

Ketamine for Depression: The Most Important Advance in Field in 50 Years?

In a new review in *Science*, the authors call the identification of the anesthetic and “club drug” ketamine as a rapid treatment for depression “arguably the most important discovery in half a century” of research on the condition

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In any given year, 7% of adults suffer from major [depression](#), and at least 1 in 10 youth will reckon with the disorder at some point during their teenage years. But about 20% of these cases will not respond to current treatments; for those that do, relief may take weeks to months to come.

There is one treatment, however, that works much faster: the anesthetic and “club drug” ketamine. It takes effect within hours. A single dose of ketamine produces relief of depression that has been shown in studies to last for up to 10 days; it also appears to reduce symptoms of [bipolar disorder](#) and suicidal thoughts. Now, a new research [review](#) published in *Science* calls the discovery of these effects of ketamine, “arguably the most important discovery in half a century” of depression research.

Ketamine doesn’t work the way traditional antidepressants do. Many such drugs affect levels of the neurotransmitter serotonin in the brain, and while the idea that depression is caused by low levels of serotonin or an “imbalance” of other key neurotransmitters has been firmly fixed in the popular imagination, scientists have known for decades that it can’t be that simple. For one, antidepressant drugs change the brain’s neurotransmitter levels immediately, yet depression doesn’t lift for several weeks, a delay that could be potentially deadly.

Another theory is that depression is caused not by neurotransmitter problems per se, but by damage to brain cells themselves in key regions critical to controlling mood. This idea fits nicely with evidence that stress can cause depression, since high levels of stress hormones can cause an overrelease of a neurotransmitter called glutamate, which damages cells and affects exactly the same suspected areas. More support for this theory comes from the fact that all known antidepressants increase cell growth in these areas too, providing an alternate explanation for their therapeutic results.

At first, ketamine seemed to throw a monkey wrench into that neat idea, however. It didn’t seem likely that a drug could repair cells within hours, but new research explored in a review paper in the journal *Science* suggests just that. Ketamine rapidly spurs the growth of new synapses, the connections between brain cells, and is associated with “reversal of the atrophy caused by chronic stress,” the authors write.

Unfortunately, the hallucinogenic and often outright unpleasant effects of ketamine mean that it can't be used in the same way typical antidepressants are, and fears about its potential for misuse also hamper its development. Researchers are frantically trying to develop compounds that have the same effects as ketamine without producing a "high."

In the meanwhile, however, ketamine is already FDA approved, so there's nothing stopping psychiatrists from trying it and patients from asking for access to it in emergency situations when all else has failed. However, it must be given by infusion and carefully monitored (nasal sprays are being developed and there is an oral form that has some effects, but is not optimally absorbed), and the drug impairs patients for hours. Still, it relieves depression for at least several days: if there's a choice between being entirely dysfunctional seven days a week or only out of commission for one or two, many people would accept that trade-off.

But while research on ketamine is ongoing, clinical use of the drug in the community remains rare. Fears about abuse continue to run high, though ketamine has never caught on as a major street drug. If the *Science* paper's authors are right that ketamine's effect on depression is a key advance — and if the drug really holds similar promise for bipolar disorder — patients might want to consider pushing for greater access. Ketamine is off patent, so no drug maker is likely to do so.

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