Medicine's psychedelic renaissance

For 50 years, virtually all medical research into psychedelic substances stopped. That research has now been renewed—and these radical therapies are again threatening to upend accepted clinical wisdom

BY TRISTAN BRONCA
Vancouver

In 2011, Health Canada threatened Dr. Gabor Maté with arrest for conducting what it believed to be an unauthorized clinical trial of the hallucinogenic tea called ayahuasca.

Fresh off the success of *In the Realm of Hungry Ghosts*, his book on addiction, Dr. Maté had begun receiving notes about how the brew, which is typically made from the South American *Banisteriopsis caapi* vine and the *Psychotria viridis* leaf, might be used to treat addiction. At first, he didn't pay much attention, but as the feedback continued to pour in, he soon received an invitation to take part in an ayahuasca ceremony in Vancouver. Dr. Maté—who had spent 12 years of his career treating addicts in the city's Downtown Eastside—accepted.

"I saw immediately why it had potential," he said. "If you told me 10 years ago there's a substance that can do what I've seen it do since, I would have said you're crazy."

Dr. Maté has staked much of his reputation as an addiction physician on a controversial hypothesis: that trauma is at the root of addiction. He theorized that ayahuasca works by breaking down the barrier between the unconscious and conscious parts of the psyche, allowing, among other things, patients to "revisit a childhood experience with the insight of an adult." The idea is that afterward, patients emerge with a clearer understanding of the nebulous pain driving their addiction and are better equipped to escape it. Dr. Maté compared it to forms of meditation or a deep-insight-oriented psychotherapy. "But (those methods) take much longer," he said. "When I do a retreat with ayahuasca, people say it's 10 years of psychotherapy in seven days." It has almost nothing to do with the brew and everything to do with the experience.

This holistic approach has shown promise. In a review of 28 human studies recently published in the *Journal of Psychopharmacology*, the researchers concluded that not only did the ayahuasca experience show "anti-depressive and anti-addictive potentials," it also had a physiological effect on the brain, affecting the size and thickness of the areas associated with impulse control, decision-making, pain and memory.

When Dr. Maté accepted an invitation to oversee a series of ayahuasca ceremonies at a First Nations community in B.C. (a group suffering from a long history of addiction), he had already been conducting psychotherapeutic work around these ceremonies for a few years. This time, however, a group of researchers from the University of British Columbia had asked to conduct an observational study. Dr. Maté obliged, and shortly after, Health Canada intervened.

"I haven't worked with it in Canada since the warning," Dr. Maté said. While Health Canada has acknowledged—publicly and in writing—that the brew is neither harmful nor addictive, it's still a banned substance, listed in the schedule of Food and Drug Regulations alongside drugs "that are considered to have no medical benefit." That list includes a number of other psychedelics that are now of particular interest to researchers.

But Dr. Maté isn't one of them. He continues to work with the brew in other parts of the world, convinced that its therapeutic potential is too powerful to be ignored, but isn't interested in trying to prove it to his medical colleagues. "I'm 72 years old," he said. "If I waited for all the research to be done and for the stuff to be officially accepted I'd be mouldering in my grave."

Buried history

Ayahuasca is one of the latest substances to emerge from a blind spot in modern medical research that has spanned nearly 50 years. It is also among a group of age-old hallucinogens that have been used in indigenous healing rituals in the Mojave Desert (peyote), the Amazon basin (ayahuasca) and the jungles of Africa (iboga) for hundreds of years. Perhaps longer. In a podcast for *Vancouver Real*, Mark Haden, chair of the board of directors for the Multidisciplinary Association for Psychedelic Studies (MAPS) Canada, said psychedelics even appear in ancient texts of Greece and India. But up until the last five years or so, they were only seriously studied for about a decade in the 1950s and '60s.

There are myriad reasons for this, but perhaps the most obvious is political. Quite simply, the public views psychedelics very suspiciously, and those views have reverberated through the scientific community. Researchers have been unwilling to risk their reputation studying them and when they did, governments often presented a barrage of logistical and regulatory obstacles that made things prohibitively expensive.

For example, in the MAPS Canada trial for MDMA (ecstasy), the only psychedelic to be studied in Canada in the last 50 years, the drug needed to be kept in what Haden half-jokingly described as a "bomb-proof safe," which required the team to make serious structural changes to the upper floor of a pharmacy. The safe held only about $2,000 worth of the drug, but the cost of storage was significantly higher.

At the root of this regulatory resistance is one substance: lysergic acid diethylamide, or LSD. Shortly after its psychedelic properties were discovered, LSD almost immediately became a sensation in medical research communities around the western world. Between 1950 and 1965, the drug was the subject of more than 1,000 scientific papers, dozens of books and six international conferences.

The problem was that it became of great interest to many others as well.

In the early 1950s, the Prairie town of Weyburn, Sask., became the home of one of the world's leading LSD research centres. It was here that psychiatrist Dr. Humphry Osmond showed it could be used to treat personality disorders and alcoholism (the founder of the famous 12-step program was said to have been inspired by an LSD trip). But farther east, at the Allan Memorial Institute in Montreal, the drug was secretly being used for more malicious purposes. In the CIA-backed MKUltra studies, some patients were unwittingly dosed in an effort to develop new interrogation techniques.

Others thought the drugs were far too important to be left in the realm of medicine alone and so began distributing them to musicians, artists and celebrities. Soon, LSD became a fixture in the American counterculture. The media caught wind of some alarming stories of drug abuse, public opinion (which had been largely positive to that point) did a half-gainer, and by 1970, the drug was banned all over the U.S. and Canada. Meanwhile, LSD vanished quietly from medical school curricula, and new research into psychedelics stopped entirely. Today, few medical students are aware that psychedelics had any history at all in western medicine.

In an interview with **continued on • page 20**

What happened to LSD?

A partial history of the far-too-popular psychedelic

- Nov. 16, 1938 – Swiss chemist Albert Hofmann synthesizes lysergic acid diethylamide in his lab.

- April 19, 1943 – Hofmann accidentally discovers the psychedelic properties of LSD after he absorbs a small amount through his fingertips.
- 1951 – Psychiatrist Dr. Humphry Osmond moves to Weyburn, Sask., to begin his studies on the drug.

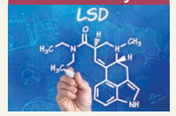
- 1953 – Project MKUltra, the CIA-sponsored initiative that would become popularly known as "the mind control studies," begins several ethically dubious experiments with LSD.
- 1957 – Dr. Osmond proposes the term "psychedelic" at a meeting of the New York Academy of Sciences. As he wrote in a letter to author Aldous Huxley: "To fathom Hell or soar angelic, just take a pinch of psychedelic."

- 1957 – Al Hubbard, a former military man and LSD enthusiast, opens a private hospital in B.C. with Vancouver's Dr. Ross MacLean, selling the drug to anyone who can cover the $500 fee. Celebrities such as Cary Grant soon come seeking their services.

- 1959 – Hubbard leaves the clinic for California, where he begins distributing the drug for free to recreational users.
- 1950 to 1965 – An estimated 40,000 patients worldwide are treated with LSD.
- 1966 – Former Harvard professor Dr. Timothy Leary (PhD), LSD's great popularizer, coins the phrase "turn on, tune in, drop out," which would be the high-water mark of the drug's role in the counterculture. Concerns over its dangers also reach a fever pitch.

- May 30, 1966 – Governors of Nevada and California sign bills outlawing the drug.
- Oct. 24, 1968 – The drug is banned in every U.S. state.
- 1969 – Canada outlaws LSD.

What the science says…



Results from some recent clinical studies of psychedelic drugs ▶

- **MDMA for PTSD**

10 of 12 patients on the drug no longer met the DSM-IV criteria for PTSD after treatment, compared with just two of eight following placebo-aided therapy—*Journal of Psychopharmacology*, Jul. 19, 2010

- **Psilocybin for anxiety in advanced-stage cancer patients**

Patients **dropped 15 points on the STAI anxiety scale** and results were still evident six months after just one dose —*Archives of General Psychiatry, Sept. 6, 2010*

- **Ibogaine for addiction**

61% of participants abstinent after treatment but length of time varied. Those who were treated only once remained abstinent for a **median of 5.5 months,** while those treated multiple times were abstinent for a **median of 8.4 months**—*Journal of Psychopharmacology, Sept. 29, 2014*

- **Ayahuasca for depression**

Depressive scores dropped by as much as **82%** and effects persisted when measured **21 days** after the drug was administered —*Revista Brasileira de Psiquiatria, 2015*

Above right: Robert Carter; lower left: CP Archive; lower right: iStockphoto

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the CBC, Dr. David Nutt, a British psychiatrist and former drug safety adviser to the U.K. government, said the research chill that occurred since LSD was criminalized amounts to the worst censorship in the history of science.

"It's even worse than when the Catholic Church found a telescope in 1616," he said. "In those days there weren't very many scientists and science wasn't progressing very fast, but in the last 50 years, brain science has increased 10-fold."

The end of the blackout

The idea that psychedelic users are predominantly rock stars, artists and aimless youth is really a holdover from Nixon-era thinking. According to Jay Stevens, the author of *Storming Heaven: LSD and the American Dream*, the majority of users in the early years of the ban were actually medical researchers and academics who had been exposed to (and taken) the drug in their work. For example, Dr. Osmond's staff—from the nurses to the ward's architects—were asked to take LSD to come to a clearer understanding of what the patients were experiencing during therapy. It was a sort of chemically aided empathy.

But after the ban, the terms of use had changed. It wasn't until Rick Doblin founded MAPS in 1986 that the flickers of serious scientific research were rekindled.

MAPS Canada chair Mark Haden first became interested in psychedelics about 10 years ago as a social worker in Vancouver Coastal Health's addiction services. That was where he was exposed to ibogaine, a psychoactive substance found in the African iboga root that is believed to suppress the effects of withdrawal from short-acting opioids such as heroin or oxycodone. Haden said the only time he's ever heard a patient say they had been healed was after that patient was treated with ibogaine.

Thus began Haden's mission to legitimize research into the drug. He began inviting physicians and other health-care providers to bimonthly dinners in hopes of sparking new discussions. But he had a difficult time getting them on board.

"This was about eight years ago," he said, "and when I retired it's interesting how the world changed. Last year, Vancouver Coastal Health invited me back to present on the exact same ideas and I got a completely different reception."

Haden credits the shift in Vancouver to Dr. Evan Wood, an internationally recognized authority on inner-city medicine and medical director of addiction services at Vancouver Coastal Health. He began talking openly about doing psychedelic research and even the possibility of starting a centre dedicated to this research at St. Paul's Hospital. (Interestingly, Dr. Wood credits the shift to new research out of Johns Hopkins University that showed certain psychedelics could help people quit smoking. "It's helped open up people's minds to the need for novel and safe approaches," he wrote in an email.)

After that, attendance at Haden's bimonthly dinners shot up. As he put it, the endorsement gave a lot of people permission.

Fathom hell or soar angelic

There is an entire Wikipedia page devoted to the urban myths used to warn against the mind-melting dangers of drugs. There's the classic tale of the man who took LSD and believed he could fly, only to jump from a balcony (or cliff or window) and plummet to his death. Or there's the myth about a group of kids who apparently got so high that they went blind staring at the sun in the middle of the day (it's no coincidence that LSD and marijuana, two of the most heavily politicized drugs in recent history, factor most heavily in these myths). Perhaps the most lurid tale is that of the hippie babysitter who, while on LSD, put a baby in the oven and an uncooked turkey in the bassinet.

Mark Haden

Most of these stories were hoaxes, while others, like the flying man, overstated the role the drug played (the original cases usually were ruled to be suicides or more modest cases of misjudgment). Still, their popularity spoke to some very powerful anxieties surrounding the use of LSD in particular. And while the concerns were overblown, they weren't entirely unwarranted. That's especially true for the class of psychedelics known as entheogens.

The entheogens include LSD, psilocybin (found in magic mushrooms), mescaline (found in peyote), and DMT (the active ingredient in ayahuasca) and are defined by their ability to induce a kind of spiritual experience. By contrast, MDMA belongs to a class of psychedelics known as the empathogens, which are named for their ability to induce feelings of connectedness with others. With the empathogens, perhaps the most notable downside is that their use is often followed by a short period of depression. However, early research has suggested that this "down" often passes unnoticed in MDMA-assisted therapy. Haden compared it to a small wave in a big ocean: people notice it when they're taking street drugs because their metaphorical ocean is calm and the next day they wake up and they have to go to work or school; but for those who are suffering from mental health disorders, there is already plenty of turbulence.

> The way practitioners frame the experience can be an especially powerful force for either healing or harm.

The entheogens are a different story. In psychedelic research parlance, they "disorient the ego." And despite the clinical applications of this, it can be terrifying.

In a study out of Johns Hopkins University published earlier this year in the *Journal of Psychopharmacology*, researchers surveyed nearly 2,000 adults about their "bad trips" on magic mushrooms (a very similar experience to taking LSD). Sixty-two per cent said it was among the 10 most difficult situations of their lives (11% said it was the most difficult).

By some accounts, ayahuasca can be worse, since it is almost always accompanied by intense feelings of sickness and vomiting. In a recent story for the *New Yorker*, one drinker described an early encounter with the brew as the most painful experience of his life "by a factor of a thousand."

"I felt like I was being torn apart," he told the reporter. He went through hours of grand mal seizures and woke up with rug burns on his face the next day.

What these nasty experiences have in common, however, is that they tend to occur in uncontrolled environments. Both Haden and Dr. Maté emphasized that the patient's mindset and the atmosphere (what they refer to as "the set and setting") of psychedelic therapy are as important as the active ingredient. Whether it's an ayahuasquero overseeing an indigenous ceremony, or a psychiatrist presiding over a psilocybin-aided therapy session, the way practitioners frame the experience can be an especially powerful force for either healing or harm.

In properly controlled settings, negative psychological effects such as psychosis are completely absent, and even in the cases of unregulated use, the physical harms aren't usually all connected to the psychedelics themselves. With most other pharmaceuticals you can often harm yourself with about six times the recommended dose, but you would have to take about 1,000 times more to overdose on LSD. (The notable exception here is ibogaine, which can have adverse cardiac effects in certain alcohol and opioid users, and so requires much more careful oversight.) With ayahuasca, the most dangerous experiences usually occur when ill-qualified ayahuasqueros attempt to intensify the experience by cutting the brew with another jungle plant called datura, which induces delirium and was used in some cultures as a poison.

Still, unpleasant experiences do happen in clinical settings, but the positive health outcomes aren't usually affected. The Johns Hopkins study found that 76% of the patients surveyed actually walked away from the bad trip with an improved sense of personal well-being and 46% said they

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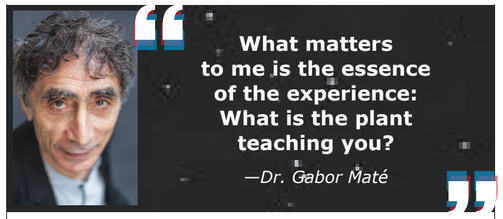
would be willing to experience it over again. Even the ayahuasca user from the *New Yorker* story would go on to use the brew regularly, claiming the anger he had held onto since childhood disappeared in the months after his initially horrific experience.

"If somebody has a vision of jaguars and anacondas and jungle plants, that's really beautiful but I don't care," said Dr. Maté of ayahuasca. "If somebody has experiences of terror and agony, I also don't care. What matters to me is the essence of the experience: What is the plant teaching you?"

The science problem

Phase II clinical trials using MDMA to treat post-traumatic stress disorder recently wrapped up, and both Haden's group and his American counterparts are now seeking approval for phase III trials. If things continue on their current trajectory, Haden is sure MDMA will be approved for psychotherapeutic use in Canada within five years.



But there continue to be unique challenges in psychedelic therapy. For example, double-blind clinical trials have always been impossible because both researchers and patients very quickly become aware of who has been given a placebo. MAPS has been able to manage this problem through creative study design in the MDMA trials, but it's difficult to say whether something like ayahuasca would be able to meet the strict criteria required by Health Canada.

Even if most entheogens could meet those criteria, it's not clear that pharmaceutical companies could make a business case for investing in them—another massive hurdle for expanding their medicinal use. With the exception of LSD and, in Vancouver at least, ibogaine, the entheogens are consumed in something very close to their natural form, which makes it difficult for any one company to control access to them. Plus, the therapeutic value lies in the experience. If that experience is life-altering, as the literature suggests, it isn't usually necessary for people to take the drug much more than once. There are few repeat customers.

Still, some clinicians are confident that these substances will slowly work their way into mainstream medicine. Although, assuming they overcome the other hurdles, such an introduction would require a change in the way we view these drugs, Western medicine, or both.

In a 2014 paper published in *Current Drug Abuse Reviews*, Dr. Kenneth Tupper (PhD), a public health professor at the University of British Columbia, and Dr. Beatriz Labate (PhD), an anthropologist in Guadalajara, Mexico, argue that scientific and legal establishments are always looking to reduce medicines to their active ingredients in the interests of safety and control. To use a common example, cannabis isn't medicine in the eyes of most doctors, but the active ingredients—cannabidiol and tetrahydrocannabinol—are. Ayahuasca defies this reductionism. Every brew is different, as is each patient experience, and to assume that the psychoactive component can be taken out, bottled and prescribed, presumes ("rather unscientifically," the authors argue) that the ceremonial aspects and the non-psychoactive elements of the brew don't have any therapeutic value (recall the importance of set and setting). But the alternative—physician-ordered attendance at an ayahuasca ceremony, for example—seems incompatible with mainstream medicine.

Nevertheless, as Dr. Tupper and Dr. Labate wrote, the scientific worldview has its own built-in biases. Whether or not physicians recognize this may determine whether psychedelics enter popular use or fade to the fringes of alternative medicine. **MP**