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Dream drug or demon brew?

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A mind-altering substance used in shamanistic rituals may hold clues to dreaming and a natural way of alleviating depression but could also trigger schizophrenic hallucinations. Lisa Melton investigates

IN THE brightly lit chapel, the ceremony is due to begin. Dennis McKenna lines up with 500 others to sip the sacrament. It takes 45 minutes before it hits him. Then, eyes closed, he finds himself hovering above the Amazon basin, aware of the massive forests and the meandering rivers beneath. A giant vine winds up towards him and he hurtles down it, shrinking as he goes until the leaves themselves seem the size of trees. Shrinking further, he finds himself surrounded by a new forest made up of molecules engaged in photosynthesis. McKenna, an ethnobotanist from the University of Minnesota in Minneapolis, is high on ayahuasca.

Ayahuasca is not the latest party drug but a foul-tasting plant concoction Amazonian people have been downing for centuries. It is the stuff of legends, credited with sending people on the most incredible trips. Today this bitter tea, also known as hoasca, has become the sacramental ritual of two modern religions in Brazil; one of them, the Unio do Vegetal (UDV) church, has invited McKenna, an expert on psychoactive plants, and other research teams, to scrutinise this sacred brew.

Their fascination with ayahuasca stems from a little-known mind-altering compound called dimethyltryptamine, or DMT, a substance the

sacred tea contains by the bucketload. When it comes to psychedelic compounds, DMT is in a league of its own, as the only hallucinogen our body produces naturally.

Scientists have found DMT pretty much everywhere they've looked in animals, plants and fungi. But despite its ubiquity, DMT's role remains a mystery. Some believe it fuels vivid dreams, mystical revelations and religious exaltation, as well as playing a part in memory. The more sinister possibility is that over-producing DMT could tip a person over the edge into insanity, inducing the psychotic symptoms of schizophrenia. McKenna and his colleagues hope the tripping churchgoers could help them find the answers.

DMT doesn't hang around long enough for people to study it easily. It acts rapidly and is broken down swiftly by the enzyme monoamine oxidase (MAO). Normally if you eat or drink it, DMT doesn't stand a chance of getting into the brain as MAO in the gut breaks it down.

Cocktail effect

Shamans, McKenna discovered, overcame this problem by carefully combining plants in the ayahuasca brew. One is the *Psychotria viridis* bush, which is packed with DMT. The other is the vine *Banisteriopsis caapi*, which contains harmine, one of the most effective MAO inhibitors. By inactivating MAO with the vine bark, DMT can be absorbed from the gut and crosses the blood-brain barrier to trigger a psychedelic response.

It turns out that harmine-like compounds are also ubiquitous in our bodies. This led some researchers to suggest that maybe our bodies regulate the levels of DMT in the same way as in the tea, sometimes boosting its activity by knocking out MAO so it can fulfil some sort of physiological role.

Pharmacologist Jordi Riba from the University of Barcelona, Spain, has been trying to work out what that physiological role might be, using brain scans

to study its effect on brain activity. His preliminary results are tantalising, showing areas lighting up that are related to memory. Riba believes DMT may be involved in retrieving facts and experiences. "When you give people ayahuasca, they re-experience memories that are there already. It's like pressing a random access button to your stored memories," he says.

Jace Callaway from the University of Kuopio in Finland has another idea. He suggests that endogenous DMT and harmine-like substances may play a role in generating dream imagery. "We experience psychedelic states on a regular basis while dreaming," he says.

But while its natural role is still uncertain, a more unnatural role is coming to the fore. The effects produced by psychedelic drugs are strikingly similar to the symptoms of psychosis. In the 1950s, these similarities led to the suggestion that psychoactive compounds like DMT were the cause of schizophrenia.

According to the theory, an enzymatic disturbance in the body could lead to overproduction of hallucinogenic compounds. And if MAO activity is low, as suspected in people with schizophrenia, the compounds would linger and the hallucinations they trigger seep into everyday existence.

But researchers had always failed to detect consistent differences in DMT levels between patients and controls. "I spent my youth collecting and analysing gallons of urine from people with schizophrenia," recalls Robin Murray from the Institute of Psychiatry in London. "The endogenous DMT hypothesis of schizophrenia was never disproved but was just overtaken by the dopamine theory, which was more immediately plausible."

But the theory is enjoying something of a comeback. Alicia Pomilio, an organic chemist, and Jorge Ciprian-Ollivier, a psychiatrist, at the University of Buenos Aires in Argentina realised that the church congregation members could help them to look for the signature of DMT in the urine

using gas chromatography and mass spectrometry. Once they knew what to look for, they were able to detect traces in the urine of patients with active schizophrenia but not in controls. It is not clear whether people with schizophrenia are producing too much DMT, or too little MAO the result would be the same. But the discovery is exciting in that it paves the way to finding new drugs to treat schizophrenia.

But if DMT might be the cause of one medical problem, it could be the cure for others. McKenna has found that DMT exerts its effect by attaching mainly to one particular type of serotonin uptake site called 5-HT_{2A}, as do other psychedelic drugs such as LSD, psilocybin and mescaline. Serotonin is a mood-altering neurotransmitter, also known to influence sleep, appetite, aggression and love. The newest class of antidepressant drugs, including Prozac, are thought to work by blocking the uptake of serotonin into nerve cells. Callaway's recent studies suggest that ayahuasca might have some of the effects of antidepressant drugs nature's very own Prozac.

He measured serotonin levels in rats after giving them ayahuasca and says the levels of the neurotransmitter "go through the roof". After drinking hoasca tea users report a feel-good effect that can last for days. Callaway found that hoasca drinkers had a greater than normal density of serotonin uptake sites on their blood platelets, where they are easier to measure than in the brain. People seem to respond, he says, by creating more receptors. When they are not getting a buzz from the tea, the additional receptors hunger for more serotonin, pushing the body to produce more.

But does the brain bump up its number of serotonin uptake sites too? Using a brain imaging technique that labels serotonin receptors, Callaway has now tested one person, and found signs of a similar upregulation in a serotonin-rich region of the brain. Of course, this observation needs following up, but it's an encouraging sign. "It's a true tonic effect," says Callaway. The sacred tea "apparently does what antidepressants fail to do. It could lead to

long-term plastic changes in the brain without having to pop a pill every day."

Charles Grob, a psychiatrist at the University of California, Los Angeles, School of Medicine, reckons that this sustained effect on mood makes ayahuasca a good candidate for treating addictions as well as alleviating depression. People with serious alcohol problems and mood disorders were transformed by the church. All religions boast life-changing stories, but Grob believes the tea itself is important. There is already one centre in Peru testing ayahuasca in clinical trials for drug abuse.

But the researchers are proceeding cautiously. Many people have been taking the hallucinogen within the supportive setting of the UDV for 30 years with seemingly no adverse side effects. But it is not always so. "If the tea is not properly prepared, or in the hands of an individual without the appropriate support, the consequences can be negative," says Grob. Even in the highly controlled lab setting it can trigger twitching, vomiting and diarrhoea. Useful if you are an Amazonian hunter wanting to rid your gut of parasites, perhaps, but not exactly convenient if you are wearing your best party gear.

Lisa Melton
Lisa Melton is a science writer at the Novartis Foundation in London, born and raised in Argentina

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