Topics in Brief
National Institute on Drug Abuse
NIDA
NATIONAL INSTITUTE ON DRUG ABUSE

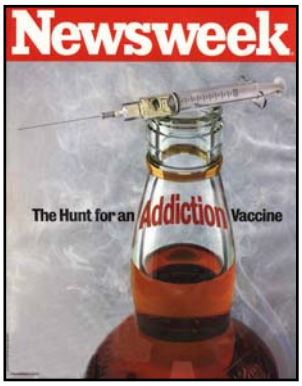
Medications Development at NIDA — July 2008

Breakthrough discoveries in the last decade have led to a profound transformation in understanding the mechanisms and consequences of drug abuse and addiction. The current picture offers a unique opportunity for the results of NIDA's collective research to be translated into new, effective pharmacotherapies that could, either by themselves or with tested behavioral therapies, help alleviate the devastating personal and social impacts of addiction.

NIDA's push to develop effective addiction medications. NIDA's program to support the discovery and testing of new addiction medications was established in response to a call by Congress "to treat the symptoms and disease of drug abuse." Given the urgent need for these medications—which still do not exist for stimulant, cannabis, or polysubstance abuse—NIDA has made the development of addiction medications a top research priority. Pharmaceutical companies have been reluctant to invest in this area, largely because of financial disincentives and associated stigma. Thus it is a gap that no one else will fill.

NIDA's approach to the development of new addiction medications

A dual strategy to medications development. NIDA's strategy focuses on: (1) medications already approved for other disorders with potential application to addiction treatment (e.g. antiepileptic drugs), and (2) new compounds that can interact with recently discovered targets in brain circuits affected by addiction. The former approach takes advantage of already approved medications' safety profile information and lower development costs, while the latter is more responsive to breakthrough discoveries.

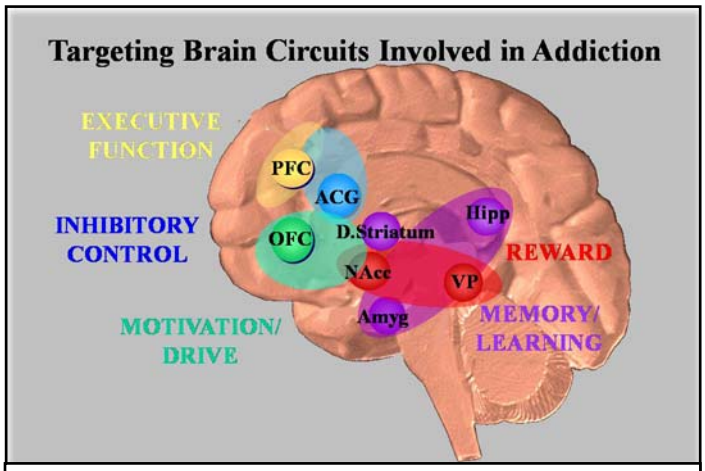


Vaccines to block drugs from reaching the brain. Vaccines are being developed that induce the body to produce drug-specific antibodies able to sequester drug molecules while they are still in the bloodstream, preventing them even from entering the brain to exert their rewarding effects. Vaccines could be useful in preventing relapse in individuals recovering from addiction. Nicotine and cocaine vaccines have already been developed and are undergoing testing in humans. A methamphetamine vaccine is in earlier stages of development.

Beyond the brain's reward system. Research shows that parts of the brain beyond the reward system are implicated in drug abuse and addiction. These include circuits involved in learning and memory, inhibition of behavior, and stress. And while the involvement of multiple brain systems makes the treatment of addiction challenging, it also offers multiple avenues for intervention and calls for new approaches to medications development. Projects include:

- **Medications to enhance cognitive processes.** Addiction changes the parts of the brain that affect our ability to think straight, control impulses, and understand consequences. These deficits can predict treatment dropout and lead to continued abuse and relapse. Modafinil is one such promising medication that may help people recover cognitive functioning and get the most from behavioral therapies—it is currently being tested for treating cocaine and methamphetamine abuse.

- **Medications to counter relapse.** Common triggers to relapse include stress and exposure to conditioned cues (i.e., the people, places, moods, or things associated with the drug experience). Medications that interfere with the biological response to stress and drug stimuli may offer promise for relapse prevention.



New knowledge about which parts of the brain are involved in drug abuse and addiction has revealed new targets for medications development. These medications aim to:

- interfere with a drug's reinforcing effects
- increase the value of natural rewards
- strengthen executive function/inhibitory control
- interfere with conditioning/create new memories
- counteract stress responses that lead to relapse

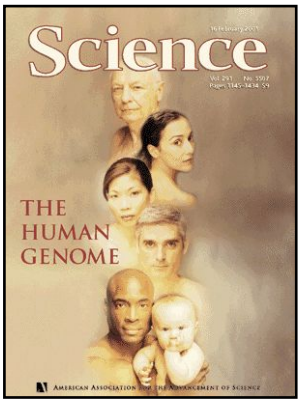
NIDA's efforts to improve the effectiveness of addiction medications

New formulations and delivery mechanisms. NIDA is continuing to explore new ways of formulating and delivering medications that will enhance their effectiveness and reduce addiction liability.

- **Suboxone** (a buprenorphine/naloxone combination) was approved in 2002 for opioid addiction. It acts on the same brain receptors as heroin and morphine, but without the same "high," physical dependence, or dangerous side effects. Its unique formulation with naloxone, an opioid antagonist, produces acute withdrawal symptoms in severely addicted persons who inject it to get high, reducing the likelihood of diversion.

- **New depot formulations** of medications, with effects that last for weeks instead of hours, are being studied in different patient populations to overcome problems of patient compliance.

- **Next-generation pharmaceuticals.** A key goal for medications development at NIDA is to use knowledge gleaned from human genome studies to elucidate how a person's genetic makeup affects his or her response to a therapeutic medication—known as pharmacogenomics. We have already seen exciting discoveries where carriers of particular gene variants showed better responses to bupropion for smoking cessation and to naltrexone for alcohol abuse, for example. Such findings herald a future in which a patient's genetic background will be a major factor in selecting the most appropriate (and therefore cost-effective) therapeutic course of action.



For further information please visit NIDA on the web at www.drugabuse.gov or contact:

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