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Psychedelic medicine: Mind bending, health giving

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JOHN HALPERN clearly remembers what made him change his mind about psychedelic drugs. It was the early 1990s and the young medical student at

a hospital in Brooklyn, New York, was getting frustrated that he could not do more to help the alcoholics and addicts in his care. He sounded off to an older psychiatrist, who mentioned that LSD and related drugs had once been considered promising treatments for addiction. "I was so fascinated that I did all this research," Halpern recalls. "I was reading all these papers from the 60s and going, whoa, wait a minute! How come nobody's talking about this?"

More than a decade later, Halpern is now an associate director of substance abuse research at Harvard University's McLean Hospital and is at the forefront of a revival of research into psychedelic medicine. He recently received approval from the US Food and Drug Administration (FDA) to give late-stage cancer patients the psychedelic drug MDMA, also known as ecstasy. He is also laying the groundwork for testing LSD as a treatment for dreaded super-migraines known as cluster headaches.

And Halpern is not alone. Clinical trials of psychedelic drugs are planned or under way at numerous centres around the world for conditions ranging from anxiety to alcoholism. It may not be long before doctors are legally prescribing hallucinogens for the first time in decades. "There are medicines here that have been overlooked, that are fundamentally valuable," says Halpern.

These developments are a remarkable turnaround. Scientists first became interested in psychedelic drugs - also called hallucinogens because of their profound effect on perception - after Albert Hofmann, a chemist working for the Swiss pharmaceutical firm Sandoz, accidentally swallowed LSD in 1943. Hofmann's description of his experience, which he found both enchanting and terrifying, spurred scientific interest in LSD as well as naturally occurring compounds with similar effects: mescaline, the active ingredient of the peyote cactus; psilocybin, found in magic mushrooms; and DMT, from the Amazonian shamans' brew ayahuasca.

At first, many scientists called these drugs "psychotomimetics" because their effects appeared to mimic the symptoms of schizophrenia and other mental illnesses. However, many users rhapsodised about the life-changing insights they achieved during their experiences, so much so that in 1957, British psychiatrist Humphry Osmond proposed that the compounds be renamed "psychedelic", from the Greek for "mind-revealing". The term caught on, and psychiatrists started experimenting with the drugs as treatments for mental illness. By the mid-1960s, more than 1000 peer-reviewed papers had been published describing the treatment of more than 40,000 patients for schizophrenia, depression, alcoholism and other disorders.

A prominent member of this movement was Harvard psychologist Timothy Leary, who among other things tested whether psilocybin and LSD could be used to treat alcoholism and rehabilitate convicts. Although his studies were initially well received, Leary eventually lost his reputation - and his job - after he began touting psychedelics as a hotline to spiritual enlightenment. Leary's antics helped trigger a backlash, and by the late 1960s psychedelics had been outlawed in the US, Canada and Europe. Unsurprisingly, clinical research ground to a halt, partly because obtaining the necessary permits became



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much more difficult, but also because few researchers were willing to risk their reputations studying demonised substances.

But to some brave souls, psychedelic medicine never lost its allure. One of them is Rick Doblin, who in 1986 founded the Multidisciplinary Association for Psychedelic Studies (MAPS) in Sarasota, Florida, and who earned a doctorate from Harvard's Kennedy School of Government after writing a dissertation on the federal regulation of psychedelics. For nearly 20 years MAPS has lobbied the FDA and other government agencies to allow research on psychedelics to resume. It has also persuaded scientists to pursue the work and raised funds to support them. A similar body, the Heffter Research Institute in Santa Fe, New Mexico, was founded in 1993 by scientists with an interest in hallucinogens.

In the past couple of years their efforts have begun to pay off. Doblin is optimistic that psychedelic research is back for good, and this time it will do things right. "This gives us the chance to show that we have learned our lessons," he says. Halpern, too, is anxious to lay to rest the ghost of Leary. "That man screwed it up for so many people," he says.

With this in mind, Halpern says the first task for him and others is to evaluate the safety of psychedelics. And they are up against an entrenched orthodoxy: a 1971 editorial in *The Journal of the American Medical Association* warned that repeated ingestion of psychedelics causes personality deterioration. "Only a few of those who experience more than 50 'trips' are spared," it warned.

"I was reading all these papers from the 60s and going, whoa, wait a minute! How come nobody's talking about this?"

So Halpern's first big foray into psychedelic research was aimed at risk-assessment. In the late 1990s he launched a study of members of the Native American Church, who are permitted by US law to consume peyote. Halpern examined 210 residents of a Navajo reservation in the south-west US, who fell into three categories: church members who had taken peyote at least 100 times but had had little exposure to other drugs or alcohol; non-church members who abstained from alcohol or drugs; and former alcoholics who had been sober for at least three months.

Halpern tested the subjects' IQ, memory, reading ability and other functions. His interim results showed that church members had no cognitive impairment compared with the abstainers, and scored significantly better than recovering alcoholics. Church members also reported no "flashbacks" - sudden recurrences of a psychedelic's effects long after the initial trip. Halpern believes this study, which he expects will be published soon, shows that contrary to the 1971 editorial, peyote at least can be taken repeatedly without adverse effects.

He is now conducting a similar assessment of MDMA. This drug is sometimes called an "empathogen" because it heightens feelings of compassion and reduces anxiety. Anecdotal reports suggest it has therapeutic potential, and some psychiatrists used it alongside psychotherapy before it was outlawed in 1985. However, anecdotal and scientific evidence have also linked MDMA with brain damage, though the research is controversial.

Ecstasy impact

Judging the true impact of MDMA is complicated by the fact that users often combine it with other drugs and alcohol. To get around this, Halpern recruited a group of American mid-westerners who admitted taking MDMA but said they shunned other substances. He separated them into "moderate" users, who had consumed MDMA 22 to 50 times, and "heavy" users, who had taken it more than 50 times.

Halpern recently reported in the journal *Drug and Alcohol Dependence* that, compared with controls, heavy users displayed "significant deficits" in mental processing speed and impulsivity. Moderate users, however, had no major problems. Halpern believes this shows that MDMA's benefits may outweigh its risks for certain patients. And apparently the FDA and the McLean Hospital agree, since both have approved Halpern's plan to test MDMA as an anti-anxiety drug for a dozen late-stage cancer patients. Halpern still needs permission from the Drug Enforcement Administration, but he expects to begin recruiting patients soon.

He is also interested in the potential benefits of the true hallucinogens. In 1996, he reviewed almost 100 substance abuse trials involving LSD, psilocybin, DMT and ibogaine, an extract of the African shrub *Tabernanthe iboga*. Halpern found tentative evidence that the drugs can reduce addicts' cravings during a

post-trip "afterglow" lasting for a month or two. Exactly how this happens is something of a mystery. A popular theory is that the benefits stem from the drugs' psychological effects, which include profound insights and cathartic emotions, but Halpern suspects that there may be a biochemical explanation too.

For now, however, Halpern isn't planning to pursue addiction therapy. He is more interested in another medical use for LSD and psilocybin: treating a debilitating condition known as cluster headaches. These attacks appear to be caused by swelling of blood vessels in the brain and are worse than migraines. Sufferers say the pain exceeds that of passing a kidney stone or giving birth without anaesthetics. They affect about 3 in every 1000 people sporadically, and 1 in 10,000 chronically. "There's a tremendous potential need for this," says Halpern, who investigated the problem after being approached by a patient group.

Many patients get little or no relief from painkillers, but some claim that small doses of LSD or psilocybin can alleviate the headaches and even prevent them from occurring. Halpern was intrigued; LSD is chemically related to ergot, a naturally occurring compound that constricts blood vessels, and the derivatives ergotamine and methysergide are commonly prescribed for migraines.

Halpern and his Harvard colleague Andrew Sewell are now gathering evidence to persuade licensing officials - and themselves - that LSD and psilocybin merit a clinical trial. Sewell has gathered more than 60 testimonials from cluster headache sufferers who have treated themselves with LSD or psilocybin.

Another member of the vanguard in the psychedelic revival is Charles Grob, a psychiatrist at the Harbor-UCLA Medical Center in Los Angeles, California, and co-founder of the Heffter Institute. After years struggling to get permits, Grob says he is slowly moving forward with a study into using psilocybin to reduce distress in terminal cancer patients. He points out that studies done in the 1960s suggested that psychedelics can help patients come to terms with their impending death. So far Grob has treated three patients, but he hopes to enrol more subjects shortly.

Grob has also led several investigations like Halpern's peyote study, but looking at ayahuasca, the DMT-rich shamanic brew. Ayahuasca often causes nausea and diarrhoea, and its psychedelic effects can be terrifying, but Amazonian shamans nonetheless prize it for its visionary properties. Since 1987 it has been a legal sacrament for several churches in Brazil, the largest of which is União Do Vegetal. UDV combines elements of Christianity with nature worship, and claims 8000 members.

In 1996 a team led by Grob reported in the *Journal of Nervous And Mental Disease* that UDV members who regularly took ayahuasca were on average physiologically and psychologically healthier than a control group of non-worshippers. The UDV followers also had more receptors for the neurotransmitter serotonin, which has been linked to lower rates of depression and other disorders. Many of the UDV members told the scientists that ayahuasca had helped them overcome alcoholism, drug addiction and other self-destructive behaviours.

“Addicts often end up filled with revulsion for their past lives and determined to change” More recently, Grob has found that adolescents who grew up participating in ayahuasca ceremonies showed no ill effects and were less likely to engage in crime and substance abuse than members of a control group. Of course, Grob acknowledges that they could be benefiting from the social effects of membership in a church as well as the effects of ayahuasca itself. Grob plans to publish these results this year.

Several other scientists are quietly pursuing psychedelic research. Since 2001, psychiatrist Francisco Moreno of the University of Arizona in Tucson has been testing psilocybin as a treatment for obsessive-compulsive disorder. Psychotherapy and antidepressants such as Prozac help many patients, but some have such severe symptoms and are so resistant to treatment that they turn to electroshock therapy and even brain surgery. As with the work on cluster headaches, Moreno's study was motivated by reports from people with OCD that psilocybin relieves their symptoms.

So far, Moreno has given both sub-psychedelic and psychedelic doses of pure psilocybin to nine treatment-resistant OCD subjects, in a total of 29 therapy sessions. His preliminary findings suggest firstly that it is safe to ingest psilocybin, which was a primary concern of the trial. Beyond that, Moreno calls his results "promising", but won't discuss them further, since he plans to submit a paper to a peer-reviewed journal this year.

“By the mid-1960s, over 1000 papers had been published describing psychedelic therapy”

Meanwhile in Charleston, South Carolina, physician Michael Mithoefer is carrying out a MAPS-sponsored clinical trial of MDMA as a treatment for post-traumatic stress disorder. PTSD affects up to 20 per cent of people who experience a traumatic event, and involves distressing symptoms such as nightmares and panic attacks. Conventional treatments typically consist of cognitive therapy and antidepressants, but many patients don't respond to these. In the past year Mithoefer has given "MDMA-assisted" psychotherapy to six treatment-resistant patients, all traumatised by violent crimes; he plans to treat 20 patients in all.

The longest-running psychedelic therapy programme started almost 20 years ago in Russia. Evgeny Krupitsky, a psychiatrist who heads a substance-abuse clinic in St Petersburg, has treated more than 300 alcoholics and about 200 heroin addicts with ketamine. Used primarily in veterinary medicine, ketamine is an anaesthetic that can trigger an extremely disorienting hallucinogenic episode lasting an hour or so. Krupitsky's subjects often emerge from their sessions filled with revulsion for their past lives and determined to change. The therapists encourage these feelings with tricks such as forcing the subjects to sniff a bottle of vodka at the peak of their session; the patients' disgust often persists long after the ketamine's effects have worn off.

In one of Krupitsky's studies, 73 out of 111 alcoholics stayed dry for at least a year after their session, compared with 24 per cent of those in a control group. Yet his programme, which was funded by MAPS and the Heffter Institute, was recently shut down because the Russian government tightened restrictions on ketamine. Although Krupitsky says he and his colleagues "are in the process of getting permission to continue", it may be several years before research resumes.

Although disappointed by this setback, Doblin is encouraged by developments elsewhere. He is lobbying officials in Spain and Israel to approve studies of MDMA for PTSD, and is raising funds for a substance-abuse trial of ibogaine outside the US together with the Heffter Institute. MAPS has also supported Frans Vollenweider, a psychiatrist at the University of Zurich in Switzerland, who has done basic research on the physiological effects of psilocybin and MDMA, and hopes to begin clinical research soon.

Doblin's primary goal is to see psychedelics legally recognised as medicines. But he also hopes that someday healthy people may take these substances for psychological or spiritual purposes, as members of the Native American Church and União Do Vegetal do, and as he did in his youth. After all, drugs such as Prozac and Viagra are already prescribed not just to heal the ill but also to enhance the lives of the healthy.

It is still an uphill struggle. Government funds for psychedelic studies are hard to come by, and drug companies have shown absolutely no interest in supporting the research. But there are signs that the wind is changing. Although psychedelics are still classified in the US as schedule-1 drugs, and so are banned for all non-research purposes, in November a US Federal Appeals Court in Colorado ruled that a branch of the UDV based in Santa Fe, New Mexico, could import ayahuasca for use in ceremonies. Among the research findings cited in the court decision were Grob's studies showing no ill effects from ayahuasca. The Department of Justice is appealing the decision, but if the Supreme Court denies the appeal, UDV members in the US will be able to ingest ayahuasca legally.

Maybe, just maybe, after more than 30 years in the wilderness, this powerful, misunderstood but potentially mind-healing class of drugs is ready to be rehabilitated.

John Horgan is a freelance science writer based in Garrison, New York. His latest book, *Rational Mysticism* (Mariner Books), was published in paperback last year
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