

DRUGS AND THE BRAIN



"After being sledgehammered repeatedly by drugs like cocaine, this system adapts. It changes, trying to preserve its equilibrium."



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DR. SHAFFER: Depending on who you read, it is estimated that the combined ill effects of addictive behaviors affect from 500,000 to 800,000 preventable deaths each year and perhaps account for the majority of hospital admissions at any given time. In addition, addictive behaviors contribute to domestic violence, crimes against person and property. Based on the news from the last five to ten years, we could all agree that addictive behaviors have become one of the most important public health concerns of our time.

We have always thought that either you're addicted or you're not. Again, the studies of the last five to ten years have proved a different story. Let me track the natural history of addictive disorders from initiation to recovery:

1. Basically, all our "Just Say No" prevention programs were focused on the first stage of addictive disorder--initiation. Obviously, if you don't start an activity you cannot become addicted to it. So, one of our primary prevention efforts should be to keep people from engaging in certain kinds of behaviors.
2. However--it is impossible to keep people from eating, risk-taking, ingesting psychoactive substances and so forth--some people move to the next phase. They experience positive consequences from the activity or the substance ingestion. Those positive consequences can be biological, sociological or psychological, depending on the setting one is in. That is a time when people use and seem to be carefree about their substance use.
3. But inevitably, adverse consequences develop. When they do, we tend to think of people as in the throes of addiction. You perhaps have heard the phrase, the "disease of denial." This is a time when they seem to be unaware of the cause of their difficulties. The reason primarily is that their subjective experience seems to be trapped in stage two; they are still experiencing some positive consequences somewhere in their awareness, while other parts of their life are starting to deteriorate.
4. Some, not all, people that experience addictive disorder reach a turning point. They reach a crisis in their life, a moment when they seem to be shamed and humiliated by their behavior; they seem to be in poor health, or at vocational or matrimonial risk. This is a time when they begin to search for ways of

Pathways In & Out of Addiction

Stages of Change

1. Initiation
2. Positive Consequences
3. Adverse Consequences
4. Turning Point(s)
5. Active Quitting
6. Relapse Prevention or Change Maintenance

changing.

5. Then they might reach the fifth stage, active quitting. They are no longer thinking about it; they are beginning to mobilize their behaviors and change in an active and purposeful way to separate from their addictive behavior.
6. Mark Twain said that it was easy to stop smoking, he had done it thousands of times. Anyone who has tried to change a behavior pattern knows exactly what he meant. Active quitting is perhaps the briefest of all phases in addictive disorder and it leads to possibly the longest phase in the natural history of addictive disorders. That is "relapse prevention" or "change maintenance"--the attempt that we all make to sustain our changed behaviors.

What is interesting about these natural stages is that these are the stages people seem to go through whether or not they separate from their addictive behavior with the guidance of self-help groups, Twelve-Step groups, for example, or on their own in a self-directed recovery process.

Dr. Hyman is going to talk about how substance use and abuse, and other potentially addictive experiences, influence the brain.

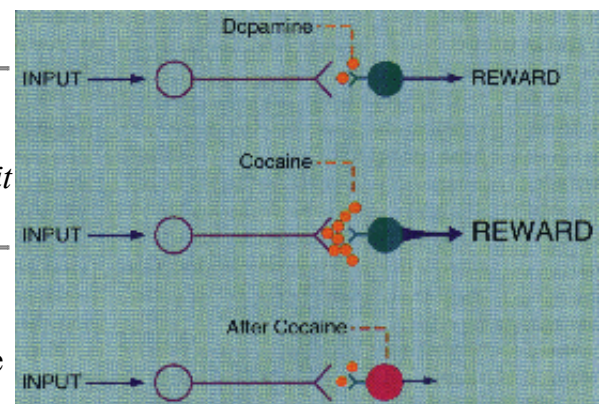
DR. HYMAN: Often we think that things like addiction are "just" psychology or just about experience, but in fact the substrate of all psychology and experience is our brain. Indeed, if we think about the positive consequences that follow the ignition of the use of addictive substances, we must think about the brain as the substrate.

What do I mean by this? Why are certain drugs profoundly addictive and other things less so? We all know that opiates, cocaine, nicotine and ethanol can be profoundly addictive, at least for a large number of human beings, whereas nobody goes around shooting up broccoli or celery. Why can essentially natural plant products have such a hold on human beings? The answer is, within these natural plant products are chemicals that mimic natural chemicals, the neurotransmitters, in the brain.

Take two nerve cells in the brain. The environment might impact on the first nerve cell. It releases a chemical, say, dopamine, which stimulates the next nerve cell in the chain. It turns out there is a particular group of nerve cells in the brain--in fact, more than one, but one key system--involved in the production of pleasure, of saying: "That was a good thing." The jargon for this is "reward."

Why do we have such a system in our brain? Clearly, certain behaviors have to be rewarded. For example, if sex didn't make people happy, Mother Nature's experiment with sexual reproduction would have been a terrible failure and the world would be dominated by yeast, which reproduce just by budding. So powerful systems in the brain reward certain actions. It turns out that the most addictive substances we know, opiates, cocaine, nicotine, ethanol, all seem to tap into this natural system in different complicated ways. The easiest example to explain is cocaine.

Process of cocaine addiction: (top) dopamine triggers reward signal; (middle) cocaine blocks reuptake, causing excess dopamine at contact point; (bottom) adapted cell does not transmit reward signal in response to normal dopamine level.



In a simplified two nerve-cell circuit leading to pleasure, dopamine is the chemical released by the neuron responding to the world and turning on this other neuron that downstream produces

pleasure. But what does cocaine do? Cocaine blocks the ability of this nerve cell to clear dopamine out of the synapse, the contact point between the cells.

As a result, in the presence of cocaine, there is an extraordinary amount of dopamine and the system is driven very, very hard. What you get, at least initially, is a great deal of pleasure.

There is one problem with all of this. Drugs like cocaine drive the system much harder than Mother Nature even intended. And one of the fundamental principles of the nervous system is "homeostasis;" that is, the system is always trying to preserve its balance, trying to maintain its own equilibrium. So, after being sledge-hammered repeatedly by drugs like cocaine, this system adapts. It changes, trying to preserve its equilibrium.

In many cases, processes of homeostasis are readily reversible. Unfortunately, this one does not easily reverse. These nerve cells adapt, but now are dependent on cocaine. In the absence of the drug the addict feels that the world is empty, meaningless. The addict can't experience pleasure, but does experience an intense craving for the drug.

In essence, addiction is a disease of the brain--in large part caused by putting drugs repetitively into the brain. And there are real neurochemical changes which are the object now of intense scientific scrutiny.

What we are trying to understand is what is this long term ratchet-like change? How can we either circumvent it or in essence break the ratchet? And, how can you have your brain back as it was before you started using addictive drugs?

One question a lot of people ask--so I'll ask Howard: Let's say we are now dependent on this drug and there is not any miraculous chemical treatment. But some people get better, and others despite very good efforts remain addicted. Why is it that some people get better and some don't?

DR. SHAFFER: Steven and I were talking about this before, and my first response was that some people are luckier than others. In fact, that certainly has some role in the recovery process, because people who are what I call "luckier" begin to find alternative reward systems to compensate for the shifts or adaptations that have occurred in their brains. These people begin to find new meaning in life in alternative ways and somehow manage to sustain this new reward system that organized their life until their brain begins to readapt, or move back to a more natural state.

It is difficult for us to predict who will recover and who will not. Our research is not nearly as precise in that regard as it might be. What we do know is that people who have failed to recover repeatedly still have the same chances as those who are attempting recovery for the first time.

I'll turn the tables and ask Steven how is it some people get addicted and others don't?

DR. HYMAN: An equally impossible question, but we have some reasonable suspects to round up. One of the things we notice is that a lot of addictions run in families. At least for the case of alcoholism, there is pretty good evidence that certain genes, we don't know what these genes are yet, certainly do give people a predisposition to become alcoholic.

You could imagine that certain unlucky genes create a set point in adaptive systems, set the thermostat in your brain so that you are more susceptible to the effects of certain drugs. We would like to know, because it might really help with both prevention and treatment efforts.

Other things that we believe really matter? The environment in which you grow up. Are drugs absolutely

proscribed? That can be both good or bad. It can give you the strength to avoid drugs but it also may mean, when somebody becomes newly independent and has no real experience they literally go crazy.

Psychiatric illnesses are a predisposing factor. When people get depressed or have other psychiatric illnesses, such as certain anxiety disorders, they may be predisposed to take drugs initially in a misguided attempt to self-medicate to feel better. Then they get caught.

Chronic pain may actually be a predisposing factor. But also there is no doubt that social context really counts. A very dramatic example of the importance of social context is the Vietnam experience. In a context where drugs were plentiful and people were miserable, a very large proportion of enlisted men in combat got literally addicted to heroin, but when they returned to the United States drugs were no longer available. Drugs were proscribed and they were less miserable--and they were able to give it up.

Those are the sorts of reasons why some people may be susceptible and others may not. But we clearly don't have a full understanding.

But I really wasn't quite finished listening to you talk about recovery. Tell us the elements of a good treatment program.

DR. SHAFFER: We have spent considerable time studying people who have successfully recovered, both in treatment programs and on their own, and there seem to be some common themes. The first might be surprising to you: the presence of exercise. Some regular program of exercise seems to be critical.

Structure building--a new relationship, a new job, a new activity, a new hobby. These are all things that bring meaning to our life and change our direction.

Spiritual commitment seems to be important. I don't necessarily mean religion, but some way of getting outside yourself and into a larger scheme of things seems to be vitally important.

People who have recovered on their own seem to have stumbled across, with trial and error, these elements of a treatment program. And professionals seem to have found a way of building these into a treatment program.

I know we are getting to questions, but give us a quick response, Steve. What about the brain chemistry makes these kinds of activities so important in recovery?

DR. HYMAN: One of the things is that in adapting to the sledgehammer of drugs, the brain loses its intrinsic ability to find meaning in life, to find pleasure. In essence, then, we suspect that a successful treatment would give something back to the addicted person. Maybe we will find a drug or a chemical which can reverse this process; that would be the easy way out. But in the meantime, environmental changes, including spiritual activities, group therapy, give something back to the addict. We would also hypothesize, and I think this has also been borne out, that therapies that are more punitive, or take everything away from the addict or restrict their access to drugs and give them nothing back are rarely, if ever, successful.

It is time for questions.

MR. RAEBURN: Smoking seems to be somehow in a different category. Doing research in addiction, do you look at smoking?

DR. HYMAN: Absolutely. From a scientific point of view, this legal drug, nicotine, leads to more unnecessary deaths than any other drug. And in the grain, it is functioning in exactly the same way. Nicotine is one of the most profoundly addicting substances--working presumably through systems like this--of any substance known.

MR. BRUZELIUS: I was fascinated by your reference to exercise and its role in treatment. Do you think that effect has something to do with, say, providing structure? Or might it actually have an independent biochemical kind of effect in the brain that helps support the recovery process? And, by the same token, might fitness have some preventive value, in terms of susceptibility?

DR. SHAFFER: I think the answer is "all of the above." People struggling with addiction are typically in poor health at the time that they decide to give it up or make a change. They have withdrawn from their social support systems or their social support systems have withdrawn from them. And they don't seem to be able to get things done the way that active, vital people can.

A program of exercise, even if it is just walking three times a week for twenty to forty minutes, does not only get the mechanisms of the brain working again and the cardiovascular system going again. It gets people to build a structure in their life that they feel productive about, that they feel they can follow through on and accomplish something, where the end result is fitness and a better self-image. So I think all three are very important.

MS. TOUFEXIS: I've heard that if you left addicts alone long enough, eventually they would physiologically outgrow the addiction. Is there any evidence to support that and what would the biological process be?

DR. HYMAN: I don't think people grown out of addictions just by the passage of time. I think that they have to undergo the kinds of processes that Howard has talked about. We really don't know how long this dependence lasts, but it certainly lasts for a very long time. It is well known that opiate addicts who are fully clean and detoxified may walk past an alley where they used to use drugs with and have an intense drug craving or a tendency to relapse. From what we know, I think that most conservative position is to say that, once you are really addicted to these drugs, your brain is really different than it was before.

MS. TOUFEXIS: Is addiction the same as compulsion or obsession?

DR. SHAFFER: There are elements of both. But obsessive/compulsive disorder is not necessarily an addictive behavior, although right now there are considerable arguments to that with respect to sexual behavior and the amount of overlap.

There are identifiable differences. For example, obsessive/compulsive behavior seems to have an "ego alien" or a self-alien quality, while addictive behavior seems to become what we call "ego syntonic"--we don't really notice that we are engaging in the behavior pattern. Obsessive/compulsive disordered people, on balance, do notice that they are behaving in a way that they would rather not.

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