Psychedelic-assisted therapy for anxiety and depression in the face of death: A critical review with an anthropological lens

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Psychedelics have been investigated for their therapeutic applications in end-of-life care as early as 1960. Recently, there have been four main groups conducting clinical trials for either lysergic acid diethylamide or psilocybin for the treatment of anxiety and depression in patients with terminal illnesses. The recent trials have higher methodological quality and demonstrate the profound impact of psychedelics for this particular patient presentation. However, a number of gaps, including understanding the meaning of death and dying in Western society; the nature of the psychedelic experience and how this lends itself to assisting those who are facing death; and how suffering and psychological distress are defined and understood in current psychiatric and medical frameworks. This article provides a critical evaluation of the recent publications and suggests how anthropology may contribute knowledge to this emerging field.

Keywords: psychedelics, anthropology, LSD, psilocybin, death and dying

INTRODUCTION

Hallucinogens, primarily lysergic acid diethylamide (LSD) and psilocybin, have been used for the treatment of anxiety and mood disturbance associated with terminal illnesses since as early as 1960, with four clinical trials occurring in recent years (Reiche et al., 2018). A systematic review of these clinical trials revealed 11 studies – 7 involving LSD, 3 using psilocybin, and 1 investigating the use of dipropyltryptamine (Reiche et al., 2018). The majority of psychedelic studies was conducted in the 1960s and 1970s, and showed a great deal of promise for psychedelics as therapeutic agents (Dutta, 2012; Gasser, Kirchener, & Passie, 2014; Reiche et al., 2018). Recently, there have been four main groups investigating the therapeutic application of LSD or psilocybin for patients with terminal illnesses at varying stages (Gasser, Kirchener, et al., 2014; Griffiths et al., 2016; Grob et al., 2011; Ross et al., 2016). This paper explores the recent trials into psychedelics for death-related anxiety and depression, in the context of current medical and psychiatric ideology. In this arena, the field of anthropology can elucidate the cultural meanings behind death and dying and methodologies that may uncover the human and experiential aspects of the psychedelic experience.

REVIEW OF LITERATURE

The recent clinical trials conducted by Grob et al. (2011), Gasser, Kirchener, et al. (2014), Griffiths et al. (2016), Ross et al. (2016), and their respective colleagues explore the use of LSD or psilocybin for the treatment of depression, anxiety, or adjustment disorders in individuals with terminal

illnesses. These studies contain higher methodological quality, more stringent assessment procedures, and higher reported safety compared to the studies of the 1960s and 1970s (Reiche et al., 2018). Early studies suggested the effectiveness of hallucinogens in treating distress in cancer patients; however, they contained no control or comparison conditions to demonstrate that the effects were any better than placebo (e.g., Grof et al., 1963; Kast, 1967; and Richards et al., 1977 – cited in Griffiths et al., 2016). It is well established that set (participant characteristics) and setting (environmental factors) lead to great variability in psychedelic experiences. It is therefore worthwhile evaluating the procedures and processes involved in the recent trials. The following section will outline the processes undertaken in the recent psychedelic studies into anxiety and depression associated with life-threatening illnesses, conducted since 2011.

Recent studies used either LSD or psilocybin, compared with either a very low dose of the active substance (e.g., Griffiths et al., 2016) or a placebo with mild physiological effects such as niacin (e.g., Grob et al., 2011). Data assessments were carried out at several time points, including well in advance of the first dose; immediately post-treatment sessions; and again days, weeks, and even several months following treatment sessions. Follow-up interviews were conducted up to 12 months following participation in LSD psychotherapy (Gasser, Kirchner, et al., 2014). Patients also took part in an extensive battery of psychometric measures for a range of constructs, including mood states, depression,

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state anxiety, trait anxiety, altered states of consciousness, psychiatric ratings, mystical experience, quality of life, and existential distress (Griffiths et al., 2016; Grob et al., 2011; Ross et al., 2016). Patients participating in the recent clinical trials were diagnosed with either cancer or other lifethreatening diseases at various stages, and also met the diagnostic criteria for a mood, anxiety, or adjustment disorder (Gasser, Holstein, et al., 2014; Griffiths et al., 2016; Grob et al., 2011; Ross et al., 2016). All participants also met the diagnostic criteria for a mood, anxiety, or adjustment disorder. The majority of participants was white, college-educated, had no prior hallucinogen use (or had not used hallucinogens for more than 30 years).

The results demonstrated long-lasting anti-depressant and anxiolytic benefit from 1 to 2 administrations of either LSD or psilocybin (Reiche et al., 2018). There were no serious adverse effects reported, and only some reports of minor short-term undesirable experiences (e.g., headaches, nausea and vomiting, transient psychological distress, discomfort, and heightened anxiety at some points; Griffiths et al., 2016). No studies reported any indications of severe anxiety reactions or a "bad trip." In fact, many of the research subjects recommended that future protocols should provide the opportunity for additional psychedelic sessions, and found the placebo sessions to be relatively unappealing (Grob et al., 2011) – it appeared that the most negative part of the study was not tripping enough. The anti-depressant response rate for psilocybin was around 80% at 6 months post follow-up (Griffiths et al., 2016; Ross et al., 2016). The clinical response for anxiety was equally as high. To put this into perspective, there are no other known pharmacological agents that can lead to immediate anti-depressant and anti-anxiolytic effects, with enduring benefits, after a single administration (Ross et al., 2016). A meta-analysis of commonly prescribed anti-depressant medication for comorbid depression and medical conditions found that for cancer patients, the anti-depressants performed only as well as the 40% placebo response (Ross et al., 2016). Themes emerging from the participants' reports of their psychedelic experiences included "examining how their illness had impacted their lives, relationships with family and close friends, and a sense of ontological security... [they] reported powerful empathic cathexis to close friends and family members and examined how they wished to address their limited life expectancy" (Griffiths et al., 2016, p. 17).

CRITIQUE OF PROCEDURES AND **INTERPRETATIONS**

Traditionally, physicians have neglected the spiritual aspect of dying, and spirituality is still largely ignored in Western medicine; meanwhile, at the end of their life, individuals frequently engage in journey inward to search for the meaning of life, death, and human existence (Rosseau, 2000). Similarly, in the recent studies into anxiety and depression in the face of death, measures of existential distress, quality of life, mystical experiences, spiritual, and even behavioral benefits were relegated to "secondary outcome measures" (Grob et al., 2011). The protocols used herein, namely the reliance on data and relegation of spiritual/mystical impacts to "secondary," are in line with the Western predisposition toward physicalist monism, dualism, and objectivity (Blainey, 2010). The following section will provide a critique of the present research in the context of dominant Western definitions of psychological suffering, the medicalization of normal experience, and the political and social fears surrounding altered states of consciousness.

The research presented herein reflects the historical, economic, scientific, and ideological meanings surrounding mental disorders (Wilson, 1993). From the 1950s to the 1970s, the biopsychosocial model was the guiding principal in Western psychiatry – underpinned by psychoanalysis, sociology, and biological knowledge (Wilson). Psychedelic research was contemporaneously explored for its utility in treating a wide range of psychological issues, and transpersonal states of consciousness were understood to catalyze the therapeutic response (Dutta, 2012; Griffiths, Richards, McCann, & Jesse, 2006). Psychedelic research was promising in its early stages and was arguably let down by a lack of scientific rigor and somewhat indiscriminate use leading to increased likelihood of adverse effects (Griffiths, Richards, Johnson, McCann, & Jesse, 2008). Political concerns around the use of psychedelics and altered states of consciousness also contributed to the demonizing and ultimate prohibition of this research. Around this time, the biopsychosocial model was under scrutiny by prominent psychiatrists for its inability to divide the mentally well from the mentally ill, a reported threat to the legitimacy of psychiatry (Wilson). The subsequent publication of the DSM-III in 1980 represented a paradigm shift to a research-based medical motel, and this descriptive model has since persisted in psychiatry (Wilson). Despite the emphasis on research, evidence, and data, which had positive scientific and economic consequences for Western psychiatry (Wilson); reliability ratings for diagnostic categories in the current version of the DSM are surprisingly low (Parry, 2018). The ideological understandings of mental health have significantly narrowed in focus (Wilson), criteria for mental illness are largely based on social norms, and there is an overmedicalization of natural and normal responses to experiences (Parry, 2018). The narrowed focus of Western psychiatry can be seen in three domains: (a) the loss of the concept of the depth of mind or unconscious; (b) the limitation of the dimension of time (relative downplaying of personal history); and (c) the constriction of what is clinically relevant to a cluster of symptoms, blind to personality, character, family dynamics, and social context (Wilson, 1993).

The Western dominance of objectivity, reductionism, and empirical sciences largely misses the subjective aspect of experience (Blainey, 2010). This reductionism of experience relates to a number of realms, including consciousness, mental well-being, and judgments of substance use, and could be perceived as a barrier to the exploration of existence and finding meaning in death and dying. For example, Blainey (2010, p. 125) argues that "the only sanctioned psychoactive substances are coffee, nicotine, alcohol and painkillers (aimed at lessening both physical and mental discomfort without prompting deep existential reflection)". Discourse surrounding altered states of consciousness is placed in opposition to words such as "normal, accurate,

real, true, objective," suggesting that any experience in altered states must be "unreal, abnormal, false, erroneous" (Horvath, Szummer, & Szabo, 2017). The mind-body dualism proposed by Descartes has persisted in medicine, relegating the spiritual realm to the church and the physical world to science (Rosseau, 2000). This leads to an overreliance on diagnostic procedures and interventions that lack empathy, where "suffering and the treatment of disease are separate from the person experiencing the suffering" (Rosseau, 2000).

The contemporary research into psychedelics for endof-life concerns is justified in a way that medicalizes and somewhat reduces the experience, and fails to take the wider sociocultural context into consideration. There is some passing mention of the spiritual qualities of psychedelics in the contemporary research (Griffiths et al., 2016); for example, Ross et al. (2016) found that more intense mystical-type experiences led to significantly greater reduction in depression and anxiety. Individuals rated their experiences as highly meaningful and spiritual, with the associated positive cognitive, affective, spiritual, and behavioral effects lasting weeks to months (Ross et al., 2016). How were such outstanding results explained by the researchers? In a return to medicalization, the neurobiological mechanisms were implicated – the serotonergic system of the brain, possibly decreased medial prefrontal cortex activity, and decreased default mode network activity (Carhart-Harris et al., 2012, 2014). Griffiths et al. (2016) argued for the need to understand the neuropsychopharmacological mechanisms of how psilocybin results in longterm alteration of cortical networks. The justification for the use of psychedelics in the treatment of death-related depression and anxiety was also somewhat lacking, with reference made to the past research of the 1950s and 1960s and no reference to the ancient cultural uses, nor how the quality of the experience lends itself to helping individuals face the ending of their lives.

A question also remains as to why there is such caution in the use of psychedelics at present, given that the results are consistently positive and beneficial. Researchers are wary of the moral panic that ensued after the first bout of psychedelic research, and make great effort to be perceived as legitimate, careful, empirical, and scientific (Dutta, 2012). There are some fears that open medical use will escalate abuse or increase recreational use of psychedelic substances. This is unlikely, considering the evidence from countries that have decriminalized non-addictive drugs and the lack of associated increases in recreational use of those drugs (e.g., the Netherlands and Portugal; Dutta, 2012). Perhaps, there is concern that psychedelic use leads to increased mental health problems? A review of the National Survey on Drug Use in the United States found that there was no significant association between psychedelic use and mental ill-health, "rather, in several cases psychedelic use was associated with a lower rate of mental health problems" (Krebs & Johansen, 2013). It has been argued that economic concerns are more relevant to the issue, considering that these drugs do not require regular use and pharmaceutical companies cannot really benefit - one to two administrations created long-term positive alterations in well-being, in contrast to the several months to years of daily dosage

required for traditional anti-depressant and anxiolytic medications (Dutta, 2012).

FUTURE DIRECTIONS

Anthropology may provide an antidote to the medical reductionism of the current psychedelic research into endof-life anxiety and depression. Spiritual suffering may present similarly to depression, experienced acutely at the end of a person's life as worthlessness, hopelessness, and meaninglessness (Rosseau, 2000). Many ancient cultures and spiritual traditions have understood the healing powers of psychedelic plants, often referred in anthropology as "entheogens," and their utility was intrinsic to many rituals including death (Dutta, 2012). Entheogenic rituals have been utilized in ancient cultures at crucial junction points in life, including puberty, onset of adulthood, marriage, mid-life, and death (Roberts, 2012). Modern Western therapeutic-shamanic communities have also formed around the use of hallucinogenic plants in hybrid communal rituals (Metzner, 2013). There are various ways in which anthropology may contribute to the present research, although specific methods for how this can occur requires an integrative, interdisciplinary approach to research design.

Anthropology has explored the use of psychoactive substances in various human cultures (Schultes, 1940). Shultes provides a discussion of the use of panaoulus, a psilocybin-containing mushroom widely used for witchcraft, and divination among the Chimatecs, Mazatecs, and Zapotecs of Southern Mexico. According to pioneering ethnographer Sahagun, these mushrooms were consumed in religious feasts and gatherings and brought on visions that were believed to constitute divine advice concerning the future (Schultes, 1940). According to Schultes, "The incoherent utterances which are made during the intoxication are interpreted as prophetic or admonitory" (p. 42). Medicinal use of the mushrooms was also reported, in treatment of rheumatism. In contrast to the Western research into the use of the same substance, the visions and phenomenological experience of participants are not regarded as highly important. Aside from one qualitative study exploring participants self-reported experiences (Gasser, Holstein, et al., 2014), most of the results of the current research have been reduced to psychometric data and neurobiological explanations. There is no evaluation of the meaning of death and dying in Western society, or the meanings and significance of altered states of consciousness, which appears to be a large gap in the present research.

Current neuroscientific and medical approaches to psychedelics for end-of-life anxiety and depression are largely reductionistic, resulting in conclusions that are often farremoved from first-person experience (Locke, 2011). This is counter to the fact that the intense experiences of facing one's own mortality and undergoing psychedelic therapy are embodied experiences that occur within a social, cultural, and historical context. The challenge for future researchers is to adopt a "non-fragmentary worldview" (Bohm, 1981, pp. xi–xiii), which integrates methodologies and theoretical perspectives from Western medical science with anthropological understandings and perhaps those of other

disciplines. For example, medical researchers could borrow from the methods in the field of the anthropology of consciousness, and incorporate a phenomenological investigation of the nature of the experience for participants (Locke, 2011). Alternatively, research could extend into the life worlds of participants, understanding their experiences of facing terminal illnesses and the systems they navigate within the medical treatment, and the dominant social and cultural meanings of death and dying that participants subscribe to. It is valuable to gain an understanding of the meaning participants assign to the psychedelic experiences (Grof, 1998; Lewis, 2008). Incorporating the methods of anthropology in the form of ethnographic enquiry (or what Geertz, 1998 referred to as "deep hanging out") and phenomenological enquiry may elicit rich knowledge that contributes to this burgeoning field.

Gallagher (2003) provides an overview of three different ways in which phenomenology may contribute to neuroscientific research: neurophenomenology, indirect phenomenology, and "front-loaded" phenomenology. Lutz (2002, cited in Gallagher, 2003, p. 89) utilizes a neurophenomenological approach, in which subjects are asked to describe their experience using an open-question format, thereby suspending preconceived beliefs or theories about experience. Clusters of descriptive categories are then correlated with objective measures of behavior and brain activity. This approach could theoretically be implemented without much alterations to the research protocols, except with the addition of applying specific phenomenological querying of the participant's psychedelic experiences. Alternatively, indirect phenomenology is incorporated in a somewhat more informal manner, by taking participants' introspective reports into consideration in analyses. This would effectively involve "testing experiential reports against all other non-experiential data, and attempting to draw a coherent picture of the subject's response" (Gallagher, 2003, p. 91). However, this raises questions regarding the scientific rigor of using introspection as a psychological research method (Gallagher). The third approach, "Front-loaded phenomenology" involves starting with the experimental design, incorporating phenomenological insights (such as Husserlian description) into initial research protocols. This would not necessarily need to include introspective reports by participants. Examples of such research involve an investigation of the neural substrates of selfhood, agency, and how individuals come to understand others (e.g., Chiao 2009, cited in Roepstorff & Frith, 2012). It is less clear how "front-loading" can contribute to the present research, and may lead to a further reductionism of experience. Overall, on face value a neurophenomenological approach is a valid consideration.

There have been a number of attempts to integrate neuroscience and anthropology in research methodology, variously called experimental anthropology, cultural neuroscience, and neuroanthropology (Roepstorff & Frith, 2012). Experimental research is increasingly complex and rigorous, and it is the control of various factors that increases the validity of results (Roepstorff & Frith, 2012). Incorporating the highly unstable variables of individuals' perceptions, life-worlds, social, and cultural understandings is problematic in this regard. One of the major lessons from anthropology has been the importance of bringing lived experience

into scientific discussion, and lived experience has been largely overlooked in the medical research into psychedelics for anxiety and depression in individuals with terminal illnesses. Perhaps future research could consider the advice of Roepstorff and Frith (2012, p. 109): "start with joint research projects, do things together, and then be sensitive to both the types of facts and the types of contexts produced."

CONCLUSIONS

Death is a natural and absolute progression of life; however, many patients endure psychospiritual suffering and anguish during the dying process (Rosseau, 2000). Rosseau (2000) highlights the need for Western medical providers of palliative care to "discard the rigid boundaries of medical care, engage in a search for meaning, and realize that they cannot always provide answers, and instead join the patient and family in the questions and mysteries that surround death" (p. 2001). In this way, "preparing for death is one of the most profoundly healing acts of a lifetime" (Levine, 1998, p. 7). The methods of anthropology that include participant observation and phenomenology may help to elucidate the meanings and experience of people undergoing psychedelic treatment for end-of-life anxiety and depression. Anthropologists can also offer the insights of ancient and modern cultural uses of psychedelics used in spiritual/mystical/ medicinal ways. These insights may further increase the efficacy, safety, and transformative power of the treatment, and lead to further improvements in quality of life for individuals facing their own death.

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