

Treating cocaine dependence: A promising new pharmacotherapy

November 28 2012

Medication development efforts for cocaine dependence have yet to result in an FDA approved treatment. The powerful rewarding effects of cocaine, the profound disruptive impact of cocaine dependence on one's lifestyle, and the tendency of cocaine to attract people who make poor life choices and then exacerbate impulsive behavior all make cocaine a vexing clinical condition.

In this battle, many candidate pharmacotherapies have been tested, but none have succeeded sufficiently to be adopted widely. Perhaps like cancer, heart disease, and AIDS, [cocaine dependence](#) is a disorder that requires combinations of medications for effective treatment.

In this issue of [Biological Psychiatry](#), researchers from Columbia University and New York State Psychiatric Institute report a step forward in this effort. They tested a medication approach that unites two themes in [addiction research](#) – amphetamine and topiramate.

There are clues that stimulants, like amphetamine, methylphenidate, and [modafinil](#), reduce reward dysfunction and deficits in executive cognitive [control mechanisms](#) associated with addiction. This approach fits with the "self-medication" hypothesis of addiction, which suggests that some people use drugs to treat symptoms that lead them to addiction or that emerge as a consequence of addiction.

There is also evidence that topiramate may be the most effective current pharmacotherapy for alcoholism. There are gaps in our understanding of

exactly how topiramate works to combat addiction, but it shows signs of efficacy in animal models of stimulant addiction. In a recent large study of methamphetamine addiction, it appeared to reduce the intensity of methamphetamine use.

Using this knowledge as building blocks, Mariani and colleagues set out to test a combination of mixed amphetamine salts and topiramate for the treatment of cocaine dependence. They recruited cocaine-dependent treatment-seeking adults who were randomized to receive either the combination treatment or a placebo for twelve weeks. It was conducted as a double-blind study, using matching capsules, so that neither participants nor the research staff knew which treatment each individual was receiving.

They found that the participants receiving the combination treatment achieved three weeks of continuous abstinence from cocaine at a rate twice that of placebo (33% versus 17%). There was a significant moderating effect of the total number of cocaine use days, which suggests that the combination treatment was most effective for participants with a high baseline frequency of cocaine use.

"The combination of mixed amphetamine salts and topiramate appears promising as a treatment for cocaine dependence," said the authors. "The positive results observed in this study need to be replicated in a larger, multicenter clinical trial. The findings also provide encouragement for the strategy of testing medication combinations, rather than single agents, for cocaine dependence."

Biological Psychiatry Editor Dr. John Krystal agreed, adding that "the challenge of developing pharmacotherapies for cocaine is daunting. Yet, this combination therapy approach is a promising new strategy."

More information: The article is "Extended-Release Mixed

Amphetamine Salts and Topiramate for Cocaine Dependence: A Randomized Controlled Trial" by John J. Mariani, Martina Pavlicova, Adam Bisaga, Edward V. Nunes, Daniel J. Brooks, and Frances R. Levin ([doi: 10.1016/j.biopsych.2012.05.032](https://doi.org/10.1016/j.biopsych.2012.05.032)). The article appears in *Biological Psychiatry*, Volume 72, Issue 11 (December 1, 2012)

Provided by Elsevier

Citation: Treating cocaine dependence: A promising new pharmacotherapy (2012, November 28) retrieved 3 May 2024 from

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