Meth vaccine shows promising results in early tests

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Scripps Research Institute Associate Professor Michael Taffe, Research Associate Michelle Miller, and colleagues have developed a promising vaccine against a methamphetamine high.

Scientists at The Scripps Research Institute (TSRI) have performed successful tests of an experimental methamphetamine vaccine on rats. Vaccinated animals that received the drug were largely protected from typical signs of meth intoxication. If the vaccine proves effective in humans too, it could become the first specific treatment for meth addiction, which is estimated to affect 25 million people worldwide.

"This is an early-stage study, but its results are comparable to those for other drug vaccines that have then gone to clinical trials," said Michael

A. Taffe, an associate professor in TSRI's addiction science group, known as the Committee on the Neurobiology of Addictive Disorders. Taffe is the senior author of the study, which is currently in press with the journal *Biological Psychiatry*.

A Common and Dangerous Drug of Abuse

Over the past two decades, methamphetamine has become one of the most common drugs of abuse around the world. In the United States alone there are said to be more than 400,000 current users, and in some states, including California, meth accounts for more primary drug abuse treatment admissions than any other drug. Meth has characteristics that make it more addictive than other common drugs of abuse, and partly for this reason, there are no approved treatments for meth addiction.

In recent years, scientists at TSRI and other institutions have taken the innovative approach of developing vaccines against addictive drugs. These vaccines evoke antibody responses against drug molecules, just as traditional vaccines evoke antibody responses against viruses or bacteria. Anti-drug antibodies are meant to grab hold of drug molecules and keep them from getting into the brain—preventing the drug from giving the user a high and removing the incentive for taking the drug.

Vaccines against nicotine and cocaine are already in clinical trials. Some meth vaccines have been tested in animals, but generally with unpromising results. The methamphetamine molecule is structurally simple, making it relatively unnoticeable to the immune system. Meth and its main metabolite, ordinary amphetamine, also tend to linger once they get into the nervous system, so that even a little drug goes a long way. "The simple structure and long half-life of this drug make it a particularly difficult vaccine target," said Kim Janda, the Ely R. Callaway, Jr. Professor of Chemistry and member of the Skaggs Institute for Chemical Biology at TSRI.

'Encouraging Results'

Two years ago Janda and his laboratory developed six candidate meth vaccines. In each, the main active ingredient was a chemical cognate of the methamphetamine molecule—that otherwise would be too small to evoke any antibody response—linked to a larger, antibody-provoking carrier molecule. Early tests in mice indicated that three of these vaccine candidates could evoke a strong antibody response to meth. Taffe's laboratory later tested these three vaccines in rats and found the one, designated MH6, that worked best at blocking two typical effects of meth—an increase in physical activity and a loss of the usual ability to regulate body temperature.

In the new study, members of Taffe's laboratory, including Research Associate Michelle L. Miller, who was lead author of the study, investigated the MH6 vaccine in more depth. Using a different experimental setup, they found again that it prevented a rise in body temperature and burst of wheel-running hyperactivity that otherwise occur after meth exposure. Underlying these promising effects on behavioral measures was a robust antibody response, which in vaccinated rats kept more of the drug in the bloodstream and out of the nervous system, compared to control rats. "These are encouraging results that we'd like to follow up with further animal tests, and, we hope, with clinical tests in humans some day," said Miller.

"I think that this vaccine has all the right features to allow it to move forward in development," said Janda. "It certainly works better than the other active vaccines for meth that have been reported so far."

The Next Big Challenge

A separate group of researchers has reported promising animal test

results for an antibody-based treatment. In this approach, the anti-meth antibodies are grown in cultured cells using standard biotechnology methods and then injected into the animal in a concentrated dose, preventing a meth high. Antibody-based therapies are commonly used to treat cancer and chronic immunological conditions. But they are typically expensive, costing thousands of dollars per dose, and the effects of a dose last for a few weeks at most. A meth treatment probably would have to be much more cost-effective to be widely useful, as addicts frequently have little money and no health insurance and receive their treatments from government health services.

In principle, an active vaccine would be cheap to make and administer and would confer protection for months per dose, rather than weeks with conventional monoclonal antibody therapy. In practice, active meth vaccine candidates don't yet last that long; for example, the MH6 candidate in the current study was given in four doses over 12 weeks. But Janda and Taffe believe that with further adjustment, an active meth vaccine could sustain an anti-meth antibody response for a much longer period.

"Extending the duration of protection is the next big scientific challenge in this field," said Taffe.

More information: "A Methamphetamine Vaccine Attenuates Methamphetamine-Induced Disruptions in Thermoregulation and Activity in Rats," www.biologicalpsychiatryjourna … (12)00803-7/abstract

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