Neuroaddiction: The Reward Pathway.

"The addicted brain is distinctly different from the nonaddicted brain," writes Alan Leshner, the former director of NIDA. "Changes in brain structure and function make it, fundamentally, a brain disease. A metaphorical switch in the brain seems to be thrown as a result of prolonged drug use."

Addiction is both a cause and a consequence of these fundamental alterations in brain function. If physical abnormalities in the brain are at the root of the problem, then any treatment program worth its weight ought to be dealing directly or indirectly with differences in brain state. Writing in Lancet, researcher Charles O'Brien has suggested a similar orientation: "Addiction must be approached more like other chronic illnesses—such as diabetes and chronic hypertension—than like an acute illness, such as a bacterial infection or a broken bone."

All this suggests we are not likely to win a war on drugs, achieve zero tolerance, or become chemical-free any time soon. The drug problem is an artifact of the basic design of the mammalian brain. Humankind is extraordinarily susceptible to drug abuse anywhere and everywhere certain drugs are widely available—and all because of a "design quirk" in the reward pathways of the central nervous system.

Any sufficiently powerful receptor-active drug is, in its way, fooling Mother Nature. This doesn't mean, in a sense, that all such drugs are illicit. They are not natural, however organic they may be. Yet, the human drive to use them is all-pervasive. We have no real built-in immunity to drugs that directly target specific receptors in the limbic and cortical pleasure pathways. The act of "liking" something is controlled by the forebrain and brainstem. If you receive a pleasant reward, your reaction is to "like" it. If, however, you are anticipating a reward, and are, in fact, engaging in behaviors motivated by that anticipation, it can be said that you "want" it. The wholly different act of wanting something strongly is a mesolimbic dopamine-serotonin phenomenon. We like to receive gifts, for example, but we want food, sex, and drugs. As Nesse and Berlidge put it, "The liking system is activated by receiving the reward, while the wanting system anticipates reward and motivates instrumental behaviors. When these two systems are exposed to drugs, the "wanting" system motivates persistent pursuit of drugs that no longer give pleasure, thus offering an explanation for a core paradox in addiction."

Under the biochemical paradigm, a runaway appetite for non-stop stimulation of the reward pathway is a prescription for disaster. The harm is physical, behavioral, and psychological—as are the symptoms. Peer pressure, disciplinary difficulties, contempt for authority—none of these conditions is necessary for drug addiction to blossom. What the drug itself does to people who are biologically vulnerable is enough. No further inducements are required.

Even this brief summary of the ways in which addictive drugs alter neurotransmission should serve to demonstrate that these substances have more in common than we ordinarily assume. All these drugs are of course rewarding, so it is perhaps not too surprising, for all their differences, that they work the limbic reward pathways. All these drugs share common mechanisms of action, which is why they are addictive.

There is more to addiction than the matter of brain chemistry, of course. Nonetheless, the neuropharmacology of addictive drugs can be spoken of with a specificity unknown of only two decades ago. Addiction is a behavior, a state of mind, a way of life—but it is not only these things. It is also a biochemical process. For all their similarities, drugs do have characteristic signatures. They make their own distinctive tracks through the reward pathways of the brain. More...
By 2000, Dr. Le's findings about dysfunctional brain chemistry in his “alcohol-prefering rats” had been borne out in human and animal laboratories and clinics worldwide. All customary levels, alcohol effects GABA transmission, dopamine release, the activation of endogenous opioids in the hypothalamus, and an alternation in the function of glutamine systems. So far, social drinking does not seem to pose similar problems.

Neurobiology has taught us that addictive drugs cause long-lasting neural changes in the brain. The problems start when sustained, heavy drinking forces the brain to accept these altered levels of neurotransmitters as the normal state of affairs. As the brain struggles to adapt to the artificial surges, it becomes more sensitized to these substances. It may grow more receptors at one site, less at another. It may cut back on the natural production of these neurotransmitters altogether, in an effort to make the best of an abnormal situation. In effect, the brain is forced to treat alcoholic drinking as normal, because that is what the drinking has become.

Take the alcohol away, and the new checks and balances, the new receptor sensitivities the brain has learned to deal with, are thrown back into disarray. In the beginning of the process of abstinence, the brain is stubborn. It has learned to deal with the new chemical state of affairs, and sends signals indicating that the drinking should continue. Add alcohol back into the mix, and the roller-coaster cycle begins anew. "I couldn't get drunk, and I couldn't get sober." is a familiar alcoholic's lament. Dr. Vaillant believes we could be doing more to help bolster "rest resistance" to alcoholism. Cultures that encourage the use of low-proof alcohol, like wines, and that sanction the use of alcohol primarily as an adjunct to food—that is, with meals—are better, Vaillant maintains, when compared with family or cultural habits which tend to separate alcohol from mealtime—bars, for example—and which emphasis the consumption of high-proof liquors like whiskey and vodka.

The likelihood that many alcoholics and other drug addicts have inherited a defect in the production and distribution of serotonin and dopamine is a far-reaching finding, because of serotonin's role with a variety of other behaviors often associated with addiction. While it is difficult to measure neurotransmitter levels directly in brains, there are indirect ways of doing so. One such method is to measure serotonin's principle metabolite breakdown product, a substance called 5-HIAA, in cerebrospinal fluid. From these measurements, scientists can make extrapolations about serotonin levels in the central nervous system as a whole.

Despite all the promising research on neurotransmission, what can physicians and health professionals do today to identify alcoholics and attempt to help them? For starters, physicians could look beyond liver damage to the many observable "tells" that are characteristic patterns of chronic alcoholism—such manifestations as constant abdominal pain, frequent nausea and vomiting, numbness or tingling in the legs, cigarette burns between the index and middle finger, jerky eye movements, and a chronically flushed or purplish face. Such signs of acute alcoholism are not always present, of course. Many practicing alcoholics are successful in their work, physically healthy, don't smoke, and come from happy homes. Despite the time, labor, and expense that have gone into the search for a better way to diagnose alcoholism, researchers have yet to come up with what may be the simplest, most accurate test for alcoholism yet devised. Developed in 1970 by Dr. John A. Ewing, it is known as the CAGE questionnaire. The questions are brief and relatively noncontroversial. The test takes less than a minute, requires only paper and pencil, and can be graded by the test takers themselves. It goes like this:

1. Have you ever felt the need to (C)ut down on your drinking?
2. Have you ever felt (A)nnoyed by someone criticizing your drinking?
3. Have you ever felt (G)uilty about your drinking?
4. Have you ever felt the need for a drink at the beginning of the day—an "(E)ye opener"?

People who answer "yes" to two or more of these questions should consider the possibility of alcoholism or alcohol abuse.

MORE...

>> Back to Top

Nicotine

If there is a single, reasonably reliable behavioral marker for alcoholism and substance abuse, it is cigarette smoking.

Nicotine, like alcohol, produces chemical changes throughout the body, and, like all other drugs of abuse, has a focused effect on the reward pathway. Nicotine lights up the usual limbic reward system activated by other drugs of abuse, but does so impressively and almost instantaneously. Dopamine and noradrenaline levels soar, endorphin concentrations...
limbic reward system activated by other drugs of abuse, but does so impressively and almost
instantaneously. Dopamine and norepinephrine levels soar, endorphin concentrations
increase, and steroid levels rise. Nicotine also has a complex impact on serotonin systems.

"In a lot of ways," said Dr. Neal Benowitz, a leading nicotine researcher at San Francisco
General Hospital Medical Center, "nicotine in the brain is doing the same thing cocaine or
amphetamine is doing."

In addition, the nicotine molecules quickly bind to receptor sites meant for acetylcholine, a
neurotransmitter involved in arousal, heart rate, and sending messages from the brain to
the muscles. This direct affinity for acetylcholine receptors is what creates the powerful nicotine rush that frequently
accompanies the first cigarette of the day. Nicotine pops into acetylcholine receptors in the brain, the adrenal glands, and
the skeletal muscles. "These are not trivial responses," said Professor Ovide Pomerleau of the University of Michigan
Medical School. "It's like lighting a match in a gasoline factory."

Acetylcholine is another neurotransmitter we share with other members of the animal kingdom. It is the Achilles' heel of the
insect world—insecticides that cause a fatal build-up of acetylcholine are among the most common in our collective chemical
arsenal against bugs. While the mechanisms of the toxic effect are not perfectly clear, acetylcholine is involved in diaphragm
control, and one of the signs of insecticide poisoning in children is difficulty breathing.

Cigarettes improve task performance and concentration, enhance memory, reduce anxiety and hunger, and increase
tolerance to pain. In laboratory tests, people given doses of nicotine perform better on complicated intellectual tasks, compared with their performance in the absence of the drug. Why? Because smoking activates additional acetylcholine
receptors in the part of the brain associated with short-term memory, for one thing. Indeed, if nicotine did not cause
cardiovascular disease, pulmonary failure, lung cancer, lip cancer, throat cancer, shortness of breath, and smelly clothing, it
might be very nearly the perfect drug.

Experiments at NIDA's Addiction Research Center in Baltimore have confirmed that nicotine withdrawal not only makes
people irritable, but also impairs intellectual performance. Logical reasoning and rapid decision-making both suffer during
nicotine withdrawal. Acetylcholine appears to enhance memory, which may help explain a common lament voiced by many
smokers during early withdrawal. As summarized by one ex-smoker, "I cannot think, cannot remember, cannot concentrate."

Both nicotine and alcohol produce similar patterns of activation at the nucleus accumbens and the prefrontal cortex.
Scientists have documented that alcohol has a strong effect on nicotinic receptors, helping to explain the link between heavy
drinking and heavy smoking. Alcohol may be making it possible for smokers to smoke more. Researchers have been able to
identify common neural substrates linking cocaine and cigarette addiction as well. Nicotine's effect is subtler than most
drugs of abuse, and because of these substrates, smoking's tenacious grip on its victims remains something of a scientific
mystery. People who have never shown an inclination toward addiction to any other drug still manage to get into trouble with

No discussion of smoking would be complete without a reference to the "Hedglett paradox"—the fact that cigarettes are
capable of producing both arousal and relaxation. In the early 1970s, researcher Paul Hedglett ran a series of tests
demonstrating that smokers could withstand an increasingly intense series of electric shocks better than non-smokers could.
If nicotine is a stimulant, why did it have a tranquilizing effect on pain? Hedglett's personal conclusion was that smoking
raises the "arousal baseline." Since smokers are already revved up, operating on "high arousal," they are better able to
withstand shocks that might strike a non-stimulated smoker with more impact.

"It's not that it's so intense," Dr. Banowitz told me, "It's just that it's so reliable. It arouses you in the morning, it
relaxes you in the afternoon. It's a drug that you can dose many times per day for the purpose of modulating your mood, and
it becomes highly conditioned, more than any other drug, because it's used every single day, multiple times per day."

Professor Pomerleau once suggested to me that the neurotransmitter changes produced by nicotine might be behind this
paradox. At low doses, nicotine stimulates acetylcholine and norepinephrine release, and that translates into arousal. But at
high doses, it starts to block acetylcholine, while increasing endorphin concentrations, and the resulting morphine-like
calm might be strong enough to swamp the initial low-dose arousal effect.

A review of various studies by Pomerleau and others tends to support the notion that short, quick puffs on a cigarette tend
to maximize nicotine's arousing properties, while long, slow drags maximize the sedative aspects of the drug. Smokers may
unconsciously learn such mechanisms as a way of matching nicotine's affects to desired moods and behaviors. MORE...

Marijuana (THC)

In the past few years, as addiction researchers have been busily mapping out the chemical
alterations caused by alcohol, cocaine, nicotine, heroin, and tranquilizers, America's most
popular illegal drug has remained largely a scientific mystery. It is a drug that millions of
Americans have been using regularly for years, and yet it is the least studied drug of all.

In the late 1980s, a team of researchers at NIMH was investigating a category of receptors
for substances called cannabinoids. This has far down the hall from the nicotine researchers.
In the late 1980s, a team of researchers at NIMH was investigating a category of receptors for substances called pain peptides. Not too far down the hall from the peptide researchers, neuroanatomist Allen E. Herman had been working with some of the powerful THC analogs Pfizer had been working with. Herman had been mapping activity under the influence of THC, and the map he was getting looked suspiciously similar to the brain distribution pattern of the mystery receptor down the hall.

When the two groups of researchers tested synthetic THC on the new receptors, they had their answer. There was a specific receptor in the brain for THC, the active ingredient in marijuana. Once they went looking for it, the NIMH scientists found the new receptor in all kinds of mammalian brains. Collaborators at the National Institutes of Health were able to make very potent forms of THC radioactive, so that Herman could use them as tracers. “No other drug we tried will recognize that receptor. Opiates won’t recognize it, nor will amphetamine, or cocaine, or POP, LSD—It’s a very unique receptor, and it’s been conserved in evolution.”

Marijuana was another drug for which the human brain seemed to be prewired. Archaeologists have discovered the remains of a 1600-year-old girl who had evidently died during childbirth, and among the remains were ashes containing THC. Scientists speculate that a midwife might have administered the drug in an attempt to ease the pain of a difficult delivery.

The NIMH researchers were struck by the relative density of cannabinoid receptors in the cerebral cortex, and the relative lack of the same receptors in the limbic system. Marijuana use, of itself, very rarely causes the kind of violent limbic explosions associated with abuse of alcohol, cocaine, and amphetamine. In a sense, marijuana is a thinking drug. The receptor for THC, which is heavily distributed in the cerebral cortex, is “a very unique receptor,” as Herman described it. “Sort of a high-brow receptor.”

Nonetheless, even fruit flies appear to have a few cannabinoid receptors. The same THC receptor has been discovered in fish and sea urchins as well, leaving researchers to puzzle over the evolutionary role played by this ancient psychoactive substance. Of what use is a THC receptor to a chicken or a trout? This... paper from Toronto’s Addiction Research Foundation attests, “and its conservation implies that the receptor serves an important biological function.” Or, as a researcher at the University of California, San Francisco summed it up: “Why would we express the receptor at high levels if it just made us stupid?”

There is little evidence in animal models for tolerance and withdrawal, the classic determinants of addiction. For at least four decades, millions of Americans have used marijuana without clear evidence of a withdrawal syndrome. Most recreational marijuana users find that too much pot in one day makes them lethargic and uncomfortable. And yet, people claiming to be addicted to marijuana—and why should we doubt them?—have been turning up in Alcoholics Anonymous and chemical dependency programs over the past twenty years or so.

While the scientific evidence weighed in against the contention that marijuana is addictive, there were a few researchers in the 1980s who were willing to concede the possibility. “Probably not, for most people,” said Dr. James Halikas, then with the University of Minnesota’s Chemical Dependency Program, “But there may be some small percentage of people who are on the same wavelength with it chemically, and who end up in some way hooked to it physically. It’s a complicated molecule.”

Different strains of grass have different effects, and there are dozens of active ingredients in addition to THC. Self-confessed marijuana addicts have tried THC pills, such as Marhum, which are sometimes prescribed for certain kinds of intractable cancer pain. Experienced users report that the effects of synthesized THC is more like a trip, Valium than a joint of marijuana. Like Herman’s monkeys, regular marijuana users don’t much care for strong synthetic THC; either. They basically just get knocked down by it.

The difference between animal models and humans may be the difference between pure THC and naturally grown marijuana. Despite the fact that rats and monkeys find whopping doses of synthesized THC aversive in the lab, psychologists Ronald Siegel has documented instances of rodents feeding happily on wild marijuana plants in the field. There are apparently other components in the psychoactive mix that makes marijuana what it is. When the lab version of THC is hundreds of times more potent than the genuine article, it is hard to know exactly what the research is telling us.

Marijuana is the odd drug out. To the early researchers, it did not look like it should be addictive. Nevertheless, for some people, it is. Recently, a group of Italian researchers succeeded in demonstrating that THC releases dopamine along the reward pathway, like all other drugs of abuse. Some of the mystery of cannabis has been resolved by the end of the 1990s, after researchers had demonstrated that marijuana definitely increased dopamine activity in the ventral tegmental area. Some of the effects of pot are produced the old-fashioned way after all-through alterations along the limbic reward pathway.

Opium

Alcohol’s range of action is diffuse, while opium’s effects are concentrated at specific receptor sites. Nonetheless, the two drugs have similar effects along the limbic reward pathway. Morphine comes right from the source, isolated from the opium poppy; heroin, morphine is known as a “pure mu agonist,” meaning it binds strongly into the “mu” subset of endorphin receptors, and activates them. This alters the transmission of pain messages, and induces a contented, euphoric state of relaxation. Codeine, another natural painkiller, is found in opium in very small concentrations. Most medical codeine is synthesized from morphine.
Amphetamine

If alcohol's impact on brain cells is wide-ranging and diffuse, the impact of cocaine and amphetamine is much more straightforward. "There is certainly lots of evidence for common neurological mechanisms of reward across a wide variety of drugs," said Dr. Robert Post, chief of the biological psychiatry branch at NIMH. Animals will readily administer cocaine and amphetamine, Dr. Post explained, but when researchers surgically block cut areas of the brain that are dense with dopamine receptors, the picture changes dramatically. "The evidence definitely incriminates dopamine in particular," said Dr. Post. "In animal models, if you make selective lesions in the dopamine-rich areas of the brain, particularly the nucleus accumbens in the limbic system, the animals won't self-administer either amphetamine or cocaine."

When you knock out large slices of the nucleus accumbens, animals no longer want the drugs. So, one cure for addiction has been discovered already—but surgically removing chunks of the midbrain won't do, of course.

The entire range of stimulative effects hits the limbic system in seconds, and the focused nature of the impact yields an astonishingly pleasurable high. But the long-term result is exactly the opposite. The body's natural stock of these neurotransmitters starts to fall as the brain, striving to compensate for the artificial flooding of the reward center, orders a general cutback in production. At the same time, the receptors for these neurotransmitters become excessively sensitive due to the frequent, often unmitigating nature of the stimulation.

In the end, says James Halikas, "It's clear that cocaine causes depletion of dopamine, norepinephrine, serotonin—it is a
In the end, says James Hallkas, “it’s clear that cocaine causes depletion of dopamine, norepinephrine, serotonin—it is a general neurotransmitter depleter. That may account for many of the effects we see after someone has stopped using cocaine. They’re tired, they’re lethargic, they sleep; they may be depressed, moody, and so on.” The continued abuse of addictive drugs only makes the problem worse. One reason why cocaine and amphetamine addicts will continue to use, even in the face of rapidly diminishing returns, is simply to avoid the crushing onset of withdrawal. Even though the drugs may no longer be working as well as they once did, the alternative—the psychological cost of withdrawal—is even worse. In the jargon used by Alcoholics Anonymous, addicts generally have to get worse before they can get better. When addicts talk about “chasing a high,” the metaphor can be extended to the lasting battle of neurotransmitter levels.

The release of dopamine and serotonin in the nucleus accumbens lies at the root of active drug addiction. It is the chemical essence of what it means to be addicted. The pattern of reward firing that results from this surge of neurotransmitters is the “high.” Dopamine is more than a primary pleasure chemical—a “happy hormone,” as it has been called. As we have seen, dopamine is also the key molecule involved in the memory of pleasurable acts. Dopamine is part of the reason why we remember how much we liked getting high yesterday.

...Speed, then, is well suited to the task of artificially stimulating the limbic reward pathway. Molecules of amphetamine displace dopamine and norepinephrine in the storage vesicles, squeezing those two neurotransmitters into the synaptic gap and keeping them there. By mechanisms less well identified, cocaine accomplishes the same feat. Both drugs also interfere with the return of dopamine, norepinephrine, and serotonin molecules to their storage sacs, a procedure known as reuptake blocking. MORE...

Cocaine

The cocaine high is a marvel of biochemical efficiency. Cocaine works primarily by blocking the reuptake of dopamine molecules in the synaptic gap between nerve cells. Dopamine remains stalled in the gap, stimulating the receptors, resulting in higher dopamine concentrations and greater sensitivity to dopamine in general.

Since dopamine is involved in moods and activities such as pleasure, alertness and movement, the primary results of using cocaine—euphoria, a sense of well being, physical alertness, and increased energy—are easily understood. Even a layperson can tell when lab rats have been on a cocaine binge. The rapid movements, sniffing, and sudden rearing at minor stimuli are not that much different in principle from the outward signs of cocaine intoxication among higher primates.

Chemically, cocaine and amphetamine are very different compounds. Psychoactively, however, they are very much alike. Of all the addictive drugs, cocaine and speed have the most direct and most devastatingly euphoric effect on the dopamine systems of the brain. Cocaine and amphetamine produce rapid classical conditioning in addicts, demonstrated by the intense cravings touched off by such stimuli as the sight of a building where the user used to buy or sell. Environmental impacts of this nature can produce marked blood flow increases to key limbic structures in abstinent addicts.

...When the crack epidemic first became news, it was clear that the old specialty of free-baseding was now within reach of existing cocaine users. No paraphernalia needed except for a small pipe; no more butane and mixing; no mace, no fuss.

...The summer of 1986 will be remembered as the season of the “crack plague,” as viewers were bombarded with long news stories and specials. NBC Nightly News offered a special report on crack, during which a correspondent told viewers: “Crack has become America’s drug of choice...it’s flooding America....”

...Crack was a refinement to free-baseding, which was, in turn, a much more expensive form of coke smoke that blew up, quite literally, in comedian Richard Pryor’s face years ago. Crack was a drug dealer’s dream. The “rush” from smoking crack was more potent, but even more transient, than the short-lived high from nasal ingestion.

...In the late 1980s, scientists at Johns Hopkins and NIDA showed that opiate receptors play a role in cocaine addiction as well. PET scans demonstrated that cocaine addicts showed increased binding activity at mu opiate receptors sites in the brain during active cocaine addiction. Take away the cocaine, and the brain must cope with too many empty dopamine and endorphin receptors.

Both the cocaine high and the amphetamine high are easily augmented with cigarettes or heroin. These combinations result in “nucleus accumbens dopamine overflow,” a state of neurochemical super saturation similar to the results obtained with the notorious “speedball”—heroin plus cocaine.

...In the short run, the use of cocaine or amphetamine causes increased activity along the dopamine, serotonin, and norepinephrine pathways in the limbic system, as we have come to expect. With a different kind of mechanism common to...
In the short run, the use of cocaine or amphetamine causes increased activity along the dopamine, serotonin, and norepinephrine pathways in the limbic system, as we have come to expect. "It's a different kind of mechanism compared to alcohol," Dr. Li explained. "Cocaine also has serotonin effects, but it's not quite clear how that works."

... By the early 1990s, the dirty little secret was a secret no longer: Most addiction treatment programs were failing. In the case of the newly arrived crack cocaine, relapse rates after formal treatment sometimes approached one hundred per cent. Clearly, a piece of the puzzle was missing; if receptors were the sites that controlled how drugs affected the mind, and if genes controlled how receptors were grown, then it made sense to examine the question of whether alcoholism and other addictions could be inherited.

One implication of the receptor theories was that sensitivity to addictive drugs could conceivably have a genetic basis. It was a large step in the right direction, because there were already good reasons for seeing alcoholism and other addictions as inherited dysfunctions in brain chemistry. MORE...

Caffeine

Until recently, coffee and tea were barely thought of as drugs of abuse, even though it is certainly possible to drink too much caffeine. Are the xanthines, the family of compounds that includes caffeine, addictive? The typical dose in a cup of coffee—between 50 and 200 milligrams, with an average of about 115 milligrams—is enough to produce a measurable metabolic effect. The side effects of overdose—excessive sweating, jittery feelings, and rapid speech—tend to be transient and benign. Withdrawal is another matter. Caffeine causes a surge in limbic dopamine and norepinephrine levels—but not solely at the nucleus accumbens. The prefrontal cortex gets involved as well. At low doses, caffeine sharpens cognitive processes—primarily mathematics, organization, and memory—just as nicotine does. The results of a ten-year study, reported in the Archives of Internal Medicine, showed that female nurses between the ages of 34 and 59 who drank coffee were less likely to commit suicide than women who drank no coffee at all.

Caffeine's psychoactive power and addictive potential are easily underestimated. The primary receptor site for caffeine is adenosine, which, like GABA, is an inhibitory neurotransmitter. Adenosine normally slows down neural firing. Caffeine blocks out adenosine at its receptors, and higher dopamine and norepinephrine levels are among the results. Taken as a whole, these neurotransmitter alterations result in the bracing lift, the coffee "buzz" that coffee drinkers experience as pleasurable.

Scientists at NIH have demonstrated that high doses of caffeine result in the growth of additional adenosine receptors in the brains of rats. In order to feel normal, the rats must continue to have caffeine. Take away the caffeine, and the brain, now excessively sensitized to adenosine, becomes sluggish without the artificial stimulation of the newly green adenosine receptors. Like alcoholics and cocaine addicts, people with an impressive tolerance for coffee and tea may find themselves chasing a caffeine high in a losing battle against fluctuating neurotransmitter growth patterns.

Increased tolerance and verifiable withdrawal symptoms, the primary determinants of addiction, are easily demonstrated in victims of caffeineism. Even casual coffee drinkers are susceptible to the familiar caffeine withdrawal headache, which is the result of caffeine's ability to restrict blood vessels and reduce the flow of blood to the head. When caffeine is withdrawn, the arteries in the head dilate, causing a headache. Caffeine's demonstrated talent for reducing headaches is one of the reasons pharmaceutical companies routinely include it in over-the-counter cold and flu remedies. The common habit of drinking coffee in the morning is not only a quick route to wakefulness, but also a means of avoiding the headaches associated with withdrawal from the caffeine of the day before. MORE...

Carbohydrates

The primary architects of the theory of carbohydrate craving are Dr. Richard Wurtman, a neuroendocrinologist at the Massachusetts Institute of Technology's Department of Applied Biological Sciences, and his wife, Judith, a biochemist at MIT. The two had been investigating eating disorders at MIT's Clinical Research Center as a team, and by the early 1990s, the ongoing results of the Wurtman's work had already cast doubt on a number of obesity myths.

...
Richard and Judith Wurtman showed that overweight people fall into distinct categories, one of which they named carbohydrate-craving obesity. In the MIT studies, the Wurtmans monitored the eating habits of student volunteers with the aid of computer-operated vending machines. Regular meals and between-meal snacks—everything from carbohydrate-packed cookies to protein-rich sandwiches—were available to the participants 24 hours a day. Everything everybody ate was meticulously recorded. Over time, the Wurtmans observed that a particular category of eater would eat normally at regular mealtimes, but would begin to snack heavily in the late afternoon and evening.

People in this category willingly ate protein-rich food during normal meals, but the snacks they chose later in the day were almost exclusively high-carbohydrate foods. More than half of the carbohydrate-cravers never selected a protein food as a snack. Other obese people in the study did not show the same marked preference for carbohydrates, and often ate heavily only at mealtimes, snacking rarely, if at all, between meals.

As the Wurtmans reported in Scientific American:

"We wondered whether the consumption of excessive amounts of snack carbohydrates leading to severe obesity might not represent a kind of substance abuse, in which the decision to consume carbohydrates for their calming and anti-depressant effects is carried to an extreme—at substantial cost to the consumer’s health and appearance.

In the case of certain carbohydrate cravers, the Wurtmans found, dietary tryptophan was being converted into serotonin, like always—but this concentrated serotonin surge was also a powerful mood-booster. It was medicine.

The Wurtmans had hit on something big. People who tended to binge late in the day on carbohydrate foods, particularly simple sugars, got a drug-like “buzz” that was highly reinforcing. In the experiments, these people quite specifically, if unconsciously, selected the kinds of foods rich in serotonin-building compounds.

The serotonin-boosting effects of carbohydrates may explain why addicts in recovery, as well as carbohydrate cravers and PMS sufferers, show a tendency to binge on sugar foods. Abstaining addicts apparently turned to the overconsumption of carbohydrates as a means of attempting to redress the neurotransmitter imbalances at the heart of their disorder. Perhaps some addicts discover early in life that carbohydrate-rich foods are their drug of choice.

Other researchers have reported that a significant number of bulimics are themselves abusers of alcohol and other drugs. What is being suggested is that carbohydrate-craving obesity and bulimia may turn out to be two additional forms of drug addiction. They may be variations on the addictive theme, and the underlying cause may be the same—irregularities in the reward system neurotransmitters.

If this proves true, traditional diet-based approaches to weight loss are likely to prove ineffective for obese carbohydrate cravers and bulimics. Such people cannot “just say no” to carbohydrates, because the underlying biochemical abnormalities that lead to the overeating are not addressed by the moral exhortation to “just eat less.” Like biological alcoholics, they must struggle against a physiology that is telling them otherwise.

A chronic deficiency of brain serotonin might be the underlying cause of carbohydrate craving, the Wurtmans have theorized. For those who may be suffering from carbohydrate-craving obesity, dietary—that is, carbohydrate withdrawal—produces the same symptoms as withdrawal from addictive drugs: depression, anxiety, irritability, and an uncontrollable obsession with the substance in question.

For women whose bodies do not regulate the production of serotonin and dopamine successfully, bulimia is one of the possible symptoms of a disordered reward pathway. Unlike anorexia, its “partner” disorder, bulimia resembles addiction in several ways. There is a definite high, which comes with the purging, and which has no analogue in anorexia. Bulimia’s impact on the brain’s reward center also seems to be quite direct, judging by the high relapse rates of bulimics. The idea that serotonin disturbances were at the root of bulimia was beginning to make sense. Preliminary twin studies were bolstering the hypothesis by showing evidence of genetic predispositions toward bulimia.

The innate drive among the addiction prone for simple sugar carbohydrate foods might reasonably be called “carbohydrolism.” In the Democratic Republic of Congo (Zaire), there is a tribe of pygmies whose natural diet is marked by the virtual absence of sugar foods. Each year, the tribe gathers for an intoxicating group celebration—and the substance they ingest is honey. “The sugar seems to affect them like a powerful drug,” an anthropologist reported in the San Francisco Chronicle. “They drop everything to get the honey, and it sure looks like a binge.” MORE...