

Ketamine is in the spotlight thanks to Elon Musk – but is it the right treatment for depression?

The entrepreneur endorses the drug, but researchers caution that it's not to be taken lightly.

The drug ketamine is enjoying a second life. First developed as an anaesthetic that was used widely by US battlefield surgeons during the Vietnam War, it is growing in popularity as a treatment for depression and other mental-health conditions. And last week, the drug got its highest-profile endorsement yet. In an interview with US journalist Don Lemon that was released online on 18 March, Elon Musk, founder of SpaceX and head of social-media platform X (formerly Twitter), spoke about his own experiences of using the drug to manage what he called a “negative chemical state” similar to depression. Musk said he has a prescription for the drug from “a real doctor” and uses “a small amount once every other week or something like that”. His comments follow the fatal drowning of *Friends* actor Matthew Perry last October, an incident that an investigation blamed on the drug’s acute effects. So, what is ketamine, how is it used and is it safe? *Nature* spoke to three specialists in the field to find out.

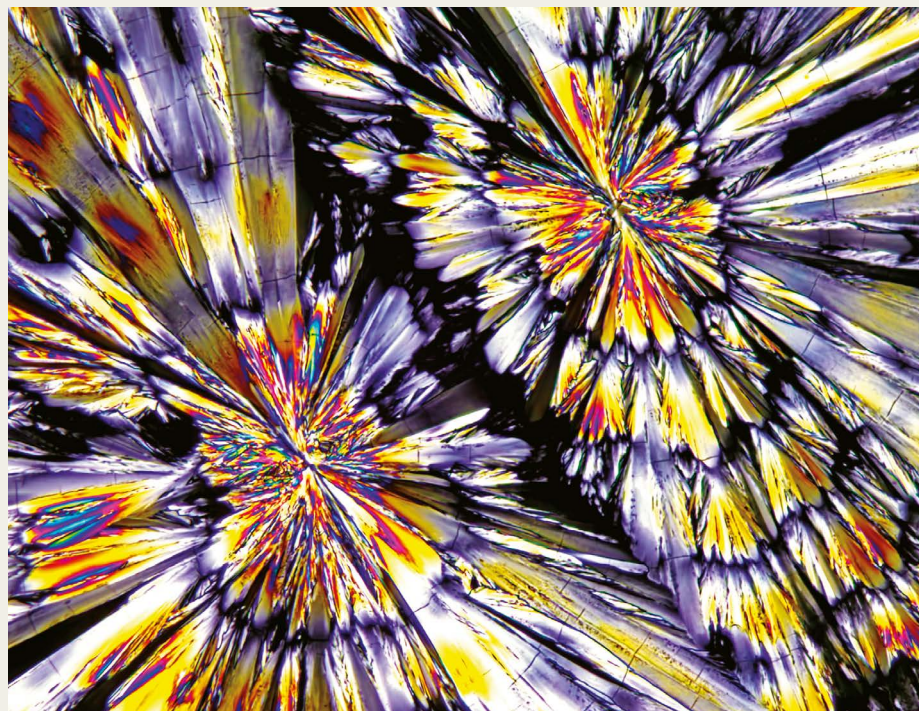
How is ketamine used to treat depression?

It’s complicated. Approved as an anaesthetic by the US Food and Drug Administration (FDA) in 1970, the drug was delivered intravenously to people undergoing surgery. Ketamine is often still given that way for depression. That requires supervision — typically people attend a private clinic and are monitored by an anaesthetist as well as the prescribing psychiatrist and members of the support staff.

Because it’s long out of patent, there’s little commercial interest in developing new versions of the drug. Some companies are trying to package it into more-convenient oral lozenges, but that’s a challenging formulation.

“The problem with ketamine is if you take it orally, by and large it doesn’t get through to the system because it’s got low bioavailability,” says Allan Young, a consultant psychiatrist at King’s College London who studies mood disorders.

In 2019, the FDA approved a nasal spray that contains a potent ketamine derivative called esketamine as a treatment for severe depression. But it’s more expensive



M. I. WALKER/SPL

Crystals of ketamine, which is growing in popularity as a treatment for depression and anxiety.

than standard ketamine, so many doctors simply prescribe the tried-and-tested anaesthetic off-label. And they are doing so increasingly often: data suggest that ketamine prescriptions in the United States rose more than fivefold from 2017 to 2022.

Does it work?

Ketamine faces a high bar, because it tends to be given to people with severe depression who have already tried standard treatments and received little or no benefit from them. But even in people who did not respond to other drugs, ketamine can be highly effective.

“We see about 50–60% of people having a very clinically meaningful response,” says Joshua Rosenblat, a staff psychiatrist and clinician-researcher at Toronto Western Hospital, Canada. “There’s been over 40 clinical trials now supporting the use of ketamine for depression. For the most part, they’ve just been very, very consistent that there’s a rapid and robust antidepressant effect.”

“We think of ketamine and electroconvulsive therapy (ECT) as quote-unquote big guns that we save for more severe cases,” he adds. (Because of its potency as an anti-depressant, some psychiatrists referred to ketamine as

liquid ECT when the drug was first developed.)

How does it work?

As is true for many psychiatric medicines, scientists aren’t sure how ketamine lifts depression at the molecular level in the brain. Its benefits seem to come from triggering what psychiatrists call a dissociative state.

People who take it “might feel removed from their body, feeling like they’re in a dream-like state or like they’re floating”, Rosenblat says.

His clinic typically offers those with treatment-resistant depression an acute course of four to six ketamine treatments over two to four weeks. For those patients who respond, the programme switches to a maintenance schedule of a treatment every two to four weeks — which fits with how often Musk said he takes the drug.

“It’s a very important alternative strategy because it works so differently to conventional medicines,” says David Nutt, a neuropsychopharmacologist at Imperial College London.

Is it used for other disorders?

Whereas esketamine is approved to treat some forms of depression, ketamine isn’t licensed

in the United States as a treatment for psychiatric conditions. However, its success in treating depression is encouraging researchers and even doctors to investigate its effects to help people with other conditions.

“When you get an effective treatment in psychiatry, you tend to look out from the initial indication, to look for benefit,” Young says. His team is studying whether it can help people with anorexia. Others are looking at the effects on people with alcohol addiction, anxiety, obsessive–compulsive disorder or post-traumatic stress disorder (PTSD).

“I don’t prescribe for those indications because I don’t think the evidence is sufficient,” Rosenblat says. “But certainly, there’s a lot of prescribers who do. I think it’s really grown in popularity for PTSD.”

Is it safe?

Regulations and medical best-practice guidelines say that ketamine should be administered only under the proper conditions, which include supervision for several hours afterwards. Some people receiving the drug for depression do react badly, even at relatively low doses.

“It’s very rare for people to have full perceptual disturbances in terms of hallucinations,” Rosenblat says. “It’s more distortion of time and space and colours and sounds.”

Some people he has treated have entered a very unpleasant state that ketamine users call a K-hole. “You feel like you’re dying, like everything goes black,” he says. “It can be distressing. And so we have staff that are trained in grounding people that sit next to them.”

Not everyone who takes ketamine receives that help. Some clinics and doctors administer the drug unsupervised. And then there’s illegal recreational use, which many see as a growing problem because the drug severely affects judgement.

“There are quite a few documented deaths from ketamine,” Nutt says. “Never take it alone or where you can be vulnerable. Not near water, as [Matthew] Perry did, or outside on a cold night admiring the stars.”

By David Adam



GETTY

Putin spoke at an event marking the 300th anniversary of the Russian Academy of Sciences.

WHAT PUTIN’S NEXT TERM MEANS FOR SCIENCE

Researchers in Russia expect growing isolation as Vladimir Putin embarks on six more years as president.

By Olga Dobrovidova

Russian President Vladimir Putin has secured a fifth term in office, claiming a landslide victory in the country’s presidential election on 18 March. Election officials say he won a record 87% of votes. This outcome came as a surprise to no one, and many international leaders have condemned the vote as not being free or fair.

Researchers interviewed by *Nature* say that another six years of Putin’s leadership does not bode well for Russian science, which has been shunned globally in response to the country’s ongoing invasion of Ukraine, and is on precarious ground at home. Those still in Russia must choose their words carefully: as one scientist, who wishes to remain anonymous, put it, “business as usual” now includes possible prison time for offhand comments.

Publicly, Putin’s government is a big supporter of research. In early February, at a celebration of the 300-year anniversary of the Russian Academy of Sciences, Putin bolstered the academy’s role, effectively reversing parts of a sweeping reform that had limited its autonomy. And at the end of last month, he signed an update to the 2030 national science and technology strategy, which calls

for funding for research and development to double to 2% of gross domestic product, and stresses an increased role for applied science amid “sanctions pressure”.

Despite being made before the election, these big announcements were framed not as campaign promises but as top-down directives, says Irina Dezhina, an economist at the Gaidar Institute for Economic Policy in Moscow. “The fact that it was set in motion back then implies no one really expected any changes at the helm.”

Fractured landscape

Although domestic support for Russian science, which remains mostly state-funded, appears to be strong, many collaborations with countries in the West have broken down since the invasion of Ukraine.

After intense internal discussions, CERN, the European particle-physics powerhouse near Geneva, Switzerland, voted in December 2023 to end ties with Russian research institutions once the current agreement expires in November this year. And the war has severely disrupted science in the Arctic, where Russia controls about half of a region that is particularly vulnerable to climate change. A study this year gave a sense of how collaborative projects