

Does neuroscience give us new insights into drug addiction?

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Becoming addicted means a life of compulsive drug seeking and use, despite the severely negative consequences of such self-medication. Research using experimental animals, from rodents to non-human primates, has shown that normal animals, never previously exposed to addictive drugs, will readily self-administer every drug that human beings abuse. When these animals are given access to these drugs of abuse (alcohol, nicotine, heroin, cocaine, and amphetamines), they will continue to self-administer these drugs compulsively.

Neuroscience research has shed new light on the biological underpinnings of drug addiction, allowing researchers to devise new interventions and develop new treatments for addictive disorders.

What is addiction?

For more than forty years, it has been known that experimental animals will do work (press levers or poke their noses in holes) in order to activate electrodes implanted in specific regions of their brains. The spots that elicit such self-rewarding behavior served to help us identify an internal reward system in the brain. This series of interconnected brain regions normally functions to reinforce life-sustaining drives, such as thirst, appetite, and reproductive behaviors.

While the anatomical circuitry associated with reward has been known for some time, modern neuroscience research has identified the chemical signaling systems used by these pathways, and specified how the drugs of abuse act to activate the brain's reward system and mislead the brain into identifying the use of the drugs as a functional reward.

This reward pathway consists of neural connections between the ventral tegmental area and the nucleus accumbens, and contains the monoamine neurotransmitters associated with mood. Addictive drugs act in the brain by increasing the interneuronal signals of dopamine, norepinephrine, or the naturally occurring endogenous opioid in the reward pathway. This increased cellular reward signaling produces a reinforcing effect on the addictive behavior.

Continuous use of addictive drugs causes the brain to take adaptive steps to overcome the effects of the drugs. The brain performs these adaptations by making active those circuits

whose effects oppose the sedating, stimulating, or mood altering effects of the abused substance. When the dependent person stops self-administering their abused drug, the overactivity in these adaptive opposing circuits continues, producing the signs and symptoms of withdrawal, and inducing the drug user to reinitiate drug use in order to suppress the withdrawal symptoms.

After understanding the biological underpinnings of addiction, researchers were able to use these animal models to devise treatments for nicotine dependence, opiate addiction and alcohol dependence. Nicotine replacement products such as chewing gums, and skin patches, release nicotine into the blood stream at levels that prevent the appearance of the withdrawal symptoms. This respite from withdrawal that would otherwise coerce further tobacco use, allows the persistent patient the time required to reduce the counter-drug adaptive processes, and restore a healthful condition.

For opiate and alcohol dependence, the appropriate brain receptors for the endogenous opiate transmitters can be occupied by the drug naloxone. Naloxone acts to block the drug effects of opioids, such as heroin, by blocking opiate receptors in the brain. This treatment has been used acutely in cases of respiratory depression in infants born to addicted mothers and in cases of morphine or heroin overdose, to reverse some of the harmful effects of heroin.

Long acting forms of naloxone can provide opiate antagonism for weeks, increasing the time of respite from withdrawal without requiring the compliance of the addict to take the drug. These advances in our understanding of addiction are leading to the development of fundamentally new treatments for addictive disorders that are already under clinical testing.

Why do some become addicted and some do not?

Drug addiction is a chronically relapsing disorder characterized by a compulsion to seek and take a drug, loss of control in limiting intake, and emergence of a negative emotional state (for example, dysphoria, anxiety and irritability) when access to the drug is prevented. An important goal of current neurobiological research is to understand the molecular, neuropharmacological, and neurocircuitry changes that mediate the transition from occasional, controlled drug use to the loss of behavioral control over drug seeking and drug taking that defines chronic addiction. For much of the twentieth century, drug addiction was regarded as a personality issue, as a habit that the addict could break if they had sufficient will power to do so.

However, beginning in the 1970s, solid research in humans and in animal models of addiction indicated that a vulnerability to becoming addicted was biologically based and inheritable. Lines of animals who were vulnerable or resistant to drug self administration were created by inbreeding, while human research indicated that children of alcoholics adopted away from their dependent parents expressed the same higher levels of drug dependence as those raised by the addicted parents.

The modern molecular research that has identified the neurotransmitters systems that underlie the specific addictive effects of opiates and alcohol has also shown that those individuals whose opiate receptors are somewhat less sensitive to opiates, especially among Caucasians, are more vulnerable to opiates and heroin addiction and more readily treatable by the opiate antagonist drug naltrexone. As this research reveals more neurotransmitter involvement in the addictive process, it is likely that additional interventions will become manifest. These biological vulnerabilities do not exonerate the person for responsibility for their addictive state since it is their choice to use the drugs, once or multiple times.

Should we punish addicts?

During the 1970s, and indeed even occasionally today, drug addiction was considered by law enforcement officers and the criminal justice system to be instant and permanent, inducing a craving so powerful that no conscious effort could overcome it. For those addicts in withdrawal, overtly criminal behavior to acquire drugs was considered justifiable.

However, research with large samples of soldiers, based on testing and interviews one and three years after their military service, provides astounding results. Initial interviews supported by urine testing indicated that nearly 80% had used marijuana, half of all enlisted men had tried morphine or opium, and that nearly 20% were symptomatic enough to have been called dependent while in the service. One year later only 5% of those who were addicted to opiates in the war zone were addicted in the United States. Of those not addicted, virtually none had received any treatment.

Lee Robbins of Washington University in St. Louis, the lead epidemiologist of those studies, concluded that the availability of cheap drugs accounted for the high rates of drug use in wartime. Clearly, the common view of the addict—once addicted, addicted for life—was erroneous. Addiction was not a lifelong dependency; it could be interrupted by a change in environment even without treatment. Perhaps, with the right agent, treatment was possible.

However, for the veterans who exhibited deviant social behavior before serving in Vietnam, the rates of re-addiction and treatment failure were as high as in the civilian and federal prison populations. In the case of alcohol dependence, the lifetime prevalence approaches 20% in the general population. To imprison an individual and provide neither treatment nor the prevention of access to the drugs to which they were dependent before imprisonment sacrifices all the knowledge that an addict can be treated and leave prison free of drugs.

Effective treatments and interventions are available, although psychostimulant dependence remains an area of intense research development.

Death from opiate overdose is a major source of mortality following release from incarceration. A prerelease program of education and the provision of an opiate antagonist, such as naltrexone, to the released prisoners helps reduce mortality.

Moreover several treatments for opiate and alcohol dependence have become available to physicians treating addicts. One, Vivitrol™, is available in a long lasting form requiring one injection a month thereby eliminating concerns for compliance. This appears to be a good alternative to an oral medication that needs to be taken one or more times daily, such as with alternate treatments like buprenorphine or acamprosate. It is even possible to predict effectiveness of this treatment option with genetic testing for alternative forms of the opiate receptor where both alcohol and opiate drugs act. In either alternative, treatment with behavioral therapy has been shown to be an important complement to medication treatment for addiction. Treatment for marijuana dependence through various medications is almost as effective as pharmaceutical treatment for dependence on opiates and alcohol.

Basic neuroscience research strongly supports the position that an untreated addict released into the social environment in which their drug use was previously undertaken will almost certainly result in a return to drug use and the accompanying criminal activity undertaken to support it. Prisoners should be treated for their addictions, given a respite from the ability to obtain the drug of choice (or any drugs), and returned to society in an environment sufficiently different from the one in which they were dependent to help break the addiction.

References

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