Intercultural, intermolecular: An ethnobotanical examination of the potential therapeutic value of LSD for the treatment of depression*

KARSTEN FATUR**

Biotechnical Faculty, University of Ljubljana, Ljubljana, Slovenia

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Lysergic acid diethylamide holds great therapeutic potential in the treatment of depression, although currently illegal in many parts of the world and seen as a recreational drug. An intercultural ethnobotanical examination of plant substances with similar chemical profiles and effects displays the true potential value of this substance and justifies an increased focus on clinical trials and studies involving it.

Keywords: psychedelic, LSD, ayahuasca, depression, serotonin

Despite its current status as an illegal substance, lysergic acid diethylamide (LSD) has an extensive history of being the subject of scientific investigation into its potential therapeutic benefits. Originally synthesized from ergot fungus known for infecting grains and causing hallucinations to those who consumed it, LSD was an accidental discovery in 1938 that rapidly gained attention and interest from the scientific community (Freedman, Ebin, & Wilson, 1962; Montagne, 1993). Despite its unconventional nature, a fair deal of acceptance for clinical use even existed at this time (Freedman et al., 1962). However, in the 1970s, LSD came to be associated with counter-cultural anti-war movements, which led to governments labeling the substance as illegal in order to tarnish public opinion of these groups (Dyck, 2005; Tupper, Wood, Yensen, & Johnson, 2015). This, combined with issues in sampling procedures from previous experiments, largely ended the scientific obsession with LSD (Dyck, 2005). In recent years, however, this interest has been rekindled, and clinical studies continue to be run to test the efficacy of this substance for the treatment of a wide range of medical problems (Garcia-Romeu, Kersgaard, & Addy, 2016). Although the older studies are limited by their sampling issues, the sheer volume of identical findings points toward clinical usefulness (Dyck, 2005). Of particular noteworthiness is the growing body of evidence that shows the utility of LSD in treating chronic treatment-resistant depression. Despite this, it continues to be classified as a restricted substance. Studies in this area have focused on clinical tests of the drug. What has been lacking, however, is an anthropological approach, which shows that LSD is likely to be a useful tool in the treatment of depression.

LSD is a substance within a broad category of chemical compounds known as hallucinogens. Despite the name, hallucinogens do not in fact produce hallucinations, but rather changes in perceptual processing (Winkelman, 2007). Specifically, LSD falls within the subcategory of psychedelics, along with psilocybin and N,N-dimethyltryptamine (DMT)

(Garcia-Romeu et al., 2016). Other groups include empathogens (3,4-methylenedioxy-methamphetamine), dissociative anesthetics (ketamine and dextromethorphan), and atypical hallucinogens (delirants such as atropine fall into this category, as does marijuana, among many others) (Garcia-Romeu et al., 2016). It is worth noting that the following argument focuses only on the psychedelics, as other groups of hallucinogens work through different biochemical processes (Garcia-Romeu et al., 2016).

Due to their chemical structure, psychedelics are able to bond with receptor sites for the neurotransmitter serotonin (5-HT)_{2A}, allowing neural impulses to pass to otherwise inaccessible regions of the brain (McClay, 1976; Nichols, 2004). It is worth noting that low serotonin levels have long been implicated as the main culprit in depression (Gorwood, Batel, Adès, Hamon, & Boni, 2000). The primary pharmaceutical interventions for depression involve the use of selective serotonin reuptake inhibitors that prevent serotonin from being absorbed back into the pre-synaptic cell. In forcing the serotonin to stay between cells longer, it is more likely to be able to bind with the post-synaptic cell's receptors and carry on the neural impulse. Despite widespread use, meta-analysis has shown that most results of the patients gain from these standard medications are due to placebo effects (Kirsch & Low, 2013). In addition, these drugs come with a plethora of side effects, some as severe as a significant increase in the risk of suicide. LSD, by contrast, has proven to have no severe side effects when properly administered (Gasser et al., 2014).

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** Corresponding address: Karsten Fatur; Biotechnical Faculty, University of Ljubljana, 101 Jamnikarjeva ulica, Ljubljana 1000, Slovenia; E-mail: karsten.fatur@gmail.com

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Of central importance to the anthropological argument for the use of LSD in treating depression is the chemical structure of this substance. As previously mentioned, LSD falls into a group with psilocybin and DMT. These substances are so similar in fact that they have identical biological effects, and even individuals well experienced in consuming all three are unable to tell them apart in blind trials (Halberstadt, 2015). The level of similarity is so high that tolerance built up for any one type applies to the others (Halberstadt, 2015). All can cause altered thinking patterns, change in emotional expression, varied manners of interpreting significance and meaning, and feelings of rejuvenation (Moxley, 1996). Although LSD has only been present since the mid 20th century, psilocybin and DMT have a much longer history. Psilocybin is found in “magic” mushrooms, which have histories of use by humans spanning back thousands of years (McKenna, 2004). Similarly, DMT is the active ingredient in ayahuasca brews (generally a combination of *Banisteriopsis caapi* and *Psychotria viridis*), which similarly spans back thousands of years, and today has even become a tourist attraction in South America (Dos Santos et al., 2011; Garcia-Romeu et al., 2016). As such, traditional knowledge of these substances and their uses has been refined over millennia. This traditional knowledge, however, is not enough to convince biomedicine.

There is a large body of research on ayahuasca pointing to its safety for use in humans (Garcia-Romeu et al., 2016). In addition, regular drinkers of ayahuasca have been observed to have an increase in the number of serotonin bonding sites in the brain, meaning more opportunities for serotonin to carry on a neural impulse (Callaway, Airaksinen, McKenna, Brito, & Grob, 1994). Those who take it regularly have also been observed to have an undeniable improvement in mental health condition, a finding present in all study participants (Baumeister, Barnes, Giaroli, & Tracy, 2014). Although it has also been used for spiritual reasons, its history as a medicine is extensive and it has proven to be more effective than placebo (Dos Santos et al., 2011). Healing with ayahuasca focuses on communal sessions that bring the group together and foster a sense of closeness between those present (Winkelman, 2007). Participants in these ceremonies tend to observe them silently, with a focus being given to their individual experiences and self-reflection (Winkelman, 2007). It is precisely this act of reflecting that shows another usefulness in treatments for depression, as the ayahuasca becomes a sort of therapist guiding the person who has taken it. Ayahuasca here is creating the mindset necessary for healing. These rituals are also often associated with self-transformation and rebirth, both of which are central to someone suffering from depression in order to escape from their preexisting and harmful ways of being (Winkelman, 2007). This is accomplished by directing neural impulses to less imprinted regions of the brain, thus helping the individual escape their engrained habitus of depressed thinking and feeling (McClay, 1976). In shifting the mental state of the participant, ayahuasca and other psychedelics are able to induce these transformative notions, as well as decreasing rumination, which is an incredibly powerful process in the maintenance of depression (Baumeister et al., 2014).

Ayahuasca is seen as a teacher, and the teacher is able to show the individual how to help themselves; interestingly,

LSD is often described in this same manner (Blackmore, 2011; Lee & Shlain, 1985). Such narratives are reminiscent of psychotherapy in which the therapist essentially functions as a teacher and shows the patient ways to think and overcome their struggles. However, while therapy is incredibly inaccessible to many due to its cost and time investment as well as being limited by the number of therapists in a given region, psychedelics provide a much more feasible alternative.

Psilocybin (magic mushrooms) has similarly played a crucial role in healing among many traditional cultures through the years. Perhaps the best studied of the psychedelics, psilocybin has been shown to bring about feelings of joy and harmony in those taking it, though technically its derivative, psilocin, which it transforms into after oral ingestion, is what causes this effect (Baumeister et al., 2014; Nichols, 2004). Unsurprisingly, it has been used traditionally to treat a range of culture-specific illnesses whose symptoms overlap with those of the Western conception of depression (Winkelman, 2007).

Both DMT and psilocybin then may unequivocally be seen as a medication, which aids in a variety of ills, including those that resemble biomedical definitions of depression. As mentioned previously, due to the similarity of their chemical structures, these two compounds and LSD all have identical neurological and cognitive effects. As such, basic deduction points to the ability of LSD to accomplish the same goal. Not only this, but all three substances have been proven to have no adverse effects on humans in an incredibly large number of studies (Garcia-Romeu et al., 2016). Unlike other substances, however, LSD is much more potent, meaning smaller doses may be administered to obtain clinically significant results (Maqueda, 2018). In addition, DMT requires the presence of a monoamine oxidase inhibitor to allow it to persist long enough in the body to be effective when consumed orally (Sayin, 2014). This naturally produces more issues in clinical trials as two substances would be involved and have to be studied simultaneously to form a complete “product.” LSD is without this drawback.

With all this in mind, the question remains as to why LSD has not seen a greater number of modern clinical trials. Research supports that it is of great benefit, and through the above intercultural perspective, we are able to see exactly why it would be so (Garcia-Romeu et al., 2016). Studies have even shown its practical effects on the symptoms of depression in participants, such as feeling like moving more, showing an increase in their level of interest, talking more, and more positive emotions emerging (Busch & Johnson, 1950). Although this is a question that cannot be answered without looking at an array of factors, it is incredibly likely that stigma plays a large role here. In branding LSD as a recreational drug needing to be controlled and making it illegal, the discourse as well as public perception naturally go in a direction that is at odds to a medical view of the substance. Even today, this stigma remains strong despite the proof of its usefulness, as well as many studies finding that legal drugs such as alcohol and nicotine are in fact injurious for humans (Garcia-Romeu et al., 2016). Although the arbitrariness of laws should appear obvious, many do not think to question them.

It is here that the value of an anthropological eye on the subject becomes immensely important. In taking a holistic

approach rather than focusing solely on one culture, we are able to draw upon information otherwise inaccessible. Comparing LSD to psilocybin and DMT within cultural contexts not only legitimizes the use of it, but also shows manners in which it could be employed. Further research is needed focusing on the medicinal aspects of traditional healing with psychedelics and how they may fit in with our own notions of mental illness. Where biomedical research largely dismisses “culture-bound syndromes” as illegitimate, an anthropological approach allows a true investigation into such conditions to occur. Thousands of years of research and experimentation have gone into the traditions with psychedelics that live today, and to ignore such a wealth of knowledge is not only illogical, but also vastly arrogant.

Still, despite the lack of appropriate research, it is plain to see that LSD holds great potential in the treatment of depression, as well as many other ailments. With the capacity to help in both cognitive and neurological manners as well as its lack of the adverse side effects so often found in modern pharmaceutical medications, LSD represents a great step forward in the ongoing development of better treatments for those living with this debilitating and widespread disorder.

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