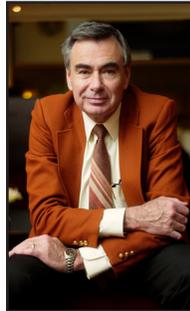


If Addictions Can Be Treated, Why Aren't They?

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The reward system is an important part of the brain, but it often receives scant attention in medical school. This neurological system is activated when we feel pleasure and it motivates us to work for and to seek out food, sex, water and other rewards. It developed early in evolution and is present in modern humans, essentially unchanged from our early ancestors. Unfortunately, certain plant products such as opioids or cocaine are, by coincidence, able to fit perfectly into receptors in the reward circuits where they can directly produce a sensation of reward or euphoria.



Normally a sense of pleasure is earned through constructive behaviors and natural drives. But even a tiny amount of cocaine can directly activate this same pleasure system without the need for the usual work. Cocaine's chemical structure blocks the normal mechanism of the neurotransmitter dopamine, with the result that, instead of the nerve cell releasing dopamine and taking it back up again after its signal is sent, cocaine blocks the reuptake of the transmitter, causing [continued high stimulation of the reward system](#). Dopamine accumulates in the space between nerve cells where signaling occurs (the synapse), and the cocaine effect takes over or "hijacks" the reward system. Other addictive drugs such as alcohol, nicotine, marijuana or opioids also directly activate the reward system through different mechanisms, but the net result is a similar "hijacking."

The reward system in mammals is very

similar to that in humans, therefore we can predict that a drug will be abused in humans by [testing it in animal models](#). If the animal "tells" us that it likes the drug by working to obtain it, it is highly probable that humans will also like the drug. We can also create "addiction" in animals and then test different treatments to see what will reduce the animal's drug taking. The [predictive value of these animal models](#) is usually quite accurate. Having good animal models is a great advantage in the development of new medications. Our understanding of addiction mechanisms is much better developed than our understanding of other mental disorders, such as depression. And this knowledge is being applied by some scientists, thereby enabling them to develop effective medications to treat addiction.

In theory this is happening, but in reality, few pharmaceutical companies have shown any interest in investing in the development of drugs to treat addiction. There is a general belief that there is not much profit in this therapeutic area because:

1. Most clinicians who treat addicted patients are counselors, not physicians; thus they cannot prescribe medication and they generally don't "believe" in the use of medication for addictive disorders. Many of them are former addicts themselves, now in recovery, who "kicked the habit" without medication and they believe that others can and should do the same.
2. Most patients have [medical insurance](#) that excludes or severely limits treatment of addictive disorders, so payment for service is not good. This situation may change in the near future with the advent of healthcare reform in the United States. Even if the Supreme

Court sends the Congress back to the drawing board on President Obama's health care law, the need for reform has become unavoidable. Reformers, including health economists, correctly realize that prevention and early treatment of substance use disorders could save a large part of our national healthcare bill that currently goes to pay for medical complications of substance abuse. A relatively small investment in early treatment of alcohol use disorders, for example, could prevent later liver failure and the need for expensive transplants.

Despite lack of interest from the pharmaceutical companies, a few effective medications have been developed. However, use by treating physicians is very low. For many decades mainstream physicians did not consider addictions to be diseases, so addictions were largely ignored. Even psychiatrists did not address alcohol as a primary problem, so self-help groups such as Alcoholics Anonymous filled the gap. Such groups can do a lot of good, but they do not replace a professionally trained physician who can address the multiple aspects of the addiction including medical, pharmacologic, psychological, occupational and social. The best treatment is usually a combination that includes medication and psychosocial support.

Current Treatment of Addiction

The most common treatment used for virtually all addictions and the intervention most likely to be covered by health insurance in the U.S. is detoxification. This is simply taking away the drug of abuse and perhaps, but not always, providing a medication to suppress withdrawal (rebound) while the drug is metabolized and gradually removed from the body. Depending on the duration of action of the drug, the patient may clear the drug in a few days or detoxification may take several weeks for drugs with a long duration.

After the drug is gone, the patient and his

family may think that the problem is over, but in truth, the addiction is still there. Modern neuroscience, informed by animal models and human brain imaging, shows that the addiction remains despite the absence of the drug, because addiction is a physical change in the brain, similar to an over-learned, long-term memory. We know some but not all of the circuits involved. When the detoxified patient is released from hospital or prison, even when months or years have passed since the last dose of the drug, the sights, sounds and smells previously associated with the drug environment activate reward circuits and evoke intense drug craving. The majority of patients relapse to compulsive drug taking soon after leaving the protected environment of the treatment program.

Relapse after detoxification is a hallmark of addictive disorders. Thus the most [successful treatment](#) strategies aimed at prevention of relapse have involved [combinations of medications and psychotherapy](#). Today, one or more medications helpful against relapse exist for several common addictions, but are underused with the most striking example being medications for alcoholism. Based on studies in animals that were experimentally addicted to alcohol, we learned that one effect of alcohol is to activate the endogenous opioid (endorphin) system. The endorphins released by alcohol produce a feeling of euphoria in some people, the "happy drunk." In different people alcohol has other effects such as sleepiness, irritability, or melancholy. The results depend on heredity and drinking environment as well as previous history of alcohol use.

In the 1980s, researchers followed up the animal studies by conducting clinical trials in people suffering from the disease of alcoholism. They administered a medication that blocks endorphin receptors or an identical placebo for comparison. All patients were treated with intensive outpatient psychotherapy delivered by trained therapists and participated in Alcoholics Anonymous (AA) groups

for 12 weeks. Half of the patients were also given naltrexone, a drug known to block opioid receptors and half were given an identical placebo in addition to psychotherapy. The patients receiving the placebo had a 50% relapse rate at the end of 12 weeks despite the psychotherapy. The group receiving naltrexone and psychotherapy had only a 23% relapse rate at follow-up. In addition, the patients receiving naltrexone reported much less alcohol craving, and if they did drink any alcohol, they reported no euphoria. The subsequent reduction in heavy drinking appeared to make the alcoholics more responsive to psychotherapy even when they did not become completely abstinent.

In order to be believed, all research has to be replicated by other scientists. This study was then repeated in another group of alcoholics treated by researchers at another university. The results were the same. Patients randomly assigned to naltrexone did significantly better than those assigned to placebo. The medication was accordingly approved by the FDA and later by regulatory agencies in other countries. Physicians in Europe recently studied another medication that also blocks opioid receptors and reported similar findings. This new opioid receptor blocker is now expected to be approved by authorities in Europe for the treatment of alcoholism.

It was noted by clinicians that some alcoholics responded beautifully to naltrexone, stopped their heavy drinking and were able to function normally in their community, but other patients reported no benefits. It was found that alcoholics with a strong family history of alcoholism and high levels of alcohol craving were more likely to respond to the medication, suggesting that there is a [genetic difference between responders and non-responders](#). Fortunately, DNA from alcoholic patients in prior clinical trials had been preserved. When DNA was examined from the good responders, they were found to have a high prevalence of a specific genetic variant of the gene for a receptor known as the μ opioid receptor. In the

clinical trials, those alcoholics with the genetic variant had a high probability of a good response to the opioid blocking medication. Those with the standard gene for the μ opioid receptor were less likely to respond to the medication. This finding was subsequently replicated by another group of investigators, but acceptance by the FDA requires a more rigorous study. The new study involves genotyping the patient first and then randomly assigning patients to naltrexone or placebo—a method called a “prospective” study. If this study also shows that those with the opioid receptor variant have a better outcome on naltrexone, the FDA will allow a labeling change stating that alcoholics with this genotype can be expected to have a superior response to naltrexone.

Unfortunately, few of the alcoholics in treatment in the United States receive any medication. Many treatment programs are adamantly against the use of medication. This philosophy was explained in a CNN television special on addiction. Five patients were followed from their entry into well-known treatment programs until their graduation, usually after 30 days of talk therapy and then interviewed again when they later relapsed. None received any relapse prevention medication. A sixth patient, not in the original five, was interviewed at the end of the series. He had been treated with naltrexone and was alcohol free for eight years working in the community. The host then brought a video recording of the interview of this successful naltrexone patient to counselors on the staffs of the five treatment programs. Each of the counselors, after viewing the interview of the naltrexone-treated patient said that, as a general rule, medication was not used in their respective programs.

So the question remains, why are effective medications being withheld from alcoholics and patients addicted to other drugs despite scientific evidence of their value? Why are patients being deprived of a treatment that could change their lives for the better? When the disease does so much damage

to so many people suffering from addiction and to their families, why are most patients not even given a trial of medication in most respected treatment programs?

The answer seems to be that there is a bias among treatment professionals, perhaps passed down from past generations when addictions were not understood to be a disease. Medically trained personnel are minimally involved in the addiction treatment system and most medical schools teach very little about addiction so most physicians are unaware of effective medications or how to use them. Numerous studies have shown that addiction treatment is cost effective so that designers of health care reform have built addiction treatment including FDA approved medications into the new system. We can only hope that medical schools will catch up with the need for education on the treatment of this common disease. Patients and their families can also help by raising questions about the availability of medication

with their treatment professionals.

Further Reading:

Addition: Life on the Edge with CNN Correspondent Dr. Sanjay Gupta - Aired April 19, 2009 <http://transcripts.cnn.com/TRANSCRIPTS/0904/19/cp.01.html>

[O'Brien, C.P.: Prospects for the Genomic Approach to the Treatment of Alcoholism \(commentary\).](#) *Archives of General Psychiatry*, 65(2):132-33, 2008.

Anton, R.F., Oroszi, G., O'Malley, S., Couper, D., Swift, R., Pettinati, H., Goldman, D. [An evaluation of \$\mu\$ -opioid receptor \(OPRM1\) as a predictor of naltrexone response in the treatment of alcohol dependence.](#) *Archives of General Psychiatry*, 65(2):135-44, 2008.

Mary C. Olmstead, "[Animal Models of Drug Addiction](#) (Neuromethods)". Humana Press (2010). (PDF, 484 pp.)