Long-term cocaine addiction therapy developed

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A pile of cocaine hydrochloride. Credit: DEA Drug Enforcement Agency, public domain

(MedicalXpress)—A team of researchers with the University of Kentucky has developed a long-term chemical treatment option for cocaine addiction. In their paper published in *Proceedings of the National*

Academy of Sciences, the team describes how they came up with a type of compound that prevents cocaine users from experiencing the high that normally comes with its use, and also lasts long enough to be of use as a treatment option.

Currently cocaine is the only illicit drug in the U.S. that does not have a long-term preventive treatment option approved by the U.S. Food and Drug Administration—scientists have tried for years to find or develop one but until now, those efforts have come up short. In this new effort, the researchers began with cocaine hydrolase enzymes, because prior studies have shown they can prevent the high associated with cocaine use—its limiting factor was that it would not remain in the body long enough to serve as a reasonable thereby treatment. The group's idea was to add another element to the enzymes to cause them to hang around longer. After much work, the team settled on human immunoglobulin G antibodies, because they are known to remain in the body for periods of time long enough to be useful as a treatment option. To make the new treatment, the researchers fused the enzymes with the antibodies to produce a therapy that would offer the benefits of both.

Testing of the new compound showed that the treatment could remain in the body of rats for up to 107 hours, whereas Cocaine hydrolase enzymes alone would last for only 8 hours. Further testing showed that in addition to preventing the rats from feeling the effects of cocaine, a single dose of the treatment also prevented the rats from suffering a lethal overdose.

The team explains that the new compound works by breaking down the cocaine metabolites, which prevents the rats from feeling the effects of cocaine administration—for up to 20 days. They note also that because of differences in metabolism, the same treatment would have to be administered to a human being every two to four weeks to be effective.

The treatment compound will have to go through more study before consideration by the FDA, of course, and even if successful it will take at least five years before it can be made available to patients.

More information: Xiabin Chen et al. Long-acting cocaine hydrolase for addiction therapy, *Proceedings of the National Academy of Sciences* (2015). DOI: 10.1073/pnas.1517713113

Abstract

Cocaine abuse is a world-wide public health and social problem without a US Food and Drug Administration-approved medication. An ideal anticocaine medication would accelerate cocaine metabolism, producing biologically inactive metabolites by administration of an efficient cocaine-specific exogenous enzyme. Our recent studies have led to the discovery of the desirable, highly efficient cocaine hydrolases (CocHs) that can efficiently detoxify and inactivate cocaine without affecting normal functions of the CNS. Preclinical and clinical data have demonstrated that these CocHs are safe for use in humans and are effective for accelerating cocaine metabolism. However, the actual therapeutic use of a CocH in cocaine addiction treatment is limited by its short biological half-life (e.g., 8 h or shorter in rats). Here we demonstrate a novel CocH form, a catalytic antibody analog, which is a fragment crystallizable (Fc)-fused CocH dimer (CocH-Fc) constructed by using CocH to replace the Fab region of human IgG1. The CocH-Fc not only has a high catalytic efficiency against cocaine but also, like an antibody, has a considerably longer biological half-life (e.g., ~107 h in rats). A single dose of CocH-Fc was able to accelerate cocaine metabolism in rats even after 20 d and thus block cocaine-induced hyperactivity and toxicity for a long period. Given the general observation that the biological half-life of a protein drug is significantly longer in humans than in rodents, the CocH-Fc reported in this study could allow dosing once every 2–4 wk, or longer, for treatment of cocaine addiction in humans.