

Yale scientists explain how ketamine vanquishes depression within hours

OCTOBER 4, 2012



Ketamine may regenerate synaptic connections between brain cells damaged by stress and depression, according to new Yale-led research.

Many chronically depressed and treatment-resistant patients experience immediate relief from symptoms after taking small amounts of the drug ketamine. For a decade, scientists have been trying to explain the observation first made at Yale University.

Today, current evidence suggests that the pediatric anesthetic helps regenerate synaptic connections between brain cells damaged by stress and depression, according to a review of scientific research written by Yale School of Medicine researchers and [published in the Oct. 5 issue of the journal Science](http://science.sciencemag.org/content/sci/338/6103/68.full.pdf) (<http://science.sciencemag.org/content/sci/338/6103/68.full.pdf>).

Ketamine works on an entirely different type of neurotransmitter system than current antidepressants, which can take months to improve symptoms of depression and do not work at all for one out of every three patients. Understanding how ketamine works in the brain could lead to the development of an entirely new class of antidepressants, offering relief for tens of millions of people suffering from chronic depression.

“The rapid therapeutic response of ketamine in treatment-resistant patients is the biggest breakthrough in depression research in a half century,” said [Ronald Duman](http://psychiatry.yale.edu/people/ronald_duman/profile) (http://psychiatry.yale.edu/people/ronald_duman/profile), the Elizabeth Mears and House Jameson Professor of Psychiatry and Professor of Neurobiology.

Duman and George K. Aghajanian, also professor of psychiatry at Yale, are co-authors of the review.

Understanding how ketamine works is crucial because of the drug’s limitations. The improvement in symptoms, which are evident just hours after ketamine is administered, lasts only a week to 10 days. In large doses, ketamine can cause short-term symptoms of psychosis and is abused as the party drug “Special K.”

In their research, Duman and others show that in a series of steps ketamine triggers release of neurotransmitter glutamate, which in turn stimulates growth of synapses. Research at Yale has shown that damage of these synaptic connections caused by chronic stress is rapidly reversed by a single dose of ketamine.

The original link between ketamine and relief of depression was made at the Connecticut Mental Health Center in New Haven by John Krystal, chair of the department of psychiatry at Yale, and Dennis Charney, now dean of Mt. Sinai School of Medicine, who helped launch clinical trials of ketamine while at the National Institute of Mental Health.

Efforts to develop drugs that replicate the effects of ketamine have produced some promising results, but they do not act as quickly as ketamine. Researchers are investigating alternatives they hope can duplicate the efficacy and rapid response of ketamine.

Watch a video of Professor Duman delivering an April 2011 lecture on the use of ketamine to treat depression below:

New Mechanisms Elicited with Ketamine in Treatment-Resistant Depression



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