

# Los Angeles Times

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*From the Los Angeles Times*

## **Drugs' double-edged sword**

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A young man reportedly taking the antidepressant Prozac has a history of significant psychiatric troubles, including self-cutting, obsessive thoughts and anxiety. But among the 27-year-old's current teachers and acquaintances, he has a reputation as a caring, dependable friend and a highly motivated student.

Surely, say mental health professionals, this recovery was brought about by [Prozac](#).

The same young man, saying the drug makes him feel "like a zombie," abruptly discontinues his antidepressant and begins to behave erratically. About three weeks later, he steps from behind a curtain in a classroom at his alma mater and begins shooting, killing five students before turning the gun on himself.

Just as surely, say critics of antidepressants' widespread use, this unraveling was brought about by Prozac.

Steven Kazmierczak's bolt-from-the-blue shooting spree on Feb. 14 reignited a long-running debate over the benefits and risks of antidepressants -- taking them and discontinuing them.

"It's sad to watch this," says Ann Blake Tracy, executive director of the International Coalition for Drug Awareness and co-founder of a website, [SSRI stories.com](#), that catalogs violent crimes like Kazmierczak's and links them to psychiatric drug use. "You find suicide, murder, rape, arson" -- all caused by drugs such as Prozac, she says. "How did they convince us that this is therapeutic?"

Most in the psychiatric profession would counter that antidepressants overwhelmingly save lives, and salvage those hobbled by sadness and anxiety. They doubt that coming off these drugs -- especially Prozac, which Kazmierczak was reported to have taken -- led the Illinois gunman to kill.

And they fret that depressed patients who believe the charges of critics like Tracy will turn their backs on medicine that can work wonders if taken -- and stopped -- correctly.

"When a story like this is brewing, people think, 'If this medication can possibly be related to a bad outcome, I'd better get off it now,' " says UCLA psychiatrist Andrew Leuchter. "We're talking about millions and millions of people who've been treated successfully with these drugs and stopped treatment without any kind of dramatic changes of behavior."

At the center of the latest tempest over psychotropic drugs is a long-recognized phenomenon called Antidepressant Discontinuation Syndrome. First identified in psychiatric journals in the late 1990s, the condition is an assortment of symptoms that can plague patients for several weeks and, in a few cases on medical record, months after coming off a wide range of antidepressants. They include dizziness, headache, fatigue, changes in sleep patterns and appetite, vivid or disturbing dreams, agitation and anxiety. Some patients experience tingling or "electric zap" sensations passing through their extremities or head and, in rare cases, spasmodic jerking in the extremities, especially while sleeping.

Though the symptoms of the syndrome can be distressing for patients, many psychiatrists insist that they are rarely dangerous and can be managed by weaning a patient off antidepressant medication very slowly. As patients taper off their meds, however, they and their doctors must assess whether symptoms such as anxiety and agitation, which may affect a patient's behavior and reactions, are a sign of the syndrome or a recurrence of the illness that led to the medication in the first place.

It's not always an easy call, says Dr. Richard Shelton of Vanderbilt University, a leading researcher on antidepressants and their effects.

### **Lightning rod for debate**

Twenty years after Prozac appeared on the U.S. landscape, roughly 10% of American women and 4% of American men take an antidepressant regularly. The selective serotonin reuptake inhibitors (SSRIs) and their close cousins have revolutionized attitudes toward mental illness and its medication in this country. But they remain a lightning rod for controversy.

The role that antidepressants played in Kazmierczak's violent end probably will never be clear. Did Prozac, which Kazmierczak's girlfriend, Jessica Baty, said he had been on but had recently discontinued, help keep the 27-year-old's mental illness in check and, when halted, allow it to roar back? Or did it distort his personality, contort his thoughts and, when abandoned, cause a chemical storm in Kazmierczak's brain that spawned a fury of aggression?

The weight of clinical observations and psychiatric research favors the view that antidepressants helped Kazmierczak until the time he abandoned them. But skeptics charge that antidepressants may have caused or contributed to Kazmierczak's spasm of violence. And mental health experts acknowledge they cannot rule out that possibility.

"You're going to get some unpredictable reactions if you have millions of people taking them and going off. The potential for violent behavior, suicide and particularly impulsive suicide exists," says Shelton, a professor of psychiatry and

psychopharmacology. "And the sicker the person is coming in the front door, the more likely they are to have a bad crash when they go off. We do see these extreme reactions."

In a category of drugs so widely used, how could potentially dangerous side effects remain a matter of uncertainty? For several reasons, experts say.

For starters, individuals' responses to antidepressants, though mostly predictable, can vary widely. Psychiatric diagnosis and medication decisions are imprecise and can be disastrously wrong; in cases where a patient with bipolar disorder is misdiagnosed and put on antidepressants, for example, the medicine has been found in some cases to bring on an episode of mania.

And, as the Food and Drug Administration acknowledged in 2007 when it warned of a heightened risk of suicide and suicidal thoughts among young patients starting on many of these drugs, 20 years after their arrival on the scene a full picture of antidepressants' side effects may still be emerging.

Research on animals points strongly to the possibility of heightened violence with the abrupt withdrawal of most antidepressants. Studies using cats and rodents have long shown that sudden declines in the neurotransmitter serotonin (the chemical that most antidepressants, in some fashion, make more available in the brain) will suppress an animal's natural caution and intensify its aggressive reactions toward other animals.

Though the human brain may have more powerful braking mechanisms than a cat's, the role of serotonin in inhibiting impulsive aggression is well established, says neuroscientist Allan Siegel of the University of Medicine and Dentistry of New Jersey, author of "The Neurobiology of Aggression and Rage."

It is expected to be several weeks before Kazmierczak's medical records and postmortem results are fully evaluated and made public. If they suggest that Kazmierczak's murderous act was linked to his abrupt discontinuance of an antidepressant, those findings may dismay the many patients who were not warned from the start of the risks they might face when going off such medicine.

Such findings could also be a sobering reminder to patients that these are not drugs to be dropped on a whim. Currently, an estimated half of patients who start on antidepressant therapy go off their medication in less than a year.

For medical professionals, the case of Steven Kazmierczak may hold other lessons: It could put physicians on alert for symptoms of Antidepressant Discontinuation Syndrome that lie at the extreme, including violence and suicide. It could underscore that when prescribing antidepressants, physicians need to alert patients that coming off these medications can be a bumpy road.

It may also remind physicians that they should take the same care to monitor a patient's state in the first several weeks off the medication as they do when a patient is just getting started.

According to a 2006 review article published in the journal *Primary Psychiatry*, the

"untoward post-treatment effects" of the syndrome are believed to affect a majority of those who have taken antidepressants in the same class as Prozac for more than six weeks and then stopped. The unnerving symptoms can be particularly acute in cases where, as Kazmierczak is believed to have done, patients abruptly stop taking their medication.

The antidepressants venlafaxine (also marketed as Effexor) and paroxetine (also marketed as Paxil) are most often associated with pronounced discontinuation reactions, which, in these cases, are usually felt quickly -- within two to three days after a patient stops taking these drugs.

Such negative post-treatment effects are considered rare among patients taking Prozac, which Kazmierczak's girlfriend said he had been taking until about three weeks before the shooting. When the effects do happen, experts said they tend to be felt several weeks after fluoxetine, Prozac's chemical name, has been discontinued, because fluoxetine lingers in the body longer than venlafaxine or paroxetine do.

While acknowledging that there is little research to show which patients are most affected by discontinuation effects, Vanderbilt psychiatrist Shelton says he has observed that those who suffer from depression coupled with obsessive-compulsive disorder "seem to be prone to pretty significant reactions."

Shelton cautions that in cases where a patient's reaction to going off an antidepressant seems extreme, a physician should taper the dose "excruciatingly slowly." In Shelton's experience, he says, a gentle reduction of medicine can not only minimize discontinuation symptoms, but may make recurrence of depressive symptoms less likely.

"It's not a horse race. No one says you have to be off medications in three weeks or even three months," Shelton says.

In the war of words over antidepressants, this may be a point of rare consensus between those who believe in the power of antidepressants and those intent on raising alarms.

"As firm as I am on the dangers of these drugs, I'm afraid of withdrawal," says Tracy of the International Coalition for Drug Awareness. "Because if people quit, and don't know how to come off the right way, we're really going to be in trouble."

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