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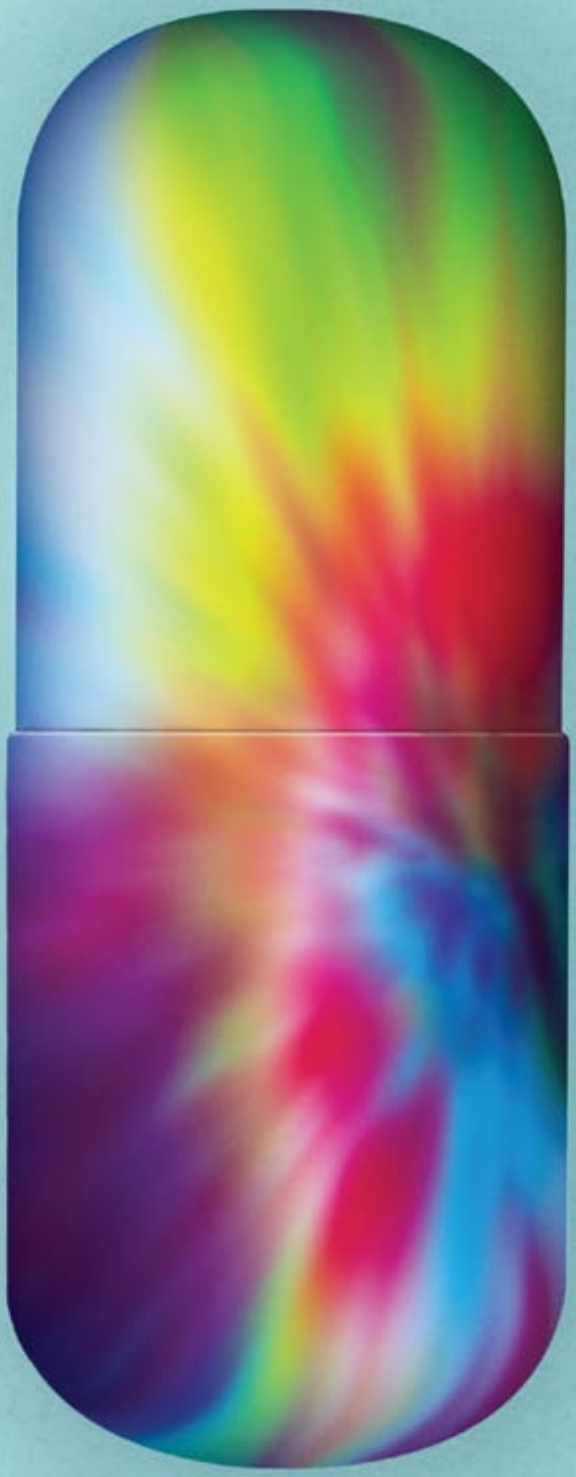

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HEALTH

Hallucinogens as Medicine

In a matter of hours, mind-altering substances may induce profound psychological realignments that can take decades to achieve on a therapist's couch

By Roland R. Griffiths and Charles S. Grob

SANDY LUNDAHL, A 50-YEAR-OLD HEALTH EDUCATOR, reported to the behavioral biology research center at the Johns Hopkins University School of Medicine one spring morning in 2004. She had volunteered to become a subject in one of the first studies of hallucinogenic drugs in the U.S. in more than three decades. She completed questionnaires, chatted with the two monitors who would be with her throughout the eight hours ahead, and settled herself in the comfortable, living-room-like space where the session would take place. She then swallowed two blue capsules and reclined on a couch. To help her relax and focus inward, she donned eyeshades and headphones, through which a program of specially selected classical music played.

The capsules contained a high dose of psilocybin, the principal constituent of "magic" mushrooms, which, like LSD and mescaline, produces changes in mood and perception yet only very rarely actual hallucinations. At the end of the session, when the psilocybin effects had dissipated, Lundahl, who had never before taken a hallucinogen, completed more questionnaires. Her responses indicated that during the time spent in the session room she had gone through a profound mystical-like experience similar to those reported by spiritual seekers in many cultures and across the ages—one characterized by a sense of interconnectedness with all people and things, accompanied by the feeling of transcending time and space, and of sacredness and joy.

IN BRIEF

Hundreds of research reports on hallucinogens appeared during the 1950s and 1960s. Illicit use resulted in outlawing of the drugs. Restrictions on research, moreover, brought studies to a halt.

Hints from the early set of studies suggesting that these chemicals might help treat patients with various psychiatric disorders were not pursued because of strictures on research.

A new wave of studies on hallucinogens, primarily psilocybin, has begun to address whether the drugs can effectively treat the anxiety of cancer patients or help addicts kick their habits.

Early results from new trials point to the promise of these therapies, with some patients reporting profound spiritual experiences and, hence , the ability to make important life changes.

Photograph by James Worrell

At a follow-up visit more than a year later, she said she continued to think about the experience every day and—most remarkably—that she regarded it as the most personally meaningful and spiritually significant event of her life. She felt it had brought on positive changes in her moods, attitudes and behaviors, as well as a noticeable increase in overall life satisfaction. "It seems like the experience triggered a quickening of my spiritual unfolding or development," she wrote. "Ripples of insight still occur… [I am] much more loving—making up for the past hurts I've inflicted… More and more I'm able to perceive people as having the light of the divine flowing through them."

Lundahl was one of 36 participants in a study conducted by one of us (Griffiths) at Johns Hopkins that began in 2001 and was published in 2006, with a follow-up report published two years later. When the initial paper appeared in the journal *Psychopharmacology,* many in the scientific community welcomed the revival of a research area that had long been dormant. Psilocybin studies at Johns Hopkins continue along two tracks: One explores the drug's psychospiritual effects in healthy volunteers. The other delves into whether hallucinogen-induced states of altered consciousness—and, in particular, mystical-like experiences—might ease various psychiatric and behavioral disorders, including some for which current therapies are not very effective. The main drug used in these studies is psilocybin, a so-called classic hallucinogen. As with other drugs in this class—psilocin, mescaline, DMT and LSD—psilocybin acts on brain cell receptors for the signaling molecule serotonin. Confusingly, substances from other drug classes that exert pharmacological effects different from those of the classic hallucinogens also bear the "hallucinogen" label in popular media and epidemiological reports. These compounds, some of which may also offer therapeutic potential, include ketamine, MDMA (which is familiar as "ecstasy"), salvinorin A and ibogaine, among others.

OVERCOMING LEARY'S LEGACY

THERAPEUTIC RESEARCH with hallucinogens pursues tantalizing evidence from studies begun in the 1950s that collectively involved thousands of participants. Some of these studies hinted that hallucinogens could help treat substance addiction and relieve the psychological distress of terminal illness. This research came to a halt in the early 1970s, as recreational use of the hallucinogens, mostly LSD, grew and garnered sensationalistic media coverage. The field had also been tainted by the widely publicized dismissal of Timothy Leary and Richard Alpert from Harvard University in 1963 in response to concerns about unconventional research methods using hallucinogens, including, in Alpert's case, giving psilocybin to a student off campus.

The burgeoning and unsupervised use of the little-understood substances, partly a result of Leary's charismatic advocacy, generated a backlash. The 1970 Controlled Substances Act placed common hallucinogens in Schedule I, its most restrictive category. New limitations were placed on human research, federal funding ceased, and investigators involved in this line of research found themselves professionally marginalized.

Decades passed before the anxiety-ridden attitudes that had blocked investigation subsided enough to allow rigorous human studies with these much storied substances. The mystical-like experiences brought about by hallucinogens interest researchers particularly because such experiences have the potential to produce rapid and enduring positive changes in moods and behavior—changes that might take years of effort to achieve with conventional psychological therapy. The Johns Hopkins work is so exciting because it demonstrates that such experiences can be elicited in a lab in most subjects studied. It permits, for the first time, rigorous, prospective scientific investigations that track volunteers before and after taking the drug. This type of study enables researchers to examine the causes and psychological and behavioral effects of these extraordinary experiences.

In its recent study the Johns Hopkins investigators used questionnaires originally designed to assess mystical experiences that occurred on their own without drugs. They also looked at overall psychological states at two and 14 months after the psilocybin session. The data showed that participants experienced increased self-confidence, a greater sense of inner contentment, a better ability to tolerate frustration, decreased nervousness and an increase in overall well-being. Ratings of their behavior by friends, family members and work colleagues uninformed about the drug experience were consistent with the participants' self-ratings. One typical comment from a subject: "The sense that all is One, that I experienced the essence of the universe and the knowing that God asks nothing of us except to receive love. I am not alone. I do not fear death. I am more patient with myself." Another participant was so inspired that she wrote an entire book about her experiences.

RELIEF OF SUFFERING

WHEN RESEARCH INTO hallucinogen-based therapy stalled some 40 years ago, it left a to-do list that included the treatment of alcoholism and other drug addictions, anxiety associated with cancer, obsessive-compulsive disorder, post-traumatic stress disorder, psychosomatic disorder, severe character pathology and autism. Back then, most published reports were anecdotal accounts of treatments with hallucinogens, furnishing much weaker evidence than that from controlled clinical trials. Even the best studies of the era did not incorporate the stringent control conditions and methodologies that have become standard in modern clinical psychopharmacology research.

With cancer, patients frequently confront severe anxiety and depression, and antidepressants and anxiety-reducing drugs may be of limited help. In the 1960s and early 1970s more than 200 cancer patients received classic hallucinogens in a series of clinical studies. In 1964 Eric Kast of Chicago Medical School, who administered LSD to terminal patients with severe pain, reported that the patients developed "a peculiar disregard for the gravity of their situations and talked freely about their impending death with an affect considered inappropriate in our Western civilization but most beneficial to their psychic states." Subsequent studies by Stanislav Grof, William Richards and their colleagues at Spring Grove State Hospital near Baltimore (and later at the Maryland Psychiatric Research Center) used LSD and another classic hallucinogen DPT (dipropyltryptamine). The trials showed decreases in depression, anxiety and fear of death, and patients who had a mystical-type experience had the most improvements in psychological measures of well-being.

One of us (Grob) has updated this work. In September a paper in the *Archives of General Psychiatry* reported on a 2004–2008 pilot study at the Harbor-UCLA Medical Center to assess whether psilocybin sessions reduced anxiety in 12 terminal cancer patients. Although the study was too small to yield definitive conclusions, it was encouraging: the patients showed diminished anxiety and

improved mood, even several months after the psilocybin session. As with studies conducted years ago, participants also reported less fear of impending death. Johns Hopkins and New York University have now undertaken studies with cancer patients using higher doses of psilocybin—ones more likely to induce the mystical-like experiences that earlier investigations indicated were pivotal to lasting therapeutic benefits. In Switzerland a similar pilot study has begun using LSD instead of psilocybin.

Alcoholics, cigarette smokers and other substance abusers sometimes report beating their addictions after a deeply affecting mystical experience that occurred spontaneously without drugs. The first wave of clinical hallucinogen research recognized the potential therapeutic power of these transformative experiences. More than 1,300 patients participated in addiction studies that yielded more than two dozen publications decades ago. Some of those studies administered high doses to minimally prepared patients with little psychological support, a few of whom were even physically strapped to their beds. Researchers who appreciated the importance of "set and setting" and who provided better support to patients tended to see better results. This earlier work yielded promising but inconclusive results.

The new generation of hallucinogen research, with its better methodologies, should be able to determine whether these drugs can in fact help people overcome their addictions. At Johns Hopkins, Griffiths, Matthew Johnson and their colleagues have begun a smoking cessation pilot study using psilocybin sessions to supplement cognitive-behavioral therapy, a form of treatment that teaches patients how to change their thoughts and behaviors to quit and remain abstinent.

Beyond treating addictions, studies have recently started to test whether psilocybin can help allay the symptoms of obsessive-compulsive disorder. Other controlled substances with different mechanisms of action are also showing therapeutic potential. Recent investigations demonstrated that ketamine, given in low doses (it is normally used as an anesthetic), could provide more rapid relief from depression than traditional antidepressants such as Prozac. A recent trial in South Carolina used MDMA to successfully treat post-traumatic stress disorder in patients whom conventional therapies had failed to help. Similar MDMA trials are under way in Switzerland and Israel.

RISKS AND THE ROAD AHEAD

FOR THERAPIES using the classic hallucinogens to gain acceptance, they will have to overcome concerns that emerged with the drug excesses of the "psychedelic '60s." Hallucinogens can sometimes induce anxiety, paranoia or panic, which in unsupervised settings can escalate to accidental injuries or suicide. In the Johns Hopkins study, even after careful screening and at least eight hours of preparation with a clinical psychologist, about a third of the participants experienced some period of significant fear and about a fifth felt paranoia sometime during the session. But in the supportive, homelike setting provided in the research center and with the constant presence of trained guides, the Johns Hopkins participants encountered no lasting ill effects.

Other potential risks of hallucinogens include prolonged psychosis, psychological distress, or disturbances in vision or other senses lasting days or even longer. Such effects occur infrequently and even more rarely in carefully screened and psychologically prepared volunteers. Although classic hallucinogens are sometimes abused (used in a manner that jeopardizes the safety of the users or others), they are not typically considered drugs of addiction, because they neither promote compulsive drug taking nor induce a withdrawal syndrome. To help minimize adverse reactions, the Johns Hopkins group recently published a set of safety guidelines for conducting high-dose hallucinogen studies. Given researchers' ability to manage drug risks, we feel that studies of these substances should continue because of their potential ability to transform the life of, say, a cancer patient or drug addict. If hallucinogens prove themselves useful in the treatment of substance abuse or the existential anxiety associated with life-threatening illness, further investigations could explore whether drug-induced experiences might be incorporated into therapies related to major public health problems, such as eating disorders, risky sexual behavior or a wider set of maladaptive behaviors.

The latest round of hallucinogen research is helping to determine whether these drugs can wean people from addictions or allay the anxiety of cancer patients.

Benefits may also come from neuroimaging and pharmacological techniques that did not exist in the 1960s, which provide a better understanding of how these drugs work. Imaging of the brain areas involved in the intense emotions and thoughts people have under the drugs' influence will provide a window into the underlying physiology of mystical-type experiences produced by hallucinogens. Further research may also yield non-pharmacological approaches that work more quickly and effectively than traditional spiritual practices such as meditation or fasting to produce mystical experiences and desired behavioral changes—the kind of experience that convinced Bill Wilson in Towns Hospital in New York City to stop drinking and inspired him to found Alcoholics Anonymous in the 1930s.

Understanding how mystical experiences can engender benevolent attitudes toward oneself and others will, in turn, aid in explaining the well-documented protective role of spirituality in psychological well-being and health. Mystical experiences can bring about a profound and enduring sense of the interconnectedness of all people and things—a perspective that underlies the ethical teachings of the world's religious and spiritual traditions. A grasp of the biology of the classic hallucinogens, then, could help clarify the mechanisms underlying human ethical and cooperative behavior—knowledge that, we believe, may ultimately be crucial to the survival of the human species. SA

MORE TO EXPLORE

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Johns Hopkins Psilocybin Cancer Project: **www.cancer-insight.org**

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