Drug Addiction:
A Chronically Relapsing Brain Disease

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Our understanding of drug addiction balances uneasily at the intersection of scientific and public knowledge. Few issues mix morality, science, public policy, and simple ignorance in such a volatile way. Older but entrenched views of addiction cast it as a moral failure, the result of weakness of will, or simply bad behavior.[1] Points of view like these logically led to the use of the criminal justice system as the solution to the addiction problem. Now, however, realizing this approach has failed, even law enforcement personnel are looking for ways to keep nonviolent drug abusers and addicts out of jail. In addition to failing to treat addiction, criminal justice approaches also reinforce the damaging stigma that surrounds addiction and which actually impairs a person's ability to seek and obtain treatment.

Recent approaches have emphasized psychological and social science hypotheses that trace the cause of addiction to a response to parental abuse or neglect or to unhealthy social conditions like poverty or inner city decay.[2] The solutions to these problems also seemed clear, though almost impossible to effectively achieve. Most recently, however, intensive neurobiological research has made an increasingly strong case that whatever other factors may play a role in the etiology of addiction, addiction itself is a brain disease.[3-5] Describing the evidence behind that conclusion will be the focus of this commentary.

The neurobiological perspective posits that whatever the initial cause of drug use or its escalation into abuse, addiction develops over time in response to repeated, high dose drug self-administration.[6] Such long-term drug abuse engages powerful conscious and unconscious learning mechanisms while at the same time altering the chemistry and microanatomy of the brain.[7,8] The resulting physical brain changes manifest themselves in changes of behavior, the most obvious being the loss of control over drug taking. While we have long known that addicts are compulsive drug users who seek and use drugs even in the face of negative personal, social, and legal consequences, the brain changes that underlie this behavioral syndrome have only recently become apparent to scientists. As a result, there is a disconnect between what the community believes about addiction and what scientists have discovered.

Recent findings indicate that the brain changes caused by long-term drug use continue to manifest themselves well into abstinence and may be a cause of the relapses into compulsive drug use that can occur long after the drug has been cleared from the body. That relapses can occur long after addicts have been detoxified is evidence of an enduring alteration of the brain, but much of the public has not yet come to clearly understand how the brain governs behavior and doesn't really understand why addicts can't simply stop, especially after they become aware of the dangers and negative consequences of drug use.

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Why is this important? Simply put, the more we allow our public policies to be influenced by the knowledge that science brings us, the more likely we are to develop policies that will be effective. In 1973, the state of New York enacted the harsh Rockefeller drug laws, which included long, mandated prison sentences for drug possession and distribution. The logic behind these laws was that once people understood the devastating consequences of being caught with drugs, they would quickly conclude that drug use just wasn't worth it. Following New York's lead, many other states have imposed similarly severe penalties on both drug users and drug dealers.

Looking back 35 years later, however, it has become apparent that incarceration represents the worst kind of policy outcome: it is both ineffective and expensive. It has ruined far

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too many lives because of convictions for simple possession, and we have had to invest billions of dollars to build and maintain prisons in part for those caught up in the extensive sentences required by these laws. Worse, prison by itself does nothing to help or rehabilitate people addicted to drugs. Indeed, the relapse rate into drug abuse among those released from prison without treatment and follow-up care approaches 95%.[9] Because it is clear that drug users being released from prison understand that continued drug use will put them at risk for prison, it seems apparent that something is interfering with their ability to act rationally on that knowledge.

Understanding the neural basis for why drugs can overcome good judgment even in the face of harsh penalties has been the subject of intense scientific interest for only about 30 years, but we are now seeing an ever-increasing payoff from all that work. It is now clear that long-term use of addictive drugs, including alcohol and tobacco, alters the activity in and structure of a specific mesolimbic neural circuit commonly referred to as the "brain reward pathway."[4] This circuit, which comprises the neural substrate for motivation and reinforcement, includes limbic structures like the amygdala and hippocampus, the dopamine-containing neurons of the ventral tegmental area (VTA), the nucleus accumbens (NAS), and the prefrontal cortex, especially its orbital and medial portions (OMPFC). An acute effect that all addictive drugs share is to increase the release of dopamine from the terminals of VTA neurons into the nucleus accumbens and prefrontal cortex. This release of dopamine is highly correlated with reward value.[10]

Long-term use of addictive drugs has profound effects on this system. Chronic cocaine self-administration, for example, decreases the densities of dopamine receptors[11,12] and increases the density of dopamine transporters in the nucleus accumbens.[13] The decrease in the density of the D2 class of dopamine receptors appears to be a universal response to the long-term use of addictive drugs,[14] and may outlast the presence of the drug in the body by many months, if not years.[15] Moreover, drugs alter the microanatomy of neurons in the nucleus accumbens and prefrontal cortex,[16] changing the way they respond to other neural signals, including those having to do with learning and memory.

Another key region of recent interest is the OMPFC.[17] Among other functions, it helps to determine the valence (want or avoid) of potential actions and rewards and their hedonic value (strength of wanting). Drug craving induced in patients who are undergoing positron emission tomography (PET) or functional magnetic resonance imaging (fMRI) scans show that the OMPFC is particularly activated during drug craving, and that the intensity of craving is proportional to the metabolic activity in the OMPFC.[10,18] Injury to the OMPFC in non-drug users causes deficits in a person's ability to select a large reward that will be available in the future rather than a small one that is available immediately.[19] The inability to put off the short-term pleasure of immediate drug use in the face of knowledge that the future will be better without drugs is one of the characteristic deficits of addiction, and recent evidence indicates that long-term drug addicts are impaired in the same way brain-injured subjects are when trying to make this type of decision. MRI changes indicative of injury in the OMPFC have also been reported and may underlie the behavioral deficit.[20] Thus, the very ability of people addicted to drugs to make sound decisions about drug use may be undermined by drug-induced damage to the brain regions most essential in making those decisions.

Common chronic relapsing diseases have a variety of things in common. For example, atherosclerosis, type 2 diabetes, and hypertension are all characterized by:

- No cure
- Genetic risk factors
- Based in voluntary behaviors
- Cause biological changes in the body
- Can be treated with medications
- Require lifestyle changes for best control
- Relapses and treatment failures are common (due to failure to adhere to treatment regimen)

Atherosclerosis, for example, cannot be cured, but it can be controlled. There are clear genetic risk factors, and poor diet, failure to manage stress, and failure to exercise are all contributing factors. Arterial plaques are an eventual result, and while medications can reduce both the risk for and incidence of plaques, ultimate control requires changes in diet, exercise, and stress management. Less than 60% of those treated for atherosclerosis adhere to their medication or diet and exercise changes, and 30% will require retreatment within one year.

This is just like addiction. Most treatment experts agree that there is no cure, per se, but it can be controlled. Genetics account for 50-70% of the risk of addiction and, once addicted, people experience clear structural and functional changes in their brains. Medications, like methadone for heroin addiction or naltrexone for either heroin or alcohol addiction, can increase the probability of treatment success, but eventual control requires changes in lifestyle, the most important being the cessation of drug use. Relapses into drug use are a characteristic of recovery for many people.

All of these points hold true for type 2 diabetes and hypertension as well, so when we look at these key characteristics, addiction is nearly indistinguishable from other chronic diseases. A huge difference, however, occurs during treatment. Whereas failure of treatment of any of the classic diseases results in a switch to other treatment regimens or an increase in intensity of treatment, people with addictions who fail to progress or who relapse are often thrown out of treatment. Health insurance will cover multiple episodes of treatment for atherosclerosis, even treatment for multiple heart attacks, but insurance companies impose such restrictive limitations on treatment for addiction as to almost assure it will fail for most of the people who need it.[21]

The way treatment for addiction is delivered and paid for in our society reflects a failure of new scientific information to alter entrenched biases against people with addictions. Even

though their behavior is quite analogous to that of people with other chronic diseases that are brought on at least in part by lifestyle choices, people with addictions are stigmatized because a drug is involved. Because people generally don't understand how the brain controls behavior and how drugs change the brain, we shortchange treatment but pay for that many times over in downstream costs for broken families, crime, incarceration, and addiction-related diseases. We can only hope that a clearer understanding of the neurobiology of addiction and the other scientific findings about the cost effectiveness of prevention and treatment will lead to policy-making that is clear-headed and cost effective, with a focus on funding effective drug abuse prevention and addiction treatment. **NCMJ**

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