Hallucinogens: An Update

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Research of hallucinogen abuse rarely extends beyond epidemiology and observed pathology. Even less research has been completed on the special circumstances surrounding the religious use of hallucinogens or on potential therapeutic applications. Rather than offer another basic review on the well-known hazards of illicit hallucinogen use, this paper provides an overview and practice recommendations on compounds the clinician may be less familiar with, such as the botanical plant *Salvia divinorum*, the drug 3,4-methylenedioxymethamphetamine ("ecstasy") and synthetic hallucinogen analogs. The often-warned, but rarely occurring, hazard of hallucinogen persisting perception disorder ("flashbacks") is also reviewed with treatment recommendations provided. The current status of clinical research with the hallucinogens is presented, with case vignettes suggesting hallucinogens may have anti-addictive applications. The special circumstances surrounding the religious, nondrug use of hallucinogens as sacred sacraments in the US and elsewhere are also presented. It is hoped that the reader will gain a more nuanced understanding of how these physiologically nonaddictive drugs may offer legitimate benefits in modern society. By appreciating that such benefits may one day be borne out by careful, methodologically sound research, clinicians should be better armed in raising the topic of hallucinogen use and abuse with their patients.

Introduction

It is time for a careful re-examination of the hallucinogens. These drugs remain widely used and abused, yet are physiologically nonaddictive. It is also uncommon to diagnose a chronic primary hallucinogen-induced or associated disorder. Nevertheless, crimes and adverse events associated with acute illicit intoxication are regularly reported by the media. Hallucinogen intoxication can be profound to disturbing and, on rare occasions, induces temporary suicidality; offering caution on the dangers of careless use of hallucinogens as drugs of recreation is an important component of drug education. These substances are also used in settings outside medical practices for nonrecreational purposes, including as spiritual sacraments, pharmacotherapies for dependence on other drugs, and to treat other medical and psychiatric conditions. Moreover, hallucinogens actually do have a long history of safe administration in legal controlled research settings [1•]. Unfortunately, there is still too little formal research on the putative dangers or benefits of the hallucinogens.

Substantial literature exists on hallucinogen abuse, related psychiatric and medical disorders, and resultant strategies for treatment. Clinicians desiring knowledge of these basic aspects of hallucinogens are referred to any of the excellent reviews contained in general psychiatry and substance abuse textbooks [2••]. This paper is written to inform the psychiatrist and other medical clinicians about the current uses of hallucinogens that some patients engage in recreationally or with serious, nonrecreational intentions. This paper also provides additional information on current trends in hallucinogen consumption, an update on the extent and treatment for hallucinogen persisting perception disorder (HHPD), and observations on some of the current clinical research in the field.

Newly Emerging Hallucinogens of Abuse

Salvia divinorum

Salvia divinorum is a small plant from the mint family, which contains the psychoactive neoclerodane diterpene, salvinorin A. *Salvia divinorum* is traditionally consumed by Mazatec Indians of Oaxaca, Mexico by chewing fresh leaves or by drinking the juice of the leaves for absorption of salvinorin A through the oral mucosa [3].

The drug is reportedly psychoactive for 15 minutes at doses of 200 to 500 μg when smoked [4], and oral absorption leads to a less intense intoxication lasting up to 1 hour. Unlike all other "major" hallucinogens, such as lysergic acid diethylamide (LSD), salvinorin A has no action at the 5HT2a serotonin receptor and, in fact, is the first known example of a naturally occurring non-nitrogenous kappa opioid receptor agonist [5]. Very little research has been conducted on this plant or salvinorin A itself, but it is an emerging intoxicant in the US and elsewhere, primarily because of Internet-based advertisements and sales, and because of repeated articles about this Internet trend appearing in the popular media.

Salvia divinorum is a powerful dissociative intoxicant with hallucinogenic properties, but so is the atropine-containing *Datura stramonium* ("Jimson Weed") growing throughout the US. Although they remain unregulated,

only *S. divinorum* is being promoted by an increasing number of web site shops [6•] and local smoke-shops, and is now being sold in concentrations two to even 10 times greater than found in its natural state. This plant does not appear addictive, and few individuals make repeat purchases. Harm most likely occurs from inadequate preparation and understanding of its safe use or from use in settings in which it is dangerous to be intoxicated with any drug at all (*eg*, such as driving).

Ecstasy

3,4-Methylenedioxymethamphetamine is most commonly referred to as "ecstasy" on the street. First synthesized by Merck in 1912 as a study compound, it often has been erroneously mentioned as a patented appetite suppressant. A dopamine-releasing agent, ecstasy is also a potent serotonin-releasing agent, as well as a selective serotonin reuptake inhibitor, and it is thought that the mood-enhancing, anxiolytic properties of this "empathogen" are primarily caused by its intense modulation of serotonin release [7].

Ecstasy is now widely used in the US, particularly among teenagers and young adults who participate in all-night dances, or "raves." The 2001 National Household Survey on Drug Abuse (NHSDA) estimated that over 8 million individuals aged 12 or older had used ecstasy at least once in their lives, including 13.1% of young adults aged 18 to 25 [8]. In the NHSDA, individuals reporting first use of ecstasy in the past year increased from fewer than 80,000 in 1992 to almost 2 million in 2000. Similarly, in the Monitoring the Future Study, rates of ecstasy use among high school seniors have risen 61% since 1996, when this study started tracking consumption in-depth [9]. A longitudinal study of students at a prestigious college also found a striking rise in ecstasy use from 1989 to 1999; approximately 10% of college seniors in 1999 had tried the drug at least once [10].

Ecstasy use is becoming a serious problem in certain special populations, such as young gay men [11,12]. In particular, some gay men are combining ecstasy with sildenafil citrate (Viagra; Pfizer Pharmaceuticals, New York, NY); erectile dysfunction is a common side effect of ecstasy, and so some men take Viagra to counteract this problem. This combination is referred to as "sextasy" [13], but it is doubtful that most people ingesting these two drugs simultaneously are also cognizant that the vascular effects from Viagra may increase the risk of cardiotoxicity from ecstasy, which already is known to increase blood pressure, core body temperature, and heart rate.

Ecstasy may lead to neurocognitive deficits in chronic users. However, most studies reporting cognitive impairments are marred by small sample size, inadequate comparison groups, testing of individuals who had used multiple drugs other than ecstasy, or those with concomitant mental disorders [14,15•]. Some studies also suggest that memory deficits found in users may be better attributable to premorbid mental illness or may not be as significant as earlier cautionary reported findings [16,17].

Including questions about the use of multiple drugs or dosages in one setting are part of the "practice recommendations" for discussing ecstasy use with patients. Patients should also be asked whether they have considered using "pill testing kits," which are specially purchased reagent tests that can verify the presence of ecstasy in a pill, but not exclude the possibility of contamination with other drugs. One should question patients carefully for claims that ecstasy assists with social awkwardness; ecstasy decreases shy and self-critical thinking, and increases impulsivity, sense of calmness, and acceptance. By inquiring further about social anxiety, researchers may be able to diagnose individuals with social phobias or social anxiety disorder and offer these individuals more long-lasting, effective pharmacotherapy [18]. If ecstasy is ingested primarily at all-night "rave" dance/music parties, these patients should be cautioned that the rave setting may pose special risks; heightened empathy and risk taking may make the intoxicated easy "prey" for abusers; euphoria and heightened stamina (ecstasy has amphetamine-like properties, as well) may falsely reassure individuals to continue dancing despite increasing dehydration, hyperthermia, and tachycardia; ecstasy also increases vasopressin release [19] and so there is also the risk of lethal over-hydration. Finally, patients should be reminded that the risk for an adverse event from taking ecstasy will increase with dosage. Over time, with successive dosing, the desirable effects of ecstasy become less intense, and this encourages some users to take two, three, five, or even 10 pills in one night!

Hallucinogen "analogs"

The most common hallucinogen used in the US is LSD and psilocybin-containing mushrooms (such as *Psilocybe cubensis*), but a number of synthetic analogs appear on the illicit market from time to time. Most of these analogs were invented and first characterized by the highly regarded forensic chemist, Alexander Shulgin, who has published two books on these compounds, much of which is also posted on the Internet [20,21]. Two such analogs that have made some inroads in the illicit market are "2C-T-7" (2,5-dimethoxy-4-(n)-propylthiophenethylamine) and 5-MeO-DIPT (N,N-diisopropyl-5-methoxytryptamine). 2C-T-7 goes by street names such as "7" or "blue mystic," and 5-MeO-DIPT is associated with names such as "foxy" and "foxy-methoxy." These drugs have been placed into Schedule 1 by the US Drug Enforcement Agency (DEA) in the past year. These drugs have anecdotally been reported to have LSD-like and ecstasy-like properties. Shulgin and Shulgin's books [20,21] provide excellent references for most hallucinogen analogs mentioned by patients, but, of course, the full profiles of drug action have not yet been characterized.

"Practice recommendations" include asking patients about their experimentation with hallucinogen analogs, as well as reviewing Internet postings on these and other newly emerging hallucinogens (the web site http://www.erowid.com is recom-

mended as a good starting point). Users should be reminded that because there are no clinical or research data on the safety of these new drugs, clinicians are unable to offer reassurances about potential drug interactions, and, of course, there are no guarantees that these pills purely, if at all, contain the stated substance. Unlike botanical hallucinogens, such as peyote (*Lophophoria williamsii*), or even synthetic LSD, these analogs have been ingested by a much smaller population of users over a much shorter period of time, and so the risk for an adverse event is much more poorly known. In scheduling 2C-T-7, the DEA associated three deaths with its experimentation—one overdose after intranasal insufflations and two deaths at raves where 2C-T-7 was taken in combination with ecstasy [22].

Hallucinogen Persisting Perception Disorder ("Flashbacks")

According to the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) [23], the diagnosis of HPPD ("flashbacks") is made if the following criteria are met.

1. The re-experiencing, after cessation of use of a hallucinogen, of one or more of the perceptual symptoms that were experienced during intoxication with the hallucinogen (*eg,* geometric hallucinations, false perceptions of movement in the peripheral visual fields, flashes of color, intensified colors, trails of images of moving objects, positive afterimages, halos around objects, and macropsia and micropsia).
2. The symptoms in criterion 1 cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
3. The symptoms are not caused by a general medical condition (*eg,* anatomic lesions and infections of the brain, visual epilepsies), and are not better accounted for by another mental disorder (*eg,* delirium, dementia, or schizophrenia) or hypnopompic hallucinations.

Hallucinogen persisting perception disorder ("flashbacks") are mentioned because this illness is often presented as a common adverse consequence of hallucinogen abuse. A recent careful review of the literature on HPPD reports that it is a rare disorder that develops in a distinctly vulnerable subpopulation of users who also were primarily exposed to LSD, in particular [24]. Those afflicted with HPPD may experience serious morbidity, but, as of yet, there have been no randomized controlled trials assessing the efficacy of any pharmacologic agent for HPPD. Improvement has been reported with use of sunglasses [25], psychotherapy and behavior modification [26], or various pharmacologic agents, the most promising of which include clonidine [27], benzodiazepines, and selective serotonin reuptake inhibitors [26].

Hallucinogen Therapy?

Drug and alcohol treatment with hallucinogens

Clinical research on the possible medicinal use of hallucinogens occurred primarily in the 1950s through the early 1970s. Much of this research focused on using LSD to treat alcoholism and, to a lesser extent, the pain and depression of patients with cancer. More recently, anecdotal reports appearing in the popular press and on the Internet have endorsed the use of the hallucinogen ibogaine, especially to interrupt the withdrawal effects and cravings associated with heroin dependence. Ibogaine, extracted from the root bark of the west African shrub *Tabernanthe iboga*, is listed as a Schedule 1 drug in the Controlled Substances Act, but this has not stopped its growing clandestine use to treat addiction in the US, as well as its legal administration in several Latin American countries and Canada. (The *Journal of the American Medical Association* recently reported on this use of ibogaine in their Medical News and Perspectives section, which the reader is encouraged to obtain [28].)

Ibogaine intoxicates much like LSD, except that the duration of intoxication extends for 8 to 12 hours or more, depending on dose. It has traditionally been used in the initiation rites and ceremonies of the Iboga cults, which have existed for centuries [29] and continue to this day in several west African countries, most especially Gabon. Two purported nonpsychoactive metabolites of ibogaine, noribogaine and 18-methoxycoronaridine, have also been shown in preclinical studies as promising anticraving agents [30]. Ibogaine has reduced cocaine intake in cocaine-dependent rats [31], attenuated naloxone- or naltrexone-precipitated withdrawal in chronic morphine-dependent rats [32], and has reversed behavioral disinhibition and neuroendocrine system stimulation in rats also exposed to methamphetamine [33].

However, the use of hallucinogens to treat drug addiction in humans has been inadequately evaluated and, like ibogaine, is deserving of closer scrutiny [34••]. Two case vignettes, which were reviewed and approved by the patients, are presented herewith. Only potentially identifying information has been altered and the patients have stated they are comfortable with the level of confidentiality contained within the text.

Case vignette 1

Patient 1 is a 38-year-old single white man with a 12-year history of heroin dependence and current nicotine and caffeine dependence. Medical history is significant for a splenectomy, "on and off" psychotherapy over many years, and multiple admissions to detoxification centers. One of three siblings also has a history of heroin dependence. This individual began smoking cannabis at age 15 and started abusing cocaine and heroin at age 18. By age 25, the patient was a daily heroin user, resulting in multiple arrests for simple possession of heroin over the ensuing years. Though dependent on illicit heroin, the patient built a successful career within the entertainment industry and achieved

abstinence once for 6 months in his late 20s with the aid of therapy, support groups, and threat of re-arrest. Despite these efforts, relapse occurred during a period of extra demands from work and in his personal life. Essentially, the patient has been addicted to heroin throughout his entire adult life and had resigned himself to remaining opiate-dependent, despite wanting to stop. At age 37, the patient heard of the use of ibogaine for the treatment of heroin dependence. Broaching the subject of ibogaine with his physician, he was discouraged from seeking it out because research is incomplete, ibogaine remains illegal in the US, and there are "more traditional" therapies that he could turn to again. Not wanting to switch to agonist therapy (methadone), frustrated with a "culture of submission to my illness" at anonymous 12-step groups, and observing that detoxification, individual and cognitive behavioral psychotherapy, and run-ins with the law, at best, help achieve abstinence for up to a few months, this patient, like many dependent on heroin, wanted to find "another way…a way that really could help heal me from what I've been doing to myself; a treatment that could stop my cravings cold." The patient decided to explore ibogaine treatment further without physician guidance. Compared with the limited information furnished by his physician, the patient discovered a wealth of postings on the Internet. After reading positive testimonials on one web site, http://www.ibogaine-therapy.net, the patient decided ibogaine was worth a try. Further Internet research led him to a treatment center operating in Latin America. Though he flew down heroin-dependent, after a brief stay at this center in which he had a single, medically supervised ibogaine session, he returned home claiming a total absence of drug cravings or desires to reuse. Subjective experience of ibogaine was described as "brutal and unpleasant; it felt like God was telling me to shut up and then to accept myself." The patient remains drug-free (10 months sobriety to-date), has steadily rebuilt connections to family members, and finds himself enjoying work: "I feel like my feelings are my own finally. I am amazed that I feel free of drug cravings rather than trying to fight off those demons to reuse. What's the difference between ibogaine and the other things I've tried before? Ibogaine has worked." This patient's opiate-dependent sibling is also now drug-free since ibogaine treatment.

Though the patient is currently in his longest period of abstinence, it must be remembered that heroin dependence typically has a chronic, relapsing cycle. Apparently a treatment responder, the patient acknowledges that he would seek out another ibogaine session should he ever ingest heroin again. Unsatisfied with the approved treatment options available, this patient typifies individuals who increasingly research health questions on the Internet and then act on their own. Because there are no large-scale studies of ibogaine in the US, this particular patient accepted extra risks not typical of patients seeking experimental therapy, including ingestion of a non–US Food and Drug Administration approved medication manufactured by unknown means from physicians offering ibogaine in a third-world country.

Case vignette 2

Patient 2 is a divorced, white woman in her 50s with a PhD in biology. While an undergraduate, she developed pyelonephritis and other chronic kidney and bladder ailments. Corrective surgeries and postsurgical treatments resulted in the patient also developing sedative-hypnotic dependence. After healing from the last procedures, her physician stopped prescribing seconal, phenobarbitol, and diazepam without a proper taper, which resulted in severe withdrawal symptoms. Fearing that the rebound insomnia would harm her school and work performance, the patient purchased seconal and methaqualone illicitly, continuing her sedative-hypnotic dependence for approximately 2 years. Confiding in a friend about her illicit use of barbiturates, she was encouraged to try psilocybin-containing mushrooms as an addiction cure. After seven treatments, she successfully stopped using barbiturates and ceased taking these mushrooms. Her sessions with hallucinogens also kindled a lasting interest in faith and spirituality; she states, "I actually read the Holy Bible (cover to cover) for the first time in my life.... To make a long story short, I didn't really go through any 'religious conversion' per se, but decided I wanted to do something more positive with my life." This patient also credits her psilocybin use with "getting my head straight" about childhood sexual abuse, depression, and thoughts of suicide, for which she had received several years of individual psychotherapy. The patient continued on to graduate school and has had a subsequent successful career teaching at the university level, working at nonprofit groups, and now is a senior university administrator. This patient has remained drug-free for 24 years and contacted the author recently to relay her story that hallucinogens aided her recovery from barbiturate dependence and deepened her work in psychotherapy. She currently receives replacement therapy for hypothyroidism and suffers chronic neck pain from a motor vehicle accident 2 years ago.

This individual was sexually abused in her youth, developed sedative-hypnotic dependence postsurgery for chronic kidney and bladder ailments, and experienced symptoms of severe depression and post-traumatic stress disorder during her 20s. In other words, she was a "dual-diagnosis" patient with drug abuse, as well as chronic physical and emotional problems. During the same period of successful work in individual psychotherapy, the patient was able to taper off of sedative-hypnotics in conjunction with the introspective insights that she feels were gleaned from her experimentation with psilocybin-containing mushrooms. She also credits her brief hallucinogen use with decreasing drug cravings, as well as contributing to a subsequent interest in faith and spirituality.

Other medical treatments with hallucinogens

Despite the clear abuse liability and potential adverse effects of most hallucinogens used outside the medical setting, tantalizing evidence—albeit uncontrolled or anecdotal—suggests that these drugs may prove useful therapies for conditions inadequately treated by other means. Before placement in Schedule 1, ecstasy, for example, was quietly used by some American psychiatrists in couples psychotherapy as an aid to enhance communication and empathy [35].

Past research also suggests that LSD and dipropyltryptamine (DPT) reduce the intensity of chronic pain in the terminally ill and may assist in coping with the special circumstances raised within the family during that time [36–39]. Several investigators in the US are planning to renew research with the terminally ill, offering synthetic psilocybin or possibly ecstasy.

Treatment of alcohol dependence is also being investigated in Russia, where one research team has administered the anesthetic agent ketamine to several thousand individuals now [40]. In subanesthetic doses, ketamine is a dissociative agent with hallucinogen-like properties. These investigators have suggested that ketamine therapy improves length of abstinence; they have recently expanded their protocol to treat opiate-dependent individuals, as well [41].

Synthetic psilocybin is currently being investigated for treating severe obsessive-compulsive disorder that has failed to respond to at least one accepted therapy. This project comes after a recent positive case report of such treatment [42].

Finally, clinical research is actively underway or in the planning stages for the treatment of post-traumatic stress disorder with ecstasy (in the US, Spain, and Israel) [43] and for eating disorders with psilocybin (in Switzerland) [44].

Hallucinogens Sometimes Are Genuine Religious Sacraments?

Every so often media reports appear of a defendant claiming his drug use or drug trafficking is protected by the First Amendment right to freedom of religion. Courts generally take a dim view of such defenses because, although the Constitution does protect religious belief, it cannot be used as a loophole to commit illegal acts. However, this First Amendment protection of religious belief can prove quite powerful in opposing the will of the government. For example, Jehovah's Witnesses can refuse to accept blood transfusions, even if they risk death by doing so. Christian Scientists can seek out their own health practitioners for their families and avoid the medications and other recommendations of a family physician (although courts have intervened in some cases where death was imminent and a potentially life-saving medical procedure was available). A number of small religions have even been formed to aid families who wish to refuse state-mandated vaccination of children. Though surprising, there are bona fide, credible religions in the US and elsewhere that ingest as holy sacrament substances that, in other circumstances, are regarded as Schedule 1, dangerous hallucinogens.

The largest such faith in the US is the Native American Church (NAC), which reveres the cactus peyote as their "sacrament" and "medicine." Full protection from any harassment or prosecution has been granted only to members of federally recognized Native American tribes through the 1994 Amendments to the American Indian Religious Freedom Act (AIRFA) passed by Congress and signed into law by President Clinton. Although some states allow for the religious use of peyote by anyone, regardless of race or ethnicity, the federal government's protection is not based on religious freedom, but instead on the special custodial relationship between the government and these tribal members who have limited sovereignty out of treaty obligations. The government is obliged to protect and promote the survival of traditional custom, culture, and ritual of these peoples; AIRFA was passed to ensure that the long-standing religious use of peyote by Native peoples cannot be obstructed by a blind application of drug control laws. Though peyote and its psychoactive constituent, mescaline, are listed as Schedule 1 drugs of abuse, each year over 2 million "buttons" (the above-ground crown of the cactus) are legally distributed throughout the US and Canada under the supervision and licensing of the Texas Department of Public Safety and the DEA. The NAC, in fact, is the largest faith among Native Americans, with over 300,000 members. Without needing "medical supervision," these American citizens safely consume their sacrament in all-night prayer vigils. The use of any drugs of abuse, including alcohol, is expressly forbidden in the NAC. Psychiatrists and anthropologists have also reported that NAC members attribute this "Peyote Way" with saving them from the ravages of alcoholism and drug abuse [45,46]. Many members are also quite successful; the current elected President and Vice President of the Navajo Nation, for example, are life-long adherents to the NAC.

Over the past several years, the author's research team has conducted the first study to screen for any residual neurocognitive deficits from exclusive peyote use versus an exclusive history of alcoholism versus comparisons who never abused alcohol or drugs and were never members of the NAC. All individuals were recruited from Navajo Nation. Although the final results of blinded neuropsychologic testing of over 200 individuals is in preparation for publication, the author's team do not expect these findings to differ from earlier reports on partial data that failed to find differences between the comparison and NAC groups [47,48]. Though anecdotal, none of the several hundred NAC members interviewed by us reported HPPD-like complaints or other harmful effects from their participation in their ceremonies.

Indigenous use of hallucinogens extends throughout the Western Hemisphere, as well, with psilocybin-containing mushrooms and, as mentioned, *S. divinorum* being used ceremonially by Mazatecs in Oaxaca. There is at least

3000 years of peyote use by some tribes in northern Mexico, most notably the Huichol. In Central and South America, traditional and shamanic use continues with other mescaline-containing cacti, dimethyltryptamine (DMT) containing snuffs and potions from seeds and barks, and with ayahuasca. Ayahuasca is a tea brewed from the leaves of *Psychotria viridis* and the vine of *Banisteriopsis caapi*, with *Psychotria* containing DMT and *Banisteriopsis* containing reversible monoamine oxidase inhibitors that are necessary for making DMT orally active.

Physician familiarity with ayahuasca is gaining importance in the US and other countries, because this brew is the sacrament of several religions that originated in Brazil over the past 100 years or so and are expanding to other countries. The two largest of these non-Native faiths are the Santo Daime and the União do Vegetal (UDV), which possess a syncretic blending of Christian and Native beliefs. There are members of these churches living in Europe, Japan, and even the US. These faiths are recognized by the Brazilian and Peruvian governments as genuine and are protected there. This permission drives some spiritual seeking tourists into the Amazon River for ayahuasca sessions and also results in ayahuasca being shipped out for ceremonies in third countries.

In 2001, The Netherlands recognized the Santo Daime as an accepted, legal religion, and the State of Oregon Board of Pharmacy also acknowledged, in a November 8, 2000 opinion, that "the sacramental use of the Santo Daime tea in the context of a bona fide religious ceremony by practitioners of the Santo Daime religion as described does not constitute abuse of a controlled substance." In 2002, the UDV even won a preliminary injunction against the DEA and the Department of Justice concerning governmental policies preventing their access and right to ingest ayahausca. This injunction has been stayed pending review by the US Court of Appeals for the Tenth Circuit. Right now, then, America's drug war pits religious tolerance and freedom against the need for drug control.

Whether or not the federal government prevails in its current quest to squelch these religions, some Americans will continue to use hallucinogens as religious sacraments. When these individuals, Native or not, become patients, clinicians must be mindful of their special circumstances, or risk alienating such patients from seeking follow-up care. The author of this paper has listened to Native Americans, for example, relate how some doctors blamed their peyote use as the cause of diseases or birth defects, even though the medical literature does not support such accusations [49•]. If physicians are devoted to the well being of their patients, then, yes, they must be among the first to extend their hands in help across any of the cultural and religious beliefs that may separate patients from good care. To act within the highest ethical traditions of medicine, it is important to learn about the set and setting within which patients use hallucinogens, as well as maintain vigilance toward cultural preconceptions that may bias against what may ultimately be reasoned lifestyle choices.

Conclusions

Alcohol, cocaine, heroin, methamphetamine, and tobacco remain the most popular drugs of abuse; they all induce physiologic dependence and form the bulk of the drug-induced morbidity and mortality that physicians battle. Of course, when hallucinogens are ingested outside of religious ritual, traditional ceremony, or controlled research settings, these drugs, too, can prove quite harmful. Psychiatrists especially know how ill-conceived hallucinogen experimentation may precipitate psychotic breaks and affect instability, especially in individuals with emerging or pre-existing psychopathology. But misuse of a drug does not preclude the possibility of a therapeutic or socially acceptable purpose, which is perhaps why all of the mentioned highly addictive drugs (save for heroin) remain in Schedule II or, for alcohol and tobacco, are unregulated by the US Food and Drug Administration.

Hallucinogens have never been properly screened for medical utility, and doing so will better inform physicians, the public, the media, and policy makers in how best to minimize misuse and abuse. Revered in shamanic tradition and even religion, yet mostly reviled by modern culture, the hallucinogens captivate, intrigue, and threaten society in ways more complicated than other drugs. That 300,000 Americans actively participate in NAC ceremonies calls into question, for example, the generally held belief that hallucinogens are too "unpredictable" for safe human consumption. Instead, hallucinogens are "predictably unpredictable," with the right conditions inducing deeply mystical and transcendent experiences. Taken in careless abandon for a "drug high," hallucinogens may induce megalomania. Taken in respectful reverence and ceremony, such as in the all night prayer vigils of the NAC and Santo Daime and UDV, the nondrug sacramental use of hallucinogens humbles and informs.

Hallucinogens hold tantalizing promise; the author believes there may be a modern role for these compounds in the treatment of drug dependence and perhaps for other psychiatric disorders. Hallucinogens may help bring "closure" and better quality of life for those struggling with end-of-life issues or to model spiritual reawakening. The author has been previously quoted referring to hallucinogens as possible "humility agonists," [50], but it may be more accurate to include among the many positive and negative effects the term *narcissilytic*, as the hallucinogens' "ego-dissolving" properties pierce through narcissism. No other drug category holds such a property and it may explain why hallucinogens are so volatile and dependent on mindset and setting.

The author of this paper remains committed to investigating how hallucinogens are abused and cause harm so as to reduce the impact of these harms, to offer more specific and accurate drug education, and to help differentiate hal-

lucinogen abuse from legitimate use. If it is apparent that better research on their harm is needed, is it not also obvious that we need better answers to these interesting threads suggestive of benefit?

Acknowledgments

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- • Of importance
- •• Of major importance

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