Can the Science of Addiction Help Reduce Stigma?

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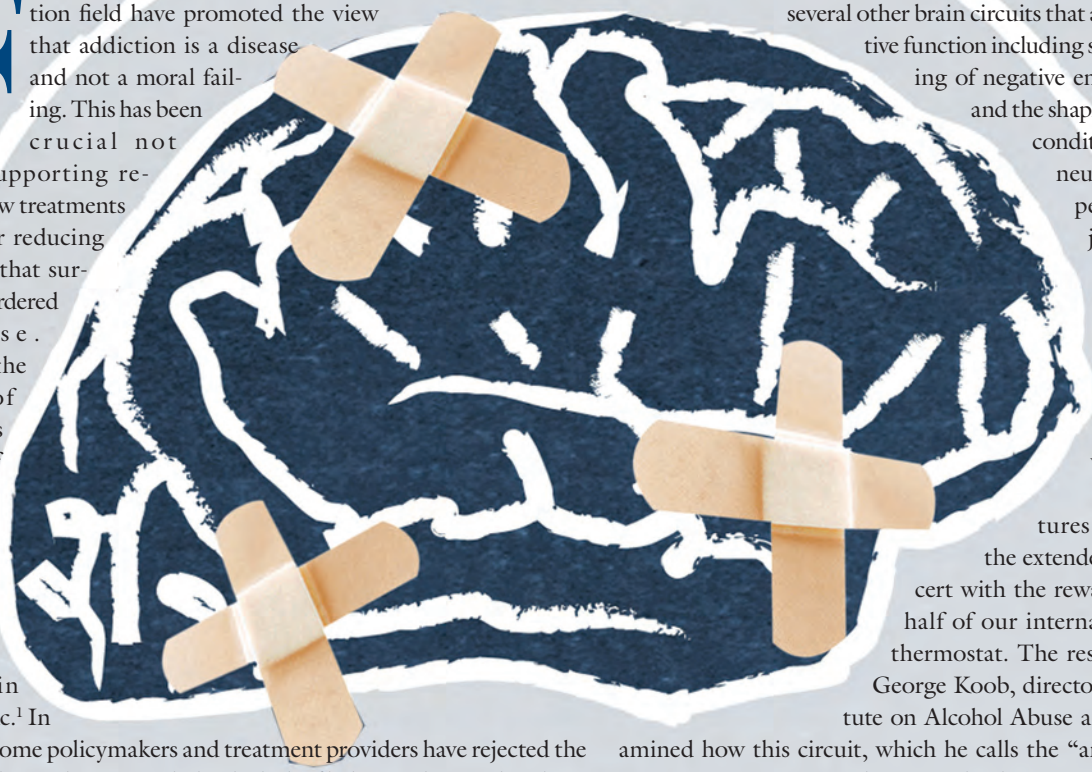

For many years, clinicians and researchers in the drug addiction field have promoted the view that addiction is a disease and not a moral failing. This has been crucial not only for supporting research in new treatments but also for reducing the stigma that surrounds disordered drug use. However, the concept of addiction as a disease of the brain has been questioned by many, both in the health care field and in the lay public.[1] In particular, some policymakers and treatment providers have rejected the notion that brain changes underlie the lack of behavioral control in those suffering from addiction. This has hindered the adoption and utilization of effective harm-reduction measures like needle exchange programs and of medications for treating drug addiction.

By focusing our past educational efforts mainly on one easy-to-understand aspect of the brain changes involved in addiction — those of the reward circuits — addiction researchers bear some of the responsibility for failing to educate the public about addiction's complexity. If the public knows anything about the brain chemistry of addiction, it is that drugs cause surges of dopamine, which we used to call the reward chemical, to flood the reward circuits — the nucleus accumbens and dorsal striatum. This is associated with extreme euphoria, which then motivates the user to seek to repeat that pleasurable experience. But more than two decades of science using advanced neuroimaging and animal models of addiction have greatly expanded our understanding of how drugs cause lasting changes to the brains of users, and dopamine flooding the reward areas is just one small part of the bigger picture. In fact, when susceptible individuals become addicted, even those surges of dopamine are often no longer experienced as pleasurable. It is necessary to convey some sense of the larger systemic imbalances that occur within the brain that drastically compromise a person's ability to control drug use.

It is now known that dopamine is not simply rewarding, but rather that it is the neurotransmitter central to *anticipation,* both of rewards and of punishments. If dopamine remains a key neurotransmitter to understanding the brain of addicted individuals, it is because we now understand that altered dopamine signaling is implicated in a whole ensemble of brain changes involving not only the reward regions but also several other brain circuits that are involved with executive function including self-control, the processing of negative emotions and memories, and the shaping of behavior through conditioning.[2] The disrupted neural circuits in addicted persons continually subject them to depressed moods, irritability, and restlessness, while dangling the faint (and usually disappointing) relief of the drug before their eyes, wherever they turn.

A group of brain structures collectively known as the extended amygdala act in concert with the reward circuit as the other half of our internal pleasure-displeasure thermostat. The research of my colleague George Koob, director of the National Institute on Alcohol Abuse and Alcoholism, has examined how this circuit, which he calls the "anti-reward" system, increases in sensitivity with repeated substance exposure.[3] The result is significant stress and suffering during the phase of withdrawal, when the person is no longer taking the drug. This is coupled with reduced sensitivity in the reward regions to the surges of dopamine mentioned earlier; these circuits get re-set so that the addicted person requires those dopamine surges just to feel a normal amount of motivation or excitement. As a result, during the state of intoxication, drugs provide a brief respite from the stress and negative moods but can no longer trigger the intense euphoria when they were first taken, and ordinary rewards such as food, sex, and other healthy behaviors no longer are capable of motivating the person much or at all. This is one reason why it is so misleading to speak of drug addiction as being about "getting high"; motivationally, it is about escaping being very low.

At the same time that the reward regions reduce their sensitivity to the drug and other rewards, they become rewired to respond to drug-related cues, or conditioned stimuli, through learning processes that Pavlov first described well over a century ago.[4] Anything associated with the drug and drug-taking — which for an addicted person may be everything in their normal routine, including friends and family, home and work environments, and a host of other daily stimuli — trigger anticipatory dopamine release, signaling the expectation of the drug and motivating the individual to seek it out. It then becomes very difficult for the addicted person to avoid this array of motivating signals related to the drug, the strength having become enhanced by the learned anticipation that the drug will relieve the negative moods that overcome them during withdrawal.

But there is still more to addiction than the unbalancing of pleasure and unpleasure and the reshaping of the individual's motivational landscape through conditioning. Addiction also involves changes to the prefrontal cortex and associated control networks necessary for self-regulation, including the control of impulses and desires.[5] It is these changes that often prevent an addicted person from being able to follow through with a sincerely made decision to endure suffering in the interest of becoming free of their dependency.

The changes in the prefrontal cortex, a key component in the control circuits, also involve a desensitization to dopamine, just as has occurred in the reward regions, but in this case the circuits using this neurotransmitter govern the individual's capacity to exert self-inhibition, to resist impulses, and to persist with plans, choices, and resolutions. When these circuits lose their sensitivity to dopamine, self-control in the face of highly motivating stimuli like drug cues, or the drug itself, becomes extraordinarily difficult to exert. The addicted individual no longer has a completely functioning guidance system that is able to steer clear of or resist threats to sobriety.

Healthy non-addicted behavioral choices and decisions are the outcome of highly orchestrated brain processes acting in concert and keeping each other in check. Just as the anti-reward circuitry feeds back on the reward circuitry in a healthy person, the prefrontal circuits also play a key regulatory role that allows to the individual to make optimal decisions that are likely to result in the best outcomes. But dopamine desensitization in these circuits, along with other changes that include the sensitization of the main excitatory neurotransmitter in the brain, glutamate, throw this regulatory process off balance, making drug seeking and drug taking an almost automatic behavior, a drive, with little or no inhibitory brake.

This ensemble of brain changes could be likened to a broken video game. Because of the conditioning processes described above, the addicted person's world is like a threatening virtual environment, a landscape calculated to pose maximal threats to their sobriety — in the form of drugs and drug cues — around every corner and lurking in every shadow. Yet the person playing the game must navigate this environment with a broken controller, such that no matter how hard they try to steer clear of hazards, their game-world avatar heads straight for the drug that will lead them to relapse.

The brain disease model of addiction has facilitated research leading to effective treatments. Restoring normal balance between reward, anti-reward, and executive systems in the brain may require behavioral interventions and, when they are available, medications. Crucial prongs in the current efforts to curb the epidemic of prescription opioid and heroin addiction include effective medications that can make the difference between recovery and relapse — or in all too many cases, death from overdose. Agonist or partial agonist medications like methadone or buprenorphine control withdrawal and cravings, and antagonists like extended-release naltrexone prevent intoxication from occurring when opioids are taken.

One of the terrible consequences of the slow acceptance of the brain disease model of addiction has been the low rate of adoption of methadone and buprenorphine. Since they are, themselves, opioids, they continue to be viewed as a "crutch," and do not fit with erroneous but all-too-common perceptions that the addicted person must simply have the strength to endure sobriety, without aid, from day one. This comes from a failure to understand that the brain, which is comprised of the various self-control and reward circuits involved in addiction, is an organ like any other in the body (albeit much more complex), requiring time as well as support to heal. In fact, we do not ask a person who has suffered severe injury as a result of a car accident to walk without aid while their bones engage in self-repair; external support — often, crutches — are needed to take the burden off healing limbs. In some cases long periods of rehabilitation, lasting years, may be needed after accidents, to restore functioning that was lost. Brain diseases are no different.

Medications including naltrexone are also available to treat alcohol addiction — although fear of stigma prevents many people with this addiction from seeking treatment that could help them — and a range of medications exist to help curb current and ex-smokers' craving for nicotine. Over the coming years, the rapidly advancing science of the brain mechanisms underlying disordered substance use and the transition to addiction are expected to produce new medications for other drug addictions like cocaine, methamphetamine, and marijuana, as well as entirely new treatment approaches like vaccines and other immunotherapies that neutralize a drug in the bloodstream, not allowing it to enter the brain, and non-drug interventions such as transcranial magnetic stimulation and direct current stimulation.

The extreme brain changes characteristic of addiction are by no means automatic, even in people who use drugs regularly. Factors contributing to an individual's unique vulnerability or resilience — both to experimenting with drugs initially and to the progressive brain changes associated with addiction — include family history of substance abuse, exposure to drugs in early adolescence, exposure to stressful environments and life circumstances across development and adulthood, and certain mental illnesses. Of those who are exposed to drugs, we roughly estimate that about 10 percent will become addicted. The non-inevitability of addiction is a point frequently emphasized by people challenging the brain disease model, with the faulty reasoning that it cannot be a disease because the condition is initiated by a decision to take a drug, which is viewed as a voluntary behavior, and also because most individuals never escalate their drug taking. However, this is no different from many other diseases that also have complex genetic, environmental, and developmental origins, may be triggered by voluntary behaviors or their omission, and may only affect a small subset of those at risk.

I often compare drug addiction to another chronic, relapsing disease, diabetes. In diabetes, the pancreas is not able to make the insulin necessary for our cells to use glucose as fuel. No one thinks that, with sufficient willpower, a person with this condition could push through without medication. Their disease, even if it had behavioral antecedents and may have involved free choices in a person's past — such as decisions about food or exercise — has a physical basis and requires medical management once it has developed. Fortunately, people often have a basic understanding that the diseased pancreas is the reason people with diabetes require constant medication, and thus no one questions when a person with diabetes excuses themselves before meals to take insulin or requires snacks at odd times. Drug addiction, despite decades of effort, still has not attained an equivalent level of social understanding: Just as the diseased pancreas cannot supply sufficient insulin, the brain affected by addiction cannot supply sufficient self-control, and the addicted person requires medical management — not judgment — to recover and lead a normal life.

But a medical approach to treating addiction by no means lessens the importance of prevention—in fact, understanding the scope and complexity of the brain changes occurring with addiction underscores how crucial prevention is. The more we learn, the more focused and skillful we can be in learning to prevent those changes from occurring. Increasing research into risk and protective factors not only in the highest periods

of vulnerability during adolescence but also in the first years of life are leading to new and effective interventions, even targeted toward pregnant women and young families. Depending on the age and population to which they are targeted, prevention interventions may enhance participants' social skills and self-control, screen them for mental illnesses or their early signs, and create opportunities for furthering their educational and emotional development.

An upcoming major prospective study to be funded by a consortium of NIH Institutes, the Adolescent Brain Cognitive Development (ABCD) study,[6] will use neuroimaging and advanced genetic and other technologies to study brain development in a large cohort of adolescents over ten years. This will teach us a great deal about the effects of various drug trajectories (including alcohol and nicotine), from abstinence through poly-drug use and substance use disorders, on the developing brain and related outcomes. It will also help inform new prevention approaches, as well as providing valuable insight into the ways drugs affect the brain during some of the most vulnerable years of life and, in a subset of cases, lead to addiction.

People suffering from addictions are not morally weak; they suffer a disease that has compromised something that the rest of us take for granted: the ability to exert will and follow through with it. The desire to be rid of the drug and its destructive influence on their life and health and relationships is usually quite sincere, but the ability to follow through on the choice to not use the drug has been compromised by their disease. I have seen all too often how the cycle of relapse and the shame and self-disappointment this disease produces can rob a person of hope and even, in extreme cases, the will to continue living.

Reducing the stigma that still surrounds drug addiction and its treatment requires getting across to the public, including policymakers, physicians, and addicted persons and their families, the complex nature of this condition. The complexity is not only biological but also philosophical, because it affects how we think about our own free will. It requires understanding that something as basic as our ability to make and follow through with choices in our own best interest is rooted in biological mechanisms that can become disrupted by drugs and, in some cases, compromised by a chronic disease.

Dr. Nora Volkow is Director of the National Institute on Drug Abuse at NIH. Dr. Volkow's work has been instrumental in demonstrating that drug addiction is a disease of the human brain. As a research psychiatrist and scientist, Dr. Volkow pioneered the use of brain imaging to investigate the toxic effects and addictive properties of abusable drugs. She has published more than 600 scientific articles and edited three books. She has received multiple awards, including membership in the Institute of Medicine, and named one of Time Magazine's "Top 100 People Who Shape our World", "One of the 20 People to Watch" by Newsweek magazine, Washingtonian Magazine's "100 Most Powerful Women" and "Innovator of the Year" by U.S. News & World Report.

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