Scientists find hyped new recreational drug 'Flakka' is as addictive as bath salts

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Scripps Research Institute Associate Professors Michael Taffe (right) and Tobin

Dickerson were senior authors of the new study. Credit: The Scripps Research Institute.

Scientists at The Scripps Research Institute (TSRI) have found using animal models that the new recreational drug alpha-PVP ("flakka") seems equivalently potent as a stimulant, and therefore as addictive, as its chemical cousin MDPV ("bath salts").

News stories in recent months have blamed flakka for incidents of extreme violence, paranoid psychoses, compulsive nudity, zombie-like behavior and even "superhuman strength." One man, allegedly high on the drug, tried to break into a police station. Another ran naked through Fort Lauderdale traffic.

"There have been assertions that flakka is somehow worse than MDPV, but this study shows that the two are very similar," said Michael A. Taffe, an associate professor at TSRI.

TSRI Associate Professor Tobin J. Dickerson, who was co-senior author of the study with Taffe, added, "That doesn't mean that flakka use is 'safe'—our data show that flakka is as potent as MDPV, making it a very good stimulant, arguably with worse addiction liability than methamphetamine."

The team's findings were published online ahead of print in the journal Psychopharmacology.

Potent and cheap

Alpha-PVP (α-pyrrolidinopentiophenone) is a synthetic stimulant; the street drug supply is reportedly made in laboratories in China, India and

Pakistan. It was designed to be slightly different, chemically, from MDPV, which has been illegal in the U.S. since 2011. The new drug's chemical difference, the lack of a cluster of atoms known as the 3,4-methylenedioxy motif, is the same as the one that distinguishes methamphetamine from MDMA ("Ecstasy").

Alpha-PVP was legal until the U.S. Drug Enforcement Administration put a ban on it early in 2014—a temporary ban that is almost certain to become permanent. Nevertheless, the drug is so potent and so cheap—reportedly as low as $5 per dose—that its use has grown in certain parts of the country, prompting concerns among police and health officials.

For the study, the research team used a standard animal model of addiction potential in which rats are trained to press a lever to infuse themselves intravenously with small doses. As expected for an addictive stimulant, the rats tended to press the drug-delivery lever more and more in each one-hour session as 20 daily sessions progressed. When the researchers increased the number of lever presses required to get another dose, the animals kept pressing—for up to hundreds of presses per dose.

In a head-to-head test of self-administration of alpha-PVP against MDPV, alpha-PVP showed an almost identical potency to induce lever presses. The drugs also showed approximately the same ability to induce two classic stimulant effects, boosting physical activity and disrupting body temperature.

Although the results suggest that scare stories over alpha-PVP may be somewhat overblown, the fact that it is comparable to MDPV makes it a highly dangerous drug. MDPV is already widely considered one of the worst-ever drugs in terms of addiction potential. In a study reported in 2013, for example, the Taffe and Dickerson labs showed that MDPV induced far more drug-seeking lever presses in rats than crystal meth.

"Animals will self-administer MDPV like no drug I have ever seen," said Dickerson.

Overshadowing other pleasures

In a related study, also published online ahead of print in Psychopharmacology, the TSRI researchers set up a test of MDPV's ability to supplant other rewarding behaviors.

"We commonly think of drug addiction as making the drug more important than anything else in the user's life, but we haven't had good rodent models of that," said Taffe. "The animals will almost always respond more to food and tasty flavors, for example, than drugs."

The team decided to get around this problem by testing the ability of MDPV to supplant a pleasurable but less fundamental behavior for rats, wheel running. The researchers found that as the animals self-administered more MDPV per session, their use of the wheel declined significantly, indicating that the drug had made this normally rewarding behavior seem much less appealing.

Remarkably, a subset of the rats didn't increase their MDPV intake gradually, but went from occasional sampling to bingeing on as much as they could get during the session. "That was when they stopped using the wheel—that very day they binged," said Taffe. "In subsequent sessions, the bingers' intake would stay high and they wouldn't run much on the wheel. We think it's a good model of the ways in which—and the speed with which—drugs can supplant other rewarding things we normally do."

Taffe and his colleagues also suspect that initial bingeing may be a predictor of individual liability for addiction, which normally affects only a minority of people who try a drug.

MDPV is related to cathinone, a natural stimulant found in the khat leaves traditionally chewed in Northeast Africa and Arabian Peninsula regions, but it also shares structural similarity to methamphetamine and MDMA. Originally developed as a potential pharmaceutical stimulant by Boehringer Ingelheim chemists in the 1960s, MDPV re-emerged as a recreational drug within the past decade. The fact that it enjoyed legal status for a time has led to the development of variants—also briefly legal—such as alpha-PVP.

In this rapidly evolving recreational drug "market," obtaining high-purity drug for laboratory research can be a challenge. In this collaboration, Dickerson designed the synthesis of drugs from precursor compounds prior to scheduling, when they are not available from research supply companies.

"There are now dozens of substituted cathinones out there that could become popular, and what we're trying to do is to study these drugs as they emerge, using our animal models, and hopefully come up with general principles for predicting their effects," said Taffe.

"These drugs are not made in garages anymore," said Dickerson. "They're made by sophisticated chemistry labs that are producing not just one drug, but also analogs of that drug, so as soon as one drug gets banned, here comes the next one, and the next one—and there's no evidence of any kind of safety testing prior to their release into the drug user population."

More information: "In vivo potency and efficacy of the novel cathinone α-pyrrolidinopentiophenone and 3,4-methylenedioxypyrovalerone: self-administration and locomotor stimulation in male rats." *Psychopharmacology* May 2015. DOI: 10.1007/s00213-015-3944-8

"Binge-like acquisition of 3,4-methylenedioxypyrovalerone (MDPV) self-administration and wheel activity in rats." *Psychopharmacology* June 2015, Volume 232, Issue 11, pp 1867-1877 DOI: 10.1007/s00213-014-3819-4