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'I Wanted To Live': New Depression Drugs Offer Hope For Toughest Cases

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This is MORNING EDITION, from NPR News. I'm Renee Montagne.

STEVE INSKEEP, HOST:

And I'm Steve Inskeep. Good morning.

For half a century now, most drugs for depression have targeted the same short list of chemicals in the brain, especially serotonin. But antidepressants like Prozac can take more than a month to kick in, and they don't work at all for up to 40 percent of people with major depression.

So researchers are looking for antidepressants that work in totally new ways. We reported yesterday on one possible drug, and we have more this morning. NPR's Jon Hamilton reports on this drug best known by its street name: Special K.

JON HAMILTON, BYLINE: The buzz about Special K has been building for several years now. Of course, researchers use the drug's proper name: ketamine. It's an FDA-approved anesthetic that's been around for decades.

Back in the 1970s, recreational drug users realized that if you take enough ketamine, you can have a mind-bending experience. But the drug's ability to relieve depression wasn't clear until just a few years ago.

I wanted to talk to someone who'd actually taken ketamine for depression. So I contacted researchers at the National Institute of Mental Health, who put me in touch with a man named Christopher Stephens. He's 28, and lives near San Francisco. Stephens told me he was diagnosed with depression when he was just 15.

CHRISTOPHER STEPHENS: My first prescription was for Paxil. Then I started on Prozac. And then, you know, at 19 when - that's when I decided that I had to go and try new medications.

HAMILTON: And what did you try?

STEPHENS: Klonopin, Ativan, Valium, Xanax, Remeron, Gabapentin, Buspar. Depakote, they had me on for a while.

HAMILTON: Stevens says some of these drugs just didn't work. Others caused nausea, headaches, insomnia - not to mention some really unpleasant sexual side effects. And despite all the drugs, Stephens' depression kept getting worse. What had been a dull ache was now a stabbing pain. Ultimately, he just couldn't function. He lost his job as a special-education assistant. Even his greatest joy, teaching martial arts, wasn't enough to keep him going.

STEPHENS: I went on the Internet, and I started researching ways to end your life. You know, a lot of people think oh, I can down a bottle of Tylenol, and that'll do it. What that'll actually do is kill your liver, and you slowly die - which is not a good way to go. I wanted to research the most efficient and painless way to do it.

HAMILTON: But Stephens wanted to do something good before he died, something that might help other people avoid the hopelessness that he was feeling. So he called up the University of California-San Francisco, and offered himself up as a sort of human lab animal. He thought maybe scientists could learn something about depression by studying his brain.

That call got Stephens referred to Carlos Zarate, a brain scientist at the National Institute of Mental Health in Bethesda, Maryland. Zarate thinks current depression drugs are misguided. I ask him why, and he offers an analogy. He says depression is a bit like a leaky faucet in the brain. And there are different ways to stop the leak.

CARLOS ZARATE: You can go straight to the faucet and you can fix it, or you can go to the water plant and shut down the water plant. The end result will be the same. Now, the current antidepressants are probably more like going to that water plant. You shut down the water, and then there's all the pipes that go through the city; eventually, it gets to your town and eventually, to your house and to the faucet.

HAMILTON: Antidepressants like Prozac act primarily on serotonin, a brain chemical once thought to be the key to depression. Other drugs affect the chemicals norepinephrine and dopamine.

But Zarate thinks all of these are a long way from the leaky faucet in the brain. He's thinks there's another chemical that gets much closer to the problem. It's called glutamate. And that's where ketamine comes in. The anesthetic-turned club drug seems to act directly on the glutamate system.

Zarate tells me he was intrigued when he began hearing anecdotal reports that ketamine could relieve depression almost instantly. But as a scientist, he says, he was thinking the reports sounded too good to be true.

ZARATE: In the field, there was really a question whether people really did believe these initial observations because it was so dramatic. And so we decided to test this in a controlled study.

HAMILTON: The study involved 17 patients with depression. They were people like Christopher Stephens, who had tried lots medications without success. After a single dose of ketamine, 12 of the 17 got better within hours. And they stayed better for a week or more.

The result got international attention. And since then, Zarate has given ketamine to many more patients, including Stephens. Stephens himself has vivid memories of the day he got ketamine. It was a Monday morning, and he woke up feeling really bad. His mood was still dark when doctors put in an IV and delivered the drug.

STEPHENS: Monday afternoon, I felt like a completely different person. It was, you know, same day – same-day effects and, you know, I woke up Tuesday morning and I said wow, there's stuff I want to do

today. And I woke up Wednesday morning and Thursday morning. And for the first time in - I don't even remember, I actually wanted to do things. I wanted to live life.

HAMILTON: About 18 months ago, researchers at Yale found a possible explanation for ketamine's effectiveness. It seems to affect the glutamate system in a way that causes brain cells to form new connections. Researchers have long suspected that stress and depression weaken some connections among brain cells. Ketamine appears to reverse the process.

But Zarate says the drug has some serious drawbacks. For one thing, patients often report alarming side effects during the infusion.

ZARATE: Feel an out-of-body experience, seeing trails of light. Their memory might be a bit foggy.

HAMILTON: Also, people can get hooked on ketamine, and habitual use has been linked to serious health problems. So scientists have been checking out other drugs that also tweak the glutamate system. One is a pill called riluzole, which is less potent than ketamine. Christopher Stephens has been taking it ever since his ketamine treatment. It has been more than a year now, and he says his depression hasn't returned.

Another possibility is a drug called scopolamine, which is used to prevent seasickness. Maura Furey, at NIH, began studying scopolamine seven or eight years ago, about the same time Zarate began looking into ketamine. [POST-BROADCAST CLARIFICATION: The National Institute of Mental Health is part of the National Institutes of Health (NIH).] Furey says when the public heard about her work, she started getting phone calls, including one from a depressed woman who had tried scopolamine by accident.

MAURA FUREY: She had gone out on a boat with her sister and used a scopolamine patch, and noticed that her symptoms had lifted. She felt better and had been treating herself with the scopolamine patch for quite some time, and was just contacting me to say: It worked for me.

HAMILTON: Furey's research found that scopolamine often does work, though not as quickly as ketamine.

Helene Najar is one of the people who has been helped by the seasickness drug. She's in her late 40s and lives in Bethesda with her family, a dog, a cat...

(SOUNDBITE OF PARROT CHIRPING)

HAMILTON: ...and a parrot named Wilbur. Najar says mainstream drugs helped her control her depression, but always came with side effects. So about five years ago, she signed up for an NIH trial. The study would give her scopolamine once a week for three weeks. Najar says the first dose didn't seem to make a difference. But after the second one, she began to feel a change.

HELENE NAJAR: By the third, I was like a new person. And then I had that - oh, my gosh, how am I going to get the scopolamine; how am I going to continue this treatment? This is like, the best thing that's ever happened to me. I haven't felt this normal in years.

HAMILTON: Najar ended up getting a prescription for the drug, which she continues to use when she feels her symptoms getting worse. Scientists are still trying to figure out precisely how scopolamine works against depression. But there's evidence that glutamate is involved. And Najar says the effect is unlike any other drug she's taken.

NAJAR: There's no doubt in my mind: However it works, or whatever receptors in the brain it works on, absolutely, it has nailed exactly where my imbalance is.

HAMILTON: Maura Furey, from NIH, says the experiments with ketamine and riluzole and scopolamine aren't intended to turn some existing drug into the next big thing for depression. She says the goal is to identify compounds that pharmaceutical companies can use as molecular models for an entirely new class of antidepressants.

FUREY: For people who actually design drugs, it would tell them chemically, what they need to focus on and develop.

HAMILTON: Drug companies have taken notice. Several are now working on glutamate drugs for depression.

Jon Hamilton, NPR News.

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