



**PSILOCYBIN, THE ACTIVE INGREDIENT IN MAGIC MUSHROOMS, IS BEING EXPLORED AS A THERAPEUTIC TOOL TO IMPROVE THE LIVES OF PEOPLE WITH A LIFE-THREATENING ILLNESS BY ERICA REX**

ILLUSTRATIONS BY PETER HORVATH



## Calming a Turbulent Mind

I was lying on a lumpy off-white sofa under a mountain of blankets, wearing an eye mask and listening to a Brahms symphony playing through my headphones. The notes of a violin solo lit three strands of deep red light, which trickled like water in my right visual field. Deeper tones poured from above in huge blue clouds in the middle distance. Another violin flourish turned the sky yellow and brought with it a comet's tail

of body parts flying from the upper left of my visual field to the lower right, disappearing behind me.

This all happened within the first hour of my swallowing a capsule of psilocybin, the psychoactive ingredient in “magic mushrooms,” as a study subject at the Johns Hopkins University School of Medicine’s Behavioral Pharmacology Research Unit (BPRU). Patients with cancer are given the drug to improve mood and outlook and to help regain a sense of existential meaning in the face of a deadly disease.

I was diagnosed with breast cancer in 2009. A year on from a lumpectomy and radiation therapy, my prognosis seemed good. But rather than cheerfully getting on with life, I was spending most days at my desk crying. I began searching the Web for a way to kill myself that wouldn’t be either messy or too painful. The man I had married, who had made it possible for me to move to England



#### FAST FACTS

### Psychedelic Solutions

- 1**» Scientists are taking a second look at the therapeutic potential of psychedelic drugs, in particular psilocybin. This hallucinogen may offer faster, more effective treatment for individuals in a spiritual deficit state.
- 2**» A spiritual deficit state encompasses the severe distress and emotional suffering associated with deeply threatening events, such as a terminal illness. Modern medicine has typically struggled to assuage this condition.
- 3**» A few doses of psilocybin, in a carefully tailored setting and with a therapist's guidance, have been shown to calm the psychological turbulence of people afflicted with a number of conditions, including depression and alcohol addiction.

and continue cancer treatment under the U.K.'s universal health plan, could not cope with my depression and left for weeks at a time.

By the time my three-year mammogram rolled around at the beginning of 2012, I was living alone. Sitting in the waiting room at Barts Cancer Center in London, I felt so alienated by the pink ribbons, the flowered wallpaper and the yapping television that I fled before being called for my scan. A staff member pursued me, first down the stairs, then later on the phone. With each imprecation to reschedule, I declined more earnestly. "You can have my breast," I'd think to myself. "I'll leave it off for you in a bag."

Both here in the U.K. and in the U.S. where I had my surgery, medicine excels at finding cures for disease and saving lives. All that excellence has created a void, however, wherein the emotional and existential needs of patients often go neglected. My demoralization is common among cancer patients. We ob-

ness about survival and what the future holds for us. The system is not structured to help doctors carry us across the minefield of emotional and personal issues that cancer lays out before us.

But I am also fortunate. After decades of banishment to the netherworld of Schedule I (Class A in the U.K.), hallucinogens are making a reprise on the clinical stage. Drugs such as psilocybin have the potential to improve patients' sense of psychospiritual well-being and with it overall quality of life, a central focus in today's palliative care protocols. We stop worrying about the future and about death. A scant handful of researchers are exploring the hallucinogenic option as an adjuvant to cancer treatment for the first time in a generation, reintroducing a means of addressing the existential crises many cancer patients experience. Hallucinogens have also been studied as treatments for other conditions: a 2005 pilot study at the University of Arizona demonstrated that psilocybin successfully treated severe refractory obsessive-compulsive disorder, and cluster headache sufferers report that psilocybin arrests the headache cycle in a way no other drugs have touched.

Before their prohibition in the 1970s—the regulatory response to the explosion in street use during the late 1960s—hallucinogens were prescribed to approximately 40,000 research subjects. The results showed remarkable promise in helping terminally ill people overcome pain, fear, psychological isolation and depression. Now researchers are revisiting some of psilocybin's forgotten virtues. Not only does it diminish patients' symptoms immediately, it also improves therapeutic outcomes for months, even years afterward. Many patients undergo what Charles S. Grob, principal investigator at Harbor-U.C.L.A. Medical Center, terms a “psychospiritual epiphany.”

These scientists have been waiting a long time for the tide to turn.

### Flesh of the Gods

Indigenous cultures have used plants with hallucinogenic powers for centuries as a chemically mediated entryway to curative religious experiences. The Aztecs of Mexico and Central America called psilocybin-containing mushrooms *teonanacatl*, meaning literally “flesh of the gods.” Then, in the 17th century, *teonanacatl* was condemned by the

Spanish Inquisition. Practitioners were forcibly converted to Christianity. For three centuries ceremonial practices were thought to have been eradicated.

In 1955 banker-cum-amateur-mycologist R. Gordon Wasson journeyed to the hills of Oaxaca, Mexico, where he was permitted to attend a ritual healing ceremony conducted by a native healer, which he described in an article for *Life* magazine. A few years later, in collaboration with French botanist Roger Heim, then director of the French National Museum of Natural History, the two men



collected and identified the families of Strophariaceae and the genus *Psilocybe* used by the native practitioners. They provided samples to chemist Albert Hoffman of Sandoz in Basel, Switzerland, who in 1938 had synthesized LSD from ergotamine, an alkaloid produced by another fungus, *Claviceps purpurea*, a rot that grows on rye. Until 1991, when a new drug was finally introduced, ergotamine was the only available treatment for migraine.

Hoffman identified and isolated two active alkaloids, psilocybin and psilocin, from the mushroom samples. Clinical experimentation on psilocybin began quickly. Both it and LSD showed immense promise when administered to terminally ill patients and subsequently to intractably depressed and alcoholic patients. They provided relief to groups previously dismissed as untreatable.

Prolonged illness is not a modern phenomenon. But now—unlike 400 years ago—most people in the Western world do not die of fast-acting infectious diseases such as typhoid and plague. Those have given way to chronic, lingering disease processes lasting months or years. The accompanying

Drugs such as psilocybin could improve patients' sense of **psychospiritual well-being** and with it overall quality of life.

psychospiritual distress also afflicts those suffering from compulsive or habit-based disorders, such as alcoholism or nicotine addiction. “The issues around alcohol addiction and terminal illness are the same thing,” says Stephen Ross, principal investigator of New York University’s Psilocybin Cancer Anxiety Study. “These are people in an acute spiritual deficit state.”

A spiritual deficit state has been defined as “severe distress and emotional suffering associated

who do. “Existential terror in the dying is the most taboo conversation in medicine,” says Anthony Bossis, clinical assistant professor of psychiatry at N.Y.U., and co-principal investigator of the study there. “You can count on clearing the room of interns the moment you mention death.”

### A Skeleton Key

In the early 1990s the FDA and the National Institute on Drug Abuse began loosening their legal

## The healing constituent of psilocybin lies within the **intrapsychic world** the drug evokes during a session.

with events that threaten the intactness of the person”; in other words, it makes many sufferers feel that life is now worthless. It destroys patients’ ability to manage their affairs or connect in any meaningful way with loved ones. The knowledge of their impending death depletes their sense of autonomy. Psychotherapy may address some of these issues, but for many patients it is a poor option—if it is available. If you are facing imminent death, talk therapy is unlikely to bring relief quickly enough.

Spiritual deficit is not modern medicine’s cup of tea. Today a patient receiving a terminal diagnosis is not likely to be offered sessions with a counselor or psychotherapist unless he or she asks for them. A very small number of hospitals give patients the option of taking part in structured palliative care, where they receive consultations with palliative care physicians and home visits by specialist nurses. Some hospitals and doctors offer support groups and meditation classes or refer patients to charities

throttle on the study of hallucinogens. Even so, psilocybin researchers today obtain funding from private rather than federal sources, among them the Heffter Research Institute in New Mexico, the Multidisciplinary Association for Psychedelic Studies in California, and the Beckley Foundation in England.

The therapeutic benefit of psilocybin lies in its capacity to provide a neurochemical bridge between spiritual guidance and talk therapy. Although questions remain about psilocybin’s precise mechanism of action, researchers agree on this point: the drug’s value depends entirely on the patient’s feelings and perceptions during the session and the way he or she processes the memories afterward. Patients who undergo a transcendent peak while taking psilocybin describe it as among the most meaningful events in their lives. “The drug is a skeleton key which unlocks an interior door to places we don’t generally have access to,” says psychologist William A. Richards of BPRU, one of the researchers who successfully treated terminally ill patients with hallucinogens from the early 1960s until 1977, when the work was shut down. “It’s a therapeutic accelerant.”

Unlike psychoactive drugs, anxiolytic medications such as Xanax help patients only while they are taking them. The effect wears off when the body clears the drug from the system. Patients must repeat the regimen, often increasing the dosage to obtain the same effect. In contrast, the healing constituent of psilocybin lies within the intrapsychic world the drug evokes during a session. Psilocybin treatment consists of only one or two doses.

Grob and his colleagues carried out the first contemporary clinical study using psilocybin to treat depression at Harbor-U.C.L.A. Medical Center between 2004 and 2008. They assessed 12 patients with advanced-stage cancer using standard-

Grassroots movements may help legalize the therapeutic use of hallucinogens. AIDS sufferers and their advocates launched the campaign for medical marijuana clinics (below).



ROBYN TWOMEY Redux Pictures



Ritual is an important part of a psilocybin session. Researchers today carefully survey a patient's mental and physical landscape to channel the drug's effects toward healing.

ized psychological measurements of depression and mood, as well as screening for other psychiatric symptoms, such as paranoia and grandiosity.

All the patients who took part in the study reported sustained mood improvement and anxiety reduction after the sessions. The effects lasted for at least six months. Everyone in this group has since died. “The profession itself forgot about the promise of the early findings,” Grob says. “Forty years later here we are.”

Psilocybin is a naturally occurring alkaloid found in several species of mushrooms. Structurally, it is similar to the neurotransmitter serotonin. Once ingested, psilocybin is rapidly metabolized to psilocin, which causes a powerful physiological reaction involving three serotonin receptors—sites on the surface of a brain cell where neurotransmitters can attach to activate a cellular function. One receptor of particular interest is known as 5-HT<sub>2A</sub>. Depressed and suicidal patients have been found (at autopsy) to have more 5-HT<sub>2A</sub> receptors than normal patients. Psilocin binds to the 5-HT<sub>2A</sub> receptor in place of serotonin, which may partly explain psilocybin's positive effect on mood.

The lasting effects of a psilocybin session are generally thought to result from psychological insights gained from the experience, although an observed physiological change may further explain the

drug's lingering benefits. Animal studies show that LSD, another potent 5-HT<sub>2A</sub> agonist, causes a prolonged decrease in the number of 5-HT<sub>2A</sub> receptors. Psilocybin very likely has the same effect.

Recently a study by researcher Robin L. Carhart-Harris of the Neuropsychopharmacology Unit at Imperial College London yielded some surprises about the way psilocybin works. He found that overall blood flow to brain regions associated with consciousness and the concept of self decreased by 20 percent, contradicting a long-standing assumption that psilocybin increases blood flow to some areas of the brain. This new information helps to explain the ego dissolution that usually accompanies subjects' descriptions of psilocybin. Instead of augmenting the brain's day job of filtering and classifying, psilocybin removes internal constraints on our perceptions, thoughts and feelings.

Carhart-Harris performed functional MRI studies in healthy volunteers who had been given

### (The Author)

ERICA REX is an American journalist based in the U.K. She has written for the *New York Times*, the *Times* (U.K.) and numerous other venues.

psilocybin. He focused on two key structural hubs, the posterior cingulate cortex (PCC) and the medial prefrontal cortex (mPFC), which tend to activate in concert, like the first violin and the kettle drum in a symphony orchestra. With psilocybin, they became far less synchronized. The mPFC, in the front part of the brain, and the PCC, tucked in the middle, participate in the brain's default-mode network (DMN), a set of regions whose activity has been closely linked to our sense of self. Looking inward at oneself, as happens in depression, activates the DMN. "Tightly constrained, ruminative thinking is associated with hyperactivity and connectivity in the DMN," Carhart-Harris says. Psilocybin reduces DMN activity and, with it, the narrowing thought processes associated with anhedonia—the inability to experience pleasure—and depression.

Although the PCC and mPFC still play together on psilocybin, it is as though the conductor has left the room. The music changes character. If the brain in its normal state is Beethoven's Violin Concerto, on psilocybin it becomes improvisational jazz. The mind no longer dwells on questions limned by the ego such as "How will I survive if I'm laid off" and "I wonder if he's having an affair?"

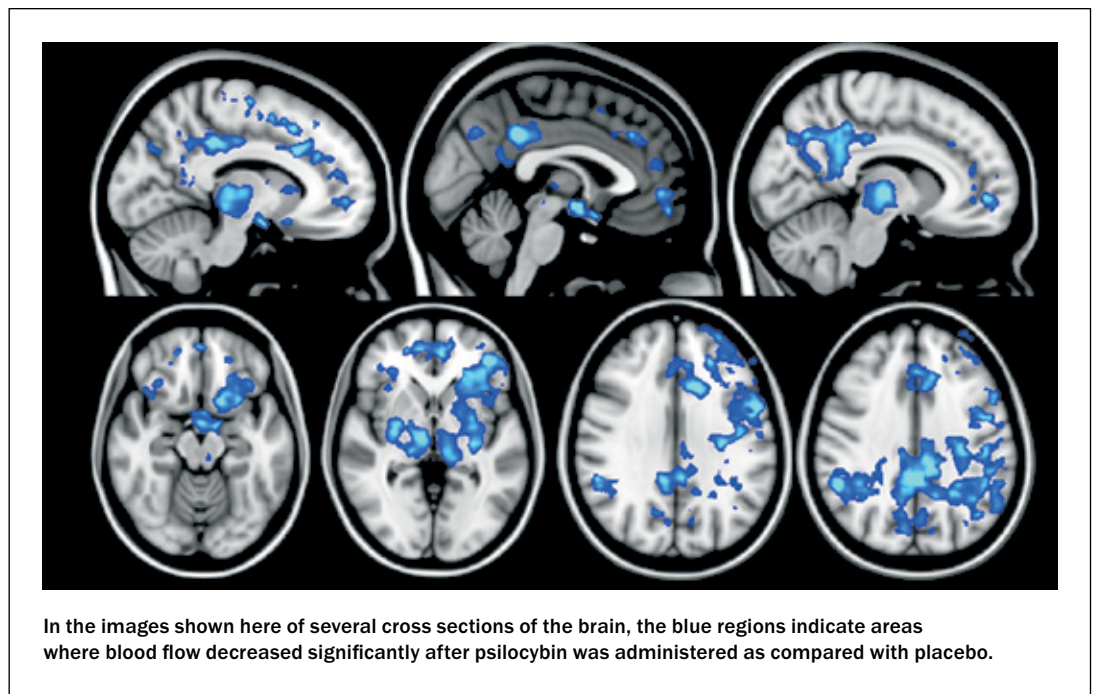
### Radical Curiosity

Subjects visit the Baltimore clinic twice, receiving a low dose of psilocybin on one visit and a moderately high dose on the next. We are screened for

mental, emotional and physical problems before we are officially admitted into the study. Giving psilocybin to people who have underlying psychotic disorders or schizophrenia can be catastrophic. Many volunteers are sent home after a day.

The researchers also brief us on "set and setting," a concept that was introduced in the early 1960s by LSD pioneer Timothy Leary to describe the optimal scenario for using hallucinogens as therapeutic tools. Set and setting are key factors in the equation. Set refers to "mind-set"—the patient's mental and emotional attitude toward the hallucinogenic experience. Setting is the physical and social environment—the room or space itself and the people who are present with the subject throughout the experience.

Set must include a willingness to move toward repellent or frightening thoughts and images, rather than trying to flee from them—either by trying to leave the room, which has happened with at least one subject at BPRU, or through emotional avoidance. For this reason, part of the set and setting equation includes complete trust in the guides, trained psychotherapists who remain throughout the entire session. The images and feelings can be beautiful and transcendent or terrifying and disgusting—or all of these over the course of a day. "Radical curiosity," said neuroscientist Roland Griffiths, study director at BPRU, when we first met. "That's how you have to approach this."



In the images shown here of several cross sections of the brain, the blue regions indicate areas where blood flow decreased significantly after psilocybin was administered as compared with placebo.

FROM "NEURAL CORRELATES OF THE PSYCHEDELIC STATE AS DETERMINED BY FMRI STUDIES WITH PSILOCYBIN," BY ROBIN L. CARHART-HARRIS ET AL., IN PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES USA, VOL. 109, NO. 6, FEBRUARY 7, 2012

“What do you think about God?” he asked me. “Where do we go **when we die?**” I didn’t know the answers.



Although modern medicine has helped prolong life for many people, including many breast cancer sufferers, it has largely failed to help patients cope with existential terror.

Four different psychotherapists and the study’s coordinator interviewed me for hours. They asked questions such as “If you had to spend the day being nauseated, could you tolerate it?” and “Do you ever think there are people or other beings who are transmitting secret coded messages to you alone?”

I filled out more than 50 pages of questionnaires, including assessments of optimism and pessimism, pain scales, depression scales, queries about my lifestyle and my habits, as well as one called Assessment of Spirituality and Religious Sentiments. My blood pressure was monitored every 15 minutes for two hours. The physical exams often uncover maladies that subjects themselves were not aware of. Borderline diabetes, heart arrhythmia or slightly off-par liver function will get you excluded, as well as traces of alcohol or drugs. All feelings and experiences—from childhood trauma to attitude to internal conflicts—are subjected to scrutiny. The guides have to know the lay of the psychic land so they can be supportive if

complex or painful feelings arise. They often do.

I met with Griffiths before my session. “What do you think about God?” he asked me. “Where do we go when we die?” I didn’t know the answers. By the end of the third day, I felt as though I had been flayed. But I’d passed, and I was in.

When my session day arrived, I was brought into a softly lit, comfortably decorated lounge, invited to lie down on a sofa and listen to music. Then I swallowed a purple capsule of psilocybin.

Some time later, when I was deeply within the world of the drug and the imagery it evoked, I found myself inside a steel industrial space. I became aware of my animosity toward my two living siblings. A woman seated at the end of a long table, wearing a net cap and white clothes and working busily, turned and handed me a Dixie cup. “You can put that in here,” she said. So I did. The cup filled itself with my bilious, sibling-directed feelings. “We’ll put it over here,” she said, and placed it on a table at the back of the room. Then she went matter-of-factly back to



work, along with now numerous busy women who occupied this space.

My guide, Fred, asked me what was happening. I sat up. As I recounted the scene, I began to laugh out loud, and my own laughter appeared to me in a midnight blue, cloud-dark sky as an effusion of twinkling gemstones, glittering in time with my peals of laughter, like a metronome.

Not all subjects have an all-encompassing transcendent experience during their sessions, wherein they feel a profound oneness with all things, a union with the universe or with God. I did not—and at first I was disappointed. But as the months have passed, I realize what I did gain is immeasurable.

harshness has ebbed. I am now able to feel more compassion both toward myself and toward others. I no longer spend my days worrying about what the future holds and whether I'll have a cancer recurrence or whether I'll die alone.

### Legal Hurdles

Grassroots movements may help push legalization of hallucinogens, as they did with medical marijuana. Initiated by AIDS sufferers and their advocates, the original California law, Proposition 215, effectively made possession of marijuana legal for pharmaceutical purposes in 1996 without prior FDA approval or the buy-in of pharmaceutical com-

## I no longer spend my days worrying about **what the future holds** and whether I'll have a cancer recurrence and die alone.

Since my session, my mood has improved, and my sense of myself as a person occupying a certain space in the universe has altered.

I have come to realize the universe consists of more than what readily meets the eye. An abiding sense of the inexplicable vastness of what is real and what is possible has affected my worldview. I no longer define myself by what has happened to my body, or even my emotional life, since my cancer diagnosis.

The vision of my own laughter producing a sky spilling jewels provided me with a kind of affirming metaphor. Shaking his finger at me at the time I told him, Fred commented: "Let that be a lesson to you, young lady."

It was.

Later on, when talking about my hallucinations with the clinicians and my guides, I found they provided me some profound truths about my life. My tendency to judge myself with a kind of murderous

panies. Seventeen other states and the District of Columbia have since followed suit.

But whereas marijuana can be safely self-administered, hallucinogens cannot. Traditional societies sequestered the experience of brain disinhibition within a ritual context supervised by shamanic healers for very good reasons. The powerful images and emotions they elicit require both context and guidance. Set and setting have to be honored because the drugs can be dangerous.

As the population ages and as more people face prolonged illness and end-of-life issues, the demand for improved palliative care and the inclusion of psychospiritual considerations is altering the way medicine will be practiced. The camel's nose is under the tent, and he's already halfway in.

Richards has far-reaching hopes for the future of hallucinogenic-assisted psychotherapy. He envisions the possibility of administering psilocybin to incarcerated sociopaths as an adjunct to talk therapy, perhaps enabling them to discover their empathic feelings toward themselves and others and eventually to reenter society's mainstream. A trial in the U.K., based at Imperial College, is recruiting patients suffering from intractable depression, whose illness has not responded to any conventional treatment.

When I asked David Nutt, director of the Neuropsychopharmacology Unit in the Division of Brain Sciences and clinical director of the upcoming Imperial College study about the obstacles presented by legal bans against psychoactive drugs, he said: "We'll change the law."

I hope he's right. **M**

### (Further Reading)

- ◆ **The Use of Psilocybin in Patients with Advanced Cancer and Existential Anxiety.** Charles S. Grob in *Psychedelic Medicine: New Evidence for Hallucinogenic Substances as Treatments*, Vol. 1. Edited by Michael Winkelman and Thomas B. Roberts. Praeger, 2007.
- ◆ **Neural Correlates of the Psychedelic State as Determined by fMRI Studies with Psilocybin.** Robin L. Carhart-Harris et al. in *Proceedings of the National Academy of Sciences USA*, Vol. 109, No. 6, pages 2138–2143; February 7, 2012.
- ◆ **Implications for Psychedelic-Assisted Psychotherapy: A Functional Magnetic Resonance Imaging Study with Psilocybin.** Robin L. Carhart-Harris et al. in *British Journal of Psychiatry*, Vol. 200, No. 3, pages 238–244; March 2012.