integrity of communication between brain regions within this network appears to be decreased by psychedelic drugs, there are also increases in connectivity between what are usually more independently functioning brain networks, and these connectivity changes are correlated with the altered state of consciousness under the influence of psychedelics (Tagliazucchi et al., 2016). Hence, it seems that in the acute drug phase, psychedelics disrupt normal or even entrenched patterns of brain activity that characterize waking experience, enabling a greater range of activity patterns to surface (Tagliazucchi et al., 2014). This may explain the unusual insights and perspectives that frequently become available under the influence of psychedelics. In support of this possibility, Lebedev et al. (2016) found that reduced organization of brain activity during the acute drug phase predicted later increases in the

personality dimension of openness, a dimension that includes facets such as intellectual curiosity and creativity. Higher magnetoencephalography signal diversity in spontaneous brain activity was also observed in participants experiencing altered states of consciousness after taking LSD, psilocybin, or ketamine, and preliminary evidence was found suggesting that these signal diversity measures were related to the intensity of the psychedelic state (Schartner et al., 2017).

Brain regions that appear most affected by the administration of psychedelics in humans overlap with sites that have a high density of serotonin 2A (5-HT_{2A}) receptors (Carhart-Harris et al., 2012; Tagliazucchi et al., 2016), corroborating animal and human research indicating that psychedelic drugs act primarily through agonistic activity at 5-HT_{2A} receptors (Glennon et al., 1984; see Nichols, 2004; Vollenweider and Kometer, 2010 for reviews). Recent research in humans provided concrete evidence for the role of 5-HT_{2A} receptors in the altered state of consciousness brought about by psychedelics: ketanserin—a 5-HT_{2A} receptor *antagonist*—completely blocked the subjective effects of LSD (Kraehenmann et al., 2017; Preller et al., 2017).

Such agonistic effects may underpin not only the acute drug state, but also longer-term changes as a result of psychedelic usage. For example, it has been found (in rodents) that repeated administration of LSD lead to the reduced expression of 5-HT_{2A} receptors, particularly in prefrontal cortical areas (Buckholtz et al., 1990). These receptors are overexpressed in the brains of humans with depression (Meyer et al., 2003), are linked to stress resilience in healthy individuals (Frokjaer et al., 2008), and are also targets of antidepressant drugs (Yamauchi et al., 2006). Hence, changes to 5-HT_{2A} receptor sites, particularly in prefrontal cortical regions involved in the regulation of emotion, could be partly responsible for long-term outcomes as a result of psychedelic use.

Effects of psychedelic drugs in healthy individuals

Though the neurobiological effects of psychedelic drugs are only recently being elucidated, interest in the psychological impact of psychedelic states has been of interest to psychologists for several decades. Early and contemporary researchers of psychedelics emphasized the therapeutic potential of psychedelic drugs in a range of disorders, ranging from depression and anxiety disorders to alcoholism and other addictions (Grinspoon and Bakalar, 1979; Nutt et al., 2013; Sessa, 2005). However, these drugs also induce profound mystical or spiritual experiences in healthy individuals, with potentially transformative effects. In this section, research on the impact of psychedelic drugs on healthy individuals will be considered.

In a classic study known as “The Good Friday experiment”, Pahnke (1963) administered psilocybin or nicotinic acid (an active placebo) to 20 students at a theological seminary in order to assess whether the drug might facilitate mystical experiences. Participants then attended the local Good Friday Mass. The majority of participants in this study found the experience very profound. A follow-up conducted between 24 and 27 years after the original study revealed that most of those who received psilocybin felt a continued benefit from their participation, with a deepened appreciation of life and nature, as well as enhanced joy and appreciation for unusual experiences and emotions (Doblin, 1991). Likewise, in a study of LSD assisted psychotherapy, Savage et al. (1966) reported data on a subset of psychiatrically healthy individuals who had complained of a lack of purpose or meaning in their lives. Following a supervised intake of LSD, the participants scored higher on self-report measures of self-actualization and creativity. As a whole, the participants in this study reported feeling a greater sense of meaning and purpose in their lives, oneness with humanity, and decreased valuation of superficial pursuits such as material gains and social status. They also reported an increase in confidence and assertiveness, with many of these changes still apparent months later.

More recent studies have largely corroborated these findings. For example, Griffiths et al. (2006) gave healthy volunteers a dose of psilocybin and supervised them during an 8-hour period in a comfortable environment. The majority of participants were found to have a “complete mystical experience”, including a sense of unity, transcendence of time and space, and positive mood. Strikingly, even at a 14-month follow-up, 58% of participants said the experience was among the five most personally significant in their lives, 67% said that it was one of the most spiritually meaningful in their lives, and 64% noted an increased sense of wellbeing and life satisfaction (Griffiths et al., 2008). Similarly, MacLean et al. (2011) determined a likely effective dose of psilocybin for reliably producing a mystical experience in an independent sample of healthy participants. These participants likewise reported increases in wellbeing and satisfaction, as well as moderate positive changes regarding behaviors in relationships and caring for themselves.

Schmid et al. (2015, and Liechti et al., 2017; see also Liechti, 2017, for a review of clinical research on LSD) assessed the acute effects of LSD in healthy subjects, and similarly found significant increases in relevant psychological states, such as a sense of oneness, disembodiment, and an increased sense of personal wellbeing and trust. Psychedelic and mystical experiences were more likely when 200 µg, rather than 100 µg, of LSD was used. Schmid et al. (2015) supplemented their

assessment of subjective effects with a range of autonomic (e.g. heart rate) and endocrine (e.g. plasma cortisol and oxytocin) measurements. Such additional physiological measures may prove informative if used more widely, potentially helping map how neural changes translate to physiological effects and subjective experiences (though it may be noted that excessive or intrusive measurement may negatively affect the “setting”, perhaps reducing positive outcomes under the influence of psychedelics).

Taking LSD in combination with listening to music may lead to particularly emotive experiences. It has long been argued that both the set (characteristics of the person taking the drug) and setting (characteristics of the environment) are strong determinants of the quality of a psychedelic experience (Pahnke, 1969). Providing an appropriate environment in which to catalyze positive and meaningful experiences can optimize the beneficial effects of psychedelics. Music may be one such environmental factor, and has been used consistently in psychedelic psychotherapy and in ritual contexts over the long history of human psychedelic usage (Kaelen et al., 2015; Nettl, 1956). In a recent study, Kaelen et al. (2015) found that feelings such as wonder, transcendence, power, and tenderness in response to music were increased under the influence of LSD, relative to placebo. The authors suggest that, given the relation of these emotions to crucial components of the psychedelic peak experience, the appropriate use of music may increase the likelihood of participants reaching this state of consciousness. Such results indicate that the environment can be carefully tailored so as to maximize the chances of achieving new and positive breakthroughs.

Consistent with the description of psychedelics as enabling new insights, it has also been suggested that their use may facilitate creative pursuits (Sessa, 2008). Both artists and scientists have reported inspiration or insights as a result of psychedelic experiences (Narby, 2002; Sessa, 2008). de Rios and Janiger (2003) found that drawings produced by visual artists after LSD sessions showed changes in some features, which were thought to reflect a greater freedom of expression. Harman and colleagues gave mescaline to 27 male participants with jobs that typically required creative problem solving, and assessed its impact on their creativity (Harman et al., 1966). This study was of particular interest because participants were not only assessed on a range of psychometric tests, but also worked on a real life issue they had been trying to solve. Many participants in this study came up with genuine solutions to their problems under the influence of mescaline, and reported an enduring impact on their creative process several weeks later. However, it is unclear the extent to which suggestion might also have contributed

towards such creativity, or to subjective reports of it: participants were specifically prepped to anticipate improvements in their creative output, and it is known that psychedelics can increase suggestibility (Carhart-Harris et al., 2014a). In a more recent study, participants were assessed before and two weeks after engaging in several ayahuasca sessions in a ritual setting (Frecska et al., 2012). Relative to a control group, participants who took ayahuasca displayed increased originality in a standardized test of creative thinking. Hence, both experimental studies and anecdotal reports indicate that psychedelics may enhance the creative process. Further controlled studies are certainly warranted.

Further studies using experimental tasks 2–3 hours after the peak effects of LSD administration have passed, but when participants are still under the influence of the drug, have shown that social and emotional processes are affected by psychedelics (Dolder et al., 2016; Mueller et al., 2017). Participants were impaired at recognizing fearful faces and showed a trend towards being less able to recognize sad faces, but had no changes in relation to angry or happy faces (Dolder et al., 2016). Relative to neutral faces, when viewing fearful faces, participants on LSD displayed reduced activation of the right medial frontal gyrus, as well as the left amygdala (Mueller et al., 2017), a brain region crucial for the detection of biologically relevant stimuli (Pessoa and Adolphs, 2010). Participants on LSD were also found to display greater feeling for and arousal over people pictured in emotionally provocative scenes (‘emotional empathy’), though they were impaired at actually inferring the mental state of the people seen in the pictures (‘theory of mind’ or ‘cognitive empathy’). Finally, these participants made more prosocial choices in a set of resource allocation tasks, and reported feeling greater trust, closeness, and a desire to be with others. Hence, important socioemotional stimuli may be processed and responded to differently when under the influence of psychedelics.

It can be seen that the effects of psychedelic drugs could go beyond the relatively small and inconsistent effects of pharmaceuticals such as SSRIs in healthy subjects, in that they not only produce improvements in mood, but may also give access to states of consciousness and insights of great significance, even after a single dose. In so doing, psychedelic drugs may cater to a major human need for meaning, connectedness, and purpose; needs which it may be argued are widely overlooked in Western, individualistic cultures. Several prominent psychologists have emphasized that these factors are central to human flourishing. For example, Maslow (1969) proposed that the peak of human actualization might be the recognition of a higher goal or purpose outside of oneself. Similarly, Frankl

(1946/1985) identified the search for meaning and purpose as a fundamental human drive. The capacity of the psychedelic experience to help resolve such existential concerns is a plausible contributor to the positive effects of psilocybin on mood and anxiety in patients with advanced cancer (Grob et al., 2011; Ross et al., 2016). In addition, the ability of psychedelic drugs to facilitate the creative process may further promote self-expression, and pave the way to solutions to both professional and personal challenges. In summary, current empirical findings indicate that psychedelics have the potential to significantly improve wellbeing among otherwise healthy individuals, and may also help foster novel perspectives, supporting the resolution of professional and personal challenges.

Possible adverse effects

With any intervention, one should always consider the associated risks. This may be especially important where drugs are taken for the purpose of ‘self improvement’ or ‘enhancement’ rather than treatment: where clear cut cases of treatment are concerned, a person may have exhausted all other avenues, and even sizable risks could be tolerated if it meant that they might be unburdened of severe pathology. People may have lower tolerance for risk when pursuing an intervention for non-therapeutic purposes. With regards to psychedelics, Griffiths et al. (2008) summarize possible risks that have been raised by other commentators, namely: (1) acute panic, leading to dangerous behavior under the influence of the drug, (2) the manifestation or exacerbation of psychiatric conditions, (3) enduring perceptual disturbances, and (4) the development of an abusive pattern of drug use. Each of these issues is discussed below.

Regarding the induction of panic and the exacerbation of psychiatric issues, it is notable, even paradoxical (Carhart-Harris et al., 2016), that the same psychedelic drugs that are being considered for the purposes of therapy and enhancement are also being utilized for their propensity to model psychotic episodes. Acute effects of psychedelic drugs can be aversive, with paranoia and the fear of going insane noted by some who take them (Hofmann and Ott, 2013). A sizable minority of participants in Griffiths and colleagues’ LSD studies noted feelings of panic while on the drug, though these feelings typically dissipated over the session, and had no lasting impact. In reviewing controlled studies of ayahuasca, dos Santos et al. (2016) also noted that participants can experience unpleasant states in the acute phase after drug intake, but emphasize that in no such studies were any lasting psychotic or otherwise highly negative outcomes observed. Other researchers likewise noted transient

increases in anxiety in participants under the influence of LSD (Carhart-Harris et al., 2016; Schmid et al., 2015). However, these participants experienced significantly greater increases in feeling a blissful state. In the aforementioned studies, negative emotions were arguably balanced or even outweighed by feelings of awe and other positive emotions, as well as longer-term improvements in wellbeing. These findings are in line with a pooled analysis of 110 healthy experimental participants who had received psilocybin (Studerus et al., 2011): strong feelings of dysphoria or panic were only observed when the highest doses were given in a small number of participants, and the psychedelic experience was mostly deemed to have been pleasurable and enriching.

Carhart-Harris et al. (2016) have suggested that some of the potentially aversive aspects of the psychedelic experience, such as thought disorganization and ego dissolution, may directly relate to later positive changes. For example, they observed a positive trend level association between thought disorganization in the acute drug state and later increases in openness. Such unusual states of consciousness could be the subjective reflection of the disordered patterns of brain activity described earlier, which are similarly predictive of later personality changes (Lebedev et al., 2016). Whatever the case, controlled studies have not found evidence for dangerous behavior under the influence of psychedelics, or of psychological damage.

While it appears that claims of common and severe negative effects of psychedelic drugs have been exaggerated (Strassman, 1984), some reports of negative effects should not be dismissed. Two subjects in Pahnke’s original ‘Good Friday’ experiment found the experience to be extremely unpleasant, with one even needing to receive a tranquilizer (Doblin, 1991). It is possible that being surrounded by several other psychedelic naïve users, as well as inadequate preparation, could have contributed to this negative outcome. Careful control over the setting in which the drug is taken can minimize such occurrences.

In case studies reporting adverse reactions to psychedelic drugs, it is often difficult to disentangle the direct effects of psychedelics from other drugs, or the influence of premorbid risk factors that should not necessarily deter psychologically healthy individuals. For example, dos Santos and Strassman (2011) describe a young man who experienced psychotic episodes on two separate occasions after having taken ayahuasca, one of which included causing superficial harm to himself. This man had no personal or family history of psychoticism. Yet, he had also been a daily user of cannabis for six years and often took cannabis in combination with ayahuasca. In addition, he had already been taking ayahuasca on a regular basis for two years

without adverse effects. Boulos et al. (2015) report a case of a 15-year-old male who made a near lethal suicide attempt shortly after having taken a synthetic psychedelic. Though he reported no prior suicidal ideation, this individual had a family history of schizophrenia and reported alcohol abuse and regular cannabis intake. In cases such as these, it can be difficult to disentangle clear psychedelic effects from drug interactions, interactions with predisposing factors, or even chance events. While such instances should not be ignored, weight should be given to controlled or at least larger scale studies of adverse effects, from which firmer conclusions can be drawn than from individual cases.

As reported in dos Santos et al.'s (2016) systematic review of ayahuasca research, beyond a few exceptional case studies, there is little evidence for serious adverse effects in relation to the use of ayahuasca, at least in ritual contexts. Gable (2007) reports psychotic incidents in relation to ayahuasca use of between approximately 0.05–0.1% over a five-year period (corresponding to an estimated 25,000 ayahuasca sessions) in the *União do Vegetal (UDV)* religious group. Lima and Tófoli (2011) also used data from a *UDV* context, and reported 29 cases with psychotic features from 1994 to 2007 (a time period corresponding to an estimated 1.56 million ayahuasca doses), of which just 19 actually appeared to have ayahuasca as a clear precipitating factor. Many of these cases were suggested to have premorbid characteristics linked with psychoticism. Regarding psychedelic use more generally, it is calculated that, in 2010, there were 32 million individuals in the US who had used a psychedelic substance at least once (Krebs and Johansen, 2013a). Consistent with the low risk of mental health problems associated with ayahuasca, independent population studies in the United States have found no evidence for a link between psychedelic use and mental health problems or suicidality (Johansen and Krebs, 2015; Krebs and Johansen, 2013b). In fact, one recent population study found that, when independent risk factors were controlled, use of psychedelics was actually associated with lower psychological distress and suicidality (Hendricks et al., 2015).

In addition to a lack of negative acute or enduring mental health effects, no evidence has been found to support the idea that the use of psychedelics leads to any kind of enduring perceptual disturbances, known as 'hallucinogen persisting perceptual disorder' (HPPD) (Krebs and Johansen, 2013b). Despite the high level of vivid mental imagery brought about under the influence of psilocybin, Studerus et al. (2011) found no evidence for enduring visual hallucinations or flashbacks in their pooled analysis of experimental psilocybin recipients. Large-scale population studies have also failed to provide any evidence of HPPD in relation to psychedelic use (Johansen and Krebs, 2015; Krebs and

Johansen, 2013b). This is true even in ritual users, who typically have much greater exposure than participants in experimental studies (dos Santos et al., 2016; Halpern et al., 2005).

Even if a drug had no direct negative physical or mental health effects, dependence and compulsive use could lead to a range of problems, such as financial difficulties, legal trouble, or simply opportunity cost in pursuing the drug. However, the current scientific consensus is that classic psychedelic drugs do not have addictive properties (Bonson, 2012; Nutt et al., 2007). In fact, psychedelic drugs are being investigated as a potential means of treating addiction (Halpern, 1996; Sessa and Johnson, 2015). It is possible that their disorganizing effects on the brain and cognition might help dismantle the well-worn neural pathways supporting drug dependence, just as they facilitate moves away from entrenched patterns of thought and behavior.

Long-term, frequent use of psychedelics might be linked to brain and personality changes. For example, Bouso et al. (2015) found that members of the Santo Daime church in Spain, who use the psychedelic ayahuasca on a roughly fortnightly basis as part of religious rituals, displayed lower cortical thickness in the PCC (the area identified as a major hub in the DMN that is affected by psychedelic drugs) relative to matched controls, and this cortical thickness was associated with levels of spirituality. These brain differences are not necessarily negative, however. The ayahuasca users in Bouso et al. (2015) actually outperformed non-users on a range of neuropsychological tests, possibly suggesting cognitive- as well as affective-enhancing capabilities of such drugs. However, as a cross-sectional study, it remains to be seen whether the observed differences between subjects reflect a predisposing factor to, or a consequence of, psychedelic use.

In summary, scientific research suggests that, when administered at appropriate doses under supervised conditions, psychedelic drugs have a very good safety profile. An overall positive experience and long-term beneficial effects typically balance acute aversive reactions. Evidence does not support a link between psychedelic use and mental health problems, and may even indicate protective effects. Moreover, use of psychedelic drugs does not lead to drug dependency. Risk factors for negative effects should certainly be investigated, and it is recognized that those with some premorbid characteristics, such as psychotic or manic/bipolar disorders might be particularly at risk (dos Santos et al., 2016). It should also be stressed that psychedelic drugs can be dangerous if used at improper dosages, in combination with other drugs, or in an unsafe environment, and that the purity of illicitly acquired drugs is rarely certain and could cause other complications. Yet, given the lack of evidence for dangers posed by psychedelics, Johansen

and Krebs (2015) summarize their view by stating that the prohibition of psychedelic drugs seems partly the result of “media sensationalization, lack of information, and cultural biases” (p. 8), and that prohibition is difficult to justify as a public health measure.

Drug policy and psychedelic use in the healthy population

In several cases in different countries, exemptions have been made for the use of psychedelics as part of religious practices. While precise exemptions differ by state, use of peyote by the Native American Church is legal in the United States. Other uses of psychedelics have become more of a global issue for lawmakers. Religious groups such as the Santo Daime and União de Vegetal, which frequently incorporate ayahuasca into their spiritual practices, have expanded outside of their native country of Brazil, prompting assessments of the rights of individuals to use psychedelic drugs in religious contexts even in countries where there is no longstanding tradition of use (Labate and Feeney, 2012). When considering the use of ayahuasca in religious ceremonies, the United States Supreme Court has ruled that drug laws may be trumped by freedom to practice religion, in accordance with the Religious Freedom Restoration Act of 1993 (Tupper, 2008). The Netherlands has also granted the right to use ayahuasca in religious and spiritual ceremonies to the Santo Daime, owing to insufficient evidence that the brew causes any harm (Adelaars, 2001). However, other countries have not always granted freedom of use. The fact that ayahuasca contains DMT was enough to suggest a public health risk that was deemed to outweigh religious freedom in Germany (Labate and Feeney, 2012; Rohde and Sander, 2011).

Exemptions for religious purposes raise questions regarding appropriate definitions of religion, and there have been concerns over whether religious pretensions might merely be used to cloak the otherwise illegal consumption of psychedelic substances (Sandberg, 2011). More libertarian commentators, however, have argued that such considerations may be beside the point. Religious and therapeutic exemptions are seen to perpetuate the notion that the state has a right to determine appropriate uses of substances even when no evidence can be furnished that their use impinges on the rights or wellbeing of individuals in wider society (Walsh, 2016). Walsh (2016) proposes that, instead of pursuing specific exemptions for psychedelic drugs in religious and therapeutic contexts, a broader exemption can be made for the use of psychedelics on the grounds of cognitive liberty. Prohibitions on psychedelic drugs may be seen to amount to prohibitions on the right to control one’s own mind and conscious experience,

precluding access to volitionally chosen but otherwise inaccessible drug states (Boire, 2001; Roberts, 1997). Given that considerations of religious legitimacy typically make distinctions between ‘merely’ philosophical perspectives and religious views, even securing the right to consume psychedelics in religious practices means that the potentially life enhancing experiences and insights that might be gained through their use is essentially off limits (without risk of legal repercussions) to those who do not hold mystical beliefs. Walsh (2010) notes that article 9 of the European Convention on Human Rights enshrines not only the right to religious freedom, but also freedom of thought. If freedom of thought is to mean anything, it is argued, it must surely incorporate freedom to direct one’s own mental states to the extent that this is possible (Boire, 2001; Roberts, 1997; Walsh, 2016).

The use of psychedelic drugs only for the purpose of treatment has also been a subject of debate. The distinction between treatment and enhancement, or between therapeutic and recreational uses, is not immediately clear. Making a binary distinction between treatment, which would be argued to be the remediation of some specific pathology, and enhancement—the improvement of a function or capacity deemed normal—begs several questions. Firstly, a clear definition of pathology would be needed to justify an intervention. This is particularly troublesome where mental health is concerned, because pathology is most frequently inferred based on the presence of symptoms that are not specific to any one disorder, which are present to varying degrees in the general population, and for which the underlying causes (i.e. pathology) are largely unknown. Secondly, it assumes that normality is synonymous with good health and wellbeing, and that this is merely the lack of (ill-defined) disease constructs. To the contrary, many authors argue that conceptions of health and wellbeing ought to encompass not only the absence of clear pathology, but also the potential of humans to develop and realize their full potential (Labate and Cavnar, 2013; Walsh, 2016). Current research on the use of psychedelics suggests that these drugs may allow otherwise healthy individuals to improve themselves and increase their wellbeing, with no apparent cost—and possibly benefits—to those around them.

A distinction between the use of psychedelics for clear cases of treatment versus enhancement may still make sense in healthcare settings, where service providers must make judgments as to the most pressing cases, and where public funds may be used to support interventions. It seems reasonable to suggest that treatments for severe mental health problems should be prioritized over less pressing desires for improvements in wellbeing in healthcare settings. From a legal

perspective, however, the nebulous boundary between treatment and enhancement, and indeed between religious and personal discovery or spiritual uses, raises problems for the clarity of law. For example, is a person who has used a psychedelic to try and gain insight into their non-clinical levels of anxiety considered to be self-medicating, or enhancing their self? Is this use to be considered wrong purely by virtue of being outside of a healthcare setting and therefore illegal? Moreover, the distinction between treatment and enhancement does not track any meaningful change in the cost to society that the law is aimed at protecting, nor benefits that might be gleaned by the individuals that make up society.

Unfortunately, some policy developments may be proceeding without due consideration of different drugs and their effects. The recent enactment of the Psychoactive Substances Act in May 2016 in the UK, which aims to prohibit psychoactive substances, not only ignores consideration of benefits people might derive from a psychoactive substance, but even sidesteps the need to demonstrate potential for harm. It is notable that this act seems to have been made to curb the proliferation of ‘new psychoactive substances’ (NPSs), also known as ‘legal highs’, whose presence in the market is the direct result of bans on existing psychoactive substances that are known to pose little danger, notably typical psychedelics LSD and magic mushrooms (DMT) (Gross, 2013). If a rational drug policy were pursued regarding existing psychoactive substances, then there would be less impetus for the development of new ones, the risk profiles and purity of which are unknown. Despite evidence indicating that psychedelic drugs pose little threat to the individual user or cost to society and may have substantial benefits, LSD, DMT, and psilocybin remain among the most strictly prohibited substances in the UK, USA, and elsewhere (Nutt et al., 2007).

Of course, it may be argued that regardless of actual drug laws, psychedelics are relatively easy to procure illegally. Nevertheless, risk to those consuming psychedelics obtained illegally is likely to be higher than where use is legalized. For example, beyond potential legal ramifications, there are no checks on the purity of illicitly obtained drugs. Furthermore, ‘copycat’ substances are sometimes produced to avoid trouble with the law, and the risk profile of these may differ markedly from known psychedelics. Beyond personal use of psychedelics in healthy subjects, current drug laws stifle the use of psychedelics for research purposes in healthy individuals. Very few research labs currently have permission to investigate psychedelics, and permissions typically impose standards that are very difficult and costly to meet (Nutt et al., 2013). Research in healthy subjects will prove highly informative in understanding

the nature of the psychedelic state and drug mechanisms, which may ultimately help in understanding how these drugs can best be utilized therapeutically.

Several suggestions have been made regarding how policy regarding psychedelics might be made more reasonable. Nutt et al. (2007) have strongly urged that drug classification should correspond to what empirical investigation actually shows to be the relative harms of different drugs. Classification also tends to consider possible benefits of usage for medical purposes. As we have discussed above, there are significant benefits that might be gained from the use of psychedelics outside of strictly medical settings, and these might also be considered when rating drugs. Some public health experts have suggested other ways that a more reasonable stance towards psychedelics might be taken, based on models of treatment administration or use in religious contexts. For example, Haden et al. (2016) have suggested that psychedelics could be administered in controlled settings to healthy individuals provided that trained individuals oversee it. Certifications advancing in their rigor and the usage of psychedelics that they allow (e.g. whether one can offer psychedelic psychotherapy, or charge for one’s services) could be earned that provide supervisors with the knowledge and skills to safely administer psychedelic drugs to healthy individuals. Production, purity, and sale of the drugs could be monitored and controlled, and tax revenue could be increased, as well as increasing safety of usage by training in set and setting. Whatever specific course of action is taken with regards to drug policy, consideration of evidence regarding risks and benefits can only improve policy.

Conclusion

Many drug researchers have urged the reclassification of psychedelic drugs so that their therapeutic potential can be fully realized (Nutt et al., 2013). From current results, it would seem that it is not only those with psychological impairments who might stand to gain from the use of psychedelics. When used appropriately, psychedelic drugs have been shown to have positive effects among healthy individuals, with single doses capable of producing lasting changes in wellbeing and purpose. A rational drug policy derived from empirical research into the potential costs and benefits of different drugs may not only facilitate the treatment of mental disorders, but the safe and enriching use of psychedelic drugs more generally.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

- Adelaars A (2001) Court case in Holland against the use of ayahuasca by the Dutch Santo Daime Church. *Journal of Clandestine Laboratory Investigating Chemists Association* 11(3): 12.
- Boire RG (2001) On cognitive liberty. *The Journal of Cognitive Liberties* 2(1): 7–22.
- Bonson KR (2012) Hallucinogenic drugs. In: *Encyclopedia of Life Sciences (eLS)*. Chichester: John Wiley & Sons Ltd.
- Boulos N, Davis MC, Hedrick R, et al. (2015) Near-lethal violent suicide attempt in a 15-year-old adolescent with no prior psychiatric history following ingestion of ‘N-Bomb’ drug. *Annals of Clinical Psychiatry* 27(3): 221–222.
- Bouso JC, Palhano-Fontes F, Rodriguez-Fornells A, et al. (2015) Long-term use of psychedelic drugs is associated with differences in brain structure and personality in humans. *European Neuropsychopharmacology* 25(4): 483–492.
- Bruhn JG, De Smet PA, El-Seedi HR, et al. (2002) Mescaline use for 5700 years. *The Lancet* 359(9320): 1866.
- Buckholtz NS, Zhou D, Freedman DX, et al. (1990) Lysergic acid diethylamide (LSD) administration selectively downregulates serotonin₂ receptors in rat brain. *Neuropsychopharmacology* 3(2): 137–148.
- Carhart-Harris RL, Erritzoe D, Williams T, et al. (2012) Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin. *Proceedings of the National Academy of Sciences* 109(6): 2138–2143.
- Carhart-Harris RL, Leech R, Hellyer PJ, et al. (2014) The entropic brain: a theory of conscious states informed by neuroimaging research with psychedelic drugs. *Frontiers in Human Neuroscience*, 8.
- Carhart-Harris RL, Kaelen M, Whalley MG, et al. (2015a) LSD enhances suggestibility in healthy volunteers. *Psychopharmacology* 232(4): 785–794.
- Carhart-Harris RL, Leech R, Hellyer PJ, et al. (2015b) The entropic brain: A theory of conscious states informed by neuroimaging research with psychedelic drugs. *Frontiers in Human Neuroscience* 8: 20.
- Carhart-Harris RL, Muthukumaraswamy S, Roseman L, et al. (2016) Neural correlates of the LSD experience revealed by multimodal neuroimaging. *Proceedings of the National Academy of Sciences* 113(17): 4853–4858.
- De Rios MD and Janiger O (2003) *LSD, Spirituality, and the Creative Process: Based on the Groundbreaking Research of Oscar Janiger, MD*. Rochester, VT: Park Street Press.
- Doblin R (1991) Pahnke’s “Good Friday experiment”: A long-term follow-up and methodological critique. *The Journal of Transpersonal Psychology* 23(1): 1–28.
- Dolder PC, Schmid Y, Müller F, et al. (2016) LSD acutely impairs fear recognition and enhances emotional empathy and sociality. *Neuropsychopharmacology* 41(11): 2638–2646.
- dos Santos RG, Balthazar FM, Bouso JC, et al. (2016) The current state of research on ayahuasca: A systematic review of human studies assessing psychiatric symptoms, neuropsychological functioning, and neuroimaging. *Journal of Psychopharmacology* 30(12): 1230–1247.
- dos Santos RG and Strassman RJ (2011) Ayahuasca and psychosis. *British Journal of Psychiatry (eLetter)*, 3 December. Available at: <http://bjp.rcpsych.org/content/190/1/81.2.e-letters#ayahuasca-and-psychosis> (accessed 9 January 2017).
- Frankl VE (1946/1985) *Man’s Search for Meaning*. New York, NY: Simon and Schuster.
- Frecska E, Móré CE, Vargha A, et al. (2012) Enhancement of creative expression and entoptic phenomena as after-effects of repeated ayahuasca ceremonies. *Journal of Psychoactive Drugs* 44(3): 191–199.
- Frokjaer VG, Mortensen EL, Nielsen F, et al. (2008) Frontolimbic serotonin 2A receptor binding in healthy subjects is associated with personality risk factors for affective disorder. *Biological Psychiatry* 63(6): 569–576.
- Gable RS (2007) Risk assessment of ritual use of oral dimethyltryptamine (DMT) and harmala alkaloids. *Addiction* 102(1): 24–34.
- Glennon RA, Titeler M and McKenney JD (1984) Evidence for 5-HT₂ involvement in the mechanism of action of hallucinogenic agents. *Life Sciences* 35(25): 2505–2511.
- Griffiths RR, Richards WA, McCann U, et al. (2006) Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. *Psychopharmacology* 187(3): 268–283.
- Griffiths RR, Richards WA, Johnson MW, et al. (2008) Mystical-type experiences occasioned by psilocybin mediate the attribution of personal meaning and spiritual significance 14 months later. *Journal of Psychopharmacology* 22(6): 621–632.
- Grinspoon L and Bakalar JB (1979) *Psychedelic Drugs Reconsidered*. New York, NY: Basic Books.
- Grob CS, Danforth AL, Chopra GS, et al. (2011) Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer. *Archives of General Psychiatry* 68(1): 71–78.
- Gross M (2013) Drugs prohibition is criminals’ gain, neuroscience’s loss. *Current Biology* 23(14): R588.
- Haden M, Emerson B and Tupper KW (2016) A public-health-based vision for the management and regulation of psychedelics. *Journal of Psychoactive Drugs* 48(4): 243–252.
- Halpern JH (1996) The use of hallucinogens in the treatment of addiction. *Addiction Research* 4(2): 177–189.
- Halpern JH, Sherwood AR, Hudson JI, et al. (2005) Psychological and cognitive effects of long-term peyote use among Native Americans. *Biological Psychiatry* 58(8): 624–631.
- Harman WW, McKim RH, Mogar RE, et al. (1966) Psychedelic agents in creative problem-solving: A pilot study. *Psychological Reports* 19(1): 211–227.
- Harmer CJ (2008) Serotonin and emotional processing: Does it help explain antidepressant drug action? *Neuropharmacology* 55(6): 1023–1028.
- Hendricks PS, Thorne CB, Clark CB, et al. (2015) Classic psychedelic use is associated with reduced psychological

- distress and suicidality in the United States adult population. *Journal of Psychopharmacology* 29(3): 280–288.
- Hofmann A and Ott J (2013) *LSD: My Problem Child*. New York, NY: McGraw-Hill.
- Ilieva I (2015) Enhancement of healthy personality through psychiatric medication: The influence of SSRIs on neuroticism and extraversion. *Neuroethics* 8(2): 127–137.
- Jaffe JH (1990) Drug addiction and drug abuse. *The Pharmacological Basis of Therapeutics* 8: 522–573.
- Johansen P and Krebs TS (2015) Psychedelics not linked to mental health problems or suicidal behavior: A population study. *Journal of Psychopharmacology* 29(3): 270–279.
- Kaelen M, Barrett FS, Roseman L, et al. (2015) LSD enhances the emotional response to music. *Psychopharmacology* 232(19): 3607–3614.
- Kraehenmann R, Pokorny D, Vollenweider L, et al. (2017) Dreamlike effects of LSD on waking imagery in humans depend on serotonin 2A receptor activation. *Psychopharmacology* 234(13): 2031–2046.
- Kramer P (1993) *Listening to Prozac: A Psychiatrist Explores Antidepressant Drugs and the Remaking of the Self*. New York: Viking.
- Krebs TS and Johansen P (2013a) Over 30 million psychedelic users in the United States. *F1000Research* 2: 98.
- Krebs TS and Johansen P (2013b) Psychedelics and mental health: A population study. *PloS One* 8(8): e63972.
- Labate BC and Carnar C (2013) *The Therapeutic use of Ayahuasca*. Berlin: Springer.
- Labate BC and Feeney K (2012) Ayahuasca and the process of regulation in Brazil and internationally: Implications and challenges. *International Journal of Drug Policy* 23(2): 154–161.
- Lebedev AV, Kaelen M, Lövdén M, et al. (2016) LSD-induced entropic brain activity predicts subsequent personality change. *Human Brain Mapping* 37(9): 3203–3213.
- Liechti ME (2017) Modern clinical research on LSD. *Neuropsychopharmacology*. Epub ahead of print 14 June 2017. DOI: 10.1038/npp.2017.86.
- Liechti ME, Dolder PC and Schmid Y (2017) Alterations of consciousness and mystical-type experiences after acute LSD in humans. *Psychopharmacology* 234(9–10): 1499–1510.
- Lima FAS and Tófoli LF (2011) An epidemiological surveillance system by the UDV: Mental health recommendations concerning the religious use of hoasca. In: Labate BC and Jungaberle H (eds) *The Internationalization of Ayahuasca*. Zurich: Lit Verlag, pp.185–199.
- MacLean KA, Johnson MW and Griffiths RR (2011) Mystical experiences occasioned by the hallucinogen psilocybin lead to increases in the personality domain of openness. *Journal of Psychopharmacology* 25(11): 1453–1461.
- Majić T, Schmidt TT and Gallinat J (2015) Peak experiences and the afterglow phenomenon: When and how do therapeutic effects of hallucinogens depend on psychedelic experiences? *Journal of Psychopharmacology* 29(3): 241–253.
- Maslow AH (1969) Various meanings of transcendence. *The Journal of Transpersonal Psychology* 1(1): 56–66.
- Meyer JH, McMain S, Kennedy SH, et al. (2003) Dysfunctional attitudes and 5-HT₂ receptors during depression and self-harm. *American Journal of Psychiatry* 160(1): 90–99.
- Mueller F, Lenz C, Dolder PC, et al. (2017) Acute effects of LSD on amygdala activity during processing of fearful stimuli in healthy subjects. *Translational Psychiatry* 7(4): e1084.
- Narby J (2002) Shamans and scientists. In: Grob CS (ed.) *Hallucinogens: A Reader*. New York, NY: Putnam, pp.159–163.
- Nettl B (1956) *Music in Primitive Culture*. Boston, MA: Harvard University Press.
- Nichols DE (2004) Hallucinogens. *Pharmacology & Therapeutics* 101(2): 131–181.
- Nutt D, King LA, Saulsbury W, et al. (2007) Development of a rational scale to assess the harm of drugs of potential misuse. *The Lancet* 369(9566): 1047–1053.
- Nutt D, King LA and Nichols DE (2013) Effects of Schedule I drug laws on neuroscience research and treatment innovation. *Nature Reviews Neuroscience* 14(8): 577–585.
- Pahnke WN (1963) *Drugs and mysticism: An analysis of the relationship between psychedelic drugs and the mystical consciousness: A thesis*. PhD Thesis, Harvard University.
- Pahnke WN (1969) The psychedelic mystical experience in the human encounter with death. *Harvard Theological Review* 62(1): 1–21.
- Palhano-Fontes F, Andrade KC, Tofoli LF, et al. (2015) The psychedelic state induced by ayahuasca modulates the activity and connectivity of the default mode network. *PLoS One* 10(2): e0118143.
- Pessoa L and Adolphs R (2010) Emotion processing and the amygdala: From a ‘low road’ to ‘many roads’ of evaluating biological significance. *Nature Reviews Neuroscience* 11(11): 773–783.
- Preller KH, Herdener M, Pokorny T, et al. (2017) The fabric of meaning and subjective effects in LSD-induced states depend on serotonin 2A receptor activation. *Current Biology* 27(3): 451–457.
- Raichle ME, MacLeod AM, Snyder AZ, et al. (2001) A default mode of brain function. *Proceedings of the National Academy of Sciences* 98(2): 676–682.
- Raichle ME and Snyder AZ (2007) A default mode of brain function: A brief history of an evolving idea. *NeuroImage* 37(4): 1083–1090.
- Repant D, Schlattmann P, Laisney O, et al. (2009) Antidepressants for neuroenhancement in healthy individuals: A systematic review. *Poiesis & Praxis* 6(3–4): 139–174.
- Roberts TB (1997) Academic and religious freedom in the study of the mind. In: Forte R (ed.) *Entheogens and the Future of Religion*. San Francisco, CA: Council on Spiritual Practices.
- Rohde SA and Sander H (2011) The development of the legal situation of Santo Daime in Germany. In: Labate BC and Jungaberle H (eds) *The Internationalization of Ayahuasca*. Münster: LIT Verlag, pp.339–352.
- Ross S, Bossis A, Guss J, et al. (2016) Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: A randomized controlled trial. *Journal of Psychopharmacology* 30(12): 1165–1180.

- Sandberg R (2011) *Judging Religious Drug use: The Misuse of the Definition of "Religion"*. In: Labate BC and Jungaberle H (eds) *The Internationalization of Ayahuasca*. Zurich, Switzerland: Lit Verlag, pp.389–401.
- Savage C, Fadiman J, Mogar R, et al. (1966) The effects of psychedelic (LSD) therapy on values, personality, and behavior. *International Journal of Neuropsychiatry* 2(3): 241–254.
- Schartner MM, Carhart-Harris RL, Barrett AB, et al. (2017) Increased spontaneous MEG signal diversity for psychoactive doses of ketamine, LSD and psilocybin. *Scientific Reports* 7: 46421.
- Schermer M (2015) Ethics of pharmacological mood enhancement. In: Clausen J and Levy N (eds) *Handbook of Neuroethics*. Dordrecht: Springer, pp.1177–1190.
- Schmid Y, Enzler F, Gasser P, et al. (2015) Acute effects of lysergic acid diethylamide in healthy subjects. *Biological Psychiatry* 78(8): 544–553.
- Schultes RE and Hofmann A (1979) *Plants of the Gods. Their Sacred, Healing and Hallucinogenic Powers*. Rochester, VT: Healing Arts Press.
- Sessa B (2005) Can psychedelics have a role in psychiatry once again? *The British Journal of Psychiatry* 186(6): 457–458.
- Sessa B (2008) Is it time to revisit the role of psychedelic drugs in enhancing human creativity? *Journal of Psychopharmacology* 22(8): 821–827.
- Sessa B and Johnson MW (2015) Can psychedelic compounds play a part in drug dependence therapy? *The British Journal of Psychiatry* 206(1): 1–3.
- Strassman RJ (1984) Adverse reactions to psychedelic drugs: A review of the literature. *The Journal of Nervous and Mental Disease* 172(10): 577–595.
- Studerus E, Komater M, Hasler F, et al. (2011) Acute, sub-acute and long-term subjective effects of psilocybin in healthy humans: A pooled analysis of experimental studies. *Journal of Psychopharmacology* 25(11): 1434–1452.
- Tagliazucchi E, Carhart-Harris R, Leech R, et al. (2014) Enhanced repertoire of brain dynamical states during the psychedelic experience. *Human Brain Mapping* 35(11): 5442–5456.
- Tagliazucchi E, Roseman L, Kaelen M, et al. (2016) Increased global functional connectivity correlates with LSD-induced ego dissolution. *Current Biology* 26(8): 1043–1050.
- Tupper KW (2008) The globalization of ayahuasca: Harm reduction or benefit maximization? *International Journal of Drug Policy* 19(4): 297–303.
- Vollenweider FX and Komater M (2010) The neurobiology of psychedelic drugs: Implications for the treatment of mood disorders. *Nature Reviews Neuroscience* 11(9): 642–651.
- Walsh C (2010) Drugs and human rights: private palliatives, sacramental freedoms and cognitive liberty. *The International Journal of Human Rights* 14(3): 425–441.
- Walsh C (2016) Psychedelics and cognitive liberty: Reimagining drug policy through the prism of human rights. *International Journal of Drug Policy* 29: 80–87.
- Yamauchi M, Miyara T, Matsushima T, et al. (2006) Desensitization of 5-HT 2A receptor function by chronic administration of selective serotonin reuptake inhibitors. *Brain Research* 1067(1): 164–169.