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Treatment of Cocaine Addiction with Viruses

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Abstract:
There are many pharmacological approaches and behavioral interventions that can limit the addiction of cocaine, but with a small success. However, there are new methods that have been studied over the past few years such as immunopharmacotherapy that target cocaine molecules which is assisted by adenoviruses, phage therapy, and the use of viral gene transfer of cocaine degrading enzymes.

Introduction:

Cocaine is an extremely addictive drug that acts on the brain causing it to release excessive levels of the neurotransmitter dopamine to produce a feeling of euphoria or extreme pleasure. A number of medications acting as agonists, antagonists, or antidepressants have been evaluated in both animal models and humans, with only limited success. However, there is a new approach to treat cocaine dependence with viruses. There are different ways to utilize viruses such as using Filamentous bacteriophages that have anti-cocaine antibodies on their surfaces, Adenovirus-based vaccine, and by viral gene transfer of butyrylcholinesterase.(1)

Discussion:

Filamentous bacteriophage fd can be produced at high titer in bacterial culture, making production simple and economical. In addition, they are extremely stable to a variety of harsh conditions, such as extremes in pH and treatment with nucleases or proteolytic enzymes. Bacteriophage can be injected multiple times into the same animal without visible toxic effects. Most importantly they have the capacity to penetrate the central nervous system when administered intranasally. This method is presented for engineering filamentous bacteriophage to display cocaine-binding proteins on its surface that sequester cocaine in the brain. These proteins are designed to bind cocaine, thereby blocking its effects, and/or degrade cocaine via hydrolysis of the benzoyl ester, thus rendering it less psychoactive. Another method is by using anticocaine antibodies that bind to cocaine in circulation, retarding its ability to enter the brain. A different antibody-based approach uses catalytic antibodies specific for cocaine and the cleavage of its benzoyl ester.(2)

Another approach is by utilizing an *Adenovirus-based anti-cocaine vaccine* to reduce cocaine self-administration. This study demonstrated that a cocaine vaccine that used a disrupted Ad gene transfer vector elicited a robust and long-lasting humoral immune response in rats. In sequestering drugs of abuse with antibodies, it is important to evoke both high titers and high-affinity antibodies to the drug to be able to counteract the bolus amount of a drug commonly used in addicts. When acutely injected with cocaine, dAd5GNE-vaccinated rats displayed a vastly reduced response to cocaine-induced stimulant behaviors. The vaccinated rats showed a progressive decrease in the psychomotor-stimulating effect of cocaine during repeated injections of cocaine, whereas the non-vaccinated rats exhibited sensitization to the effect.(3)

Another method is by the use of *viral gene transfer of butyrylcholinesterase*. Butyrylcholinesterase (BChE) is a plasma enzyme that hydrolyses the neurotransmitter, acetylcholine with a lower efficiency than acetylcholinesterase (AChE) but with the capability to degrade a broad range of bioactive esters. BChE hydrolyzes cocaine. Actually, it is a major factor in cocaine metabolism by humans and rodents. Normal BChE levels in liver and plasma are enough to limit cocaine-induced euphoria to just a few minutes after drug intake. This feature encouraged exploration of treatments for cocaine addiction and overdose, by raising BChE blood

levels and enhancing its efficiency by modifying key residues in and around the enzyme's catalytic site. Scientists have developed a mutated form of the enzyme that is 20-fold enhanced to hydrolyse cocaine, and called it *cocaine hydrolase*, "CocH."
Delivering enzyme protein to mice by direct injection proved highly effective in reducing cocaine's behavioral impact, as measured in reduced drug-stimulated motor activity. Then they enhanced vector expression efficiency by optimizing promotor elements. An AAV-VIP vector was more effective than AAV-CMV. It raised plasma levels of CocH activity in a dose-dependent fashion and sustained a 10-fold increase for an entire 3-month period of observation. These outcomes encouraged further study of CocH gene transfer to determine if it could deliver equivalent amounts of enzyme for a year or more.(4)

Conclusion:

Cocaine dependence continues to be a major public health problem. There're many methods used to limit the addiction. New approaches have been widely studied to help stop the self-administration or the abuse of the drug, such as the use of anti-cocaine antibodies, filamentous bacteriophages, anti-cocaine vaccines, and others. Although they have not been used in clinical trials, but the laboratory results are promising.

References:

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