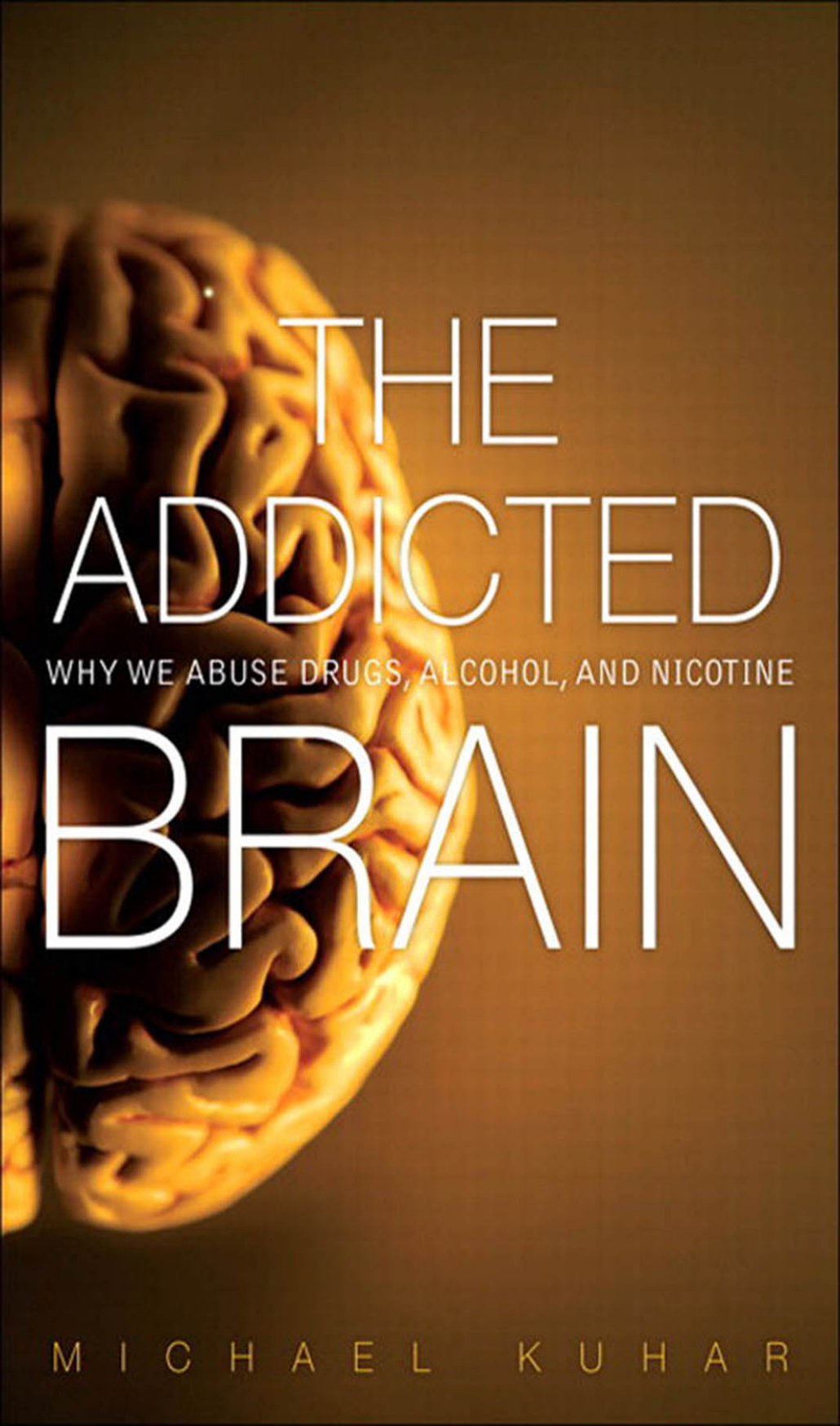
THE
ADDICTED
WHY WE ABUSE DRUGS, ALCOHOL, AND NICOTINE
BRAIN
MICHAEL KUHAR

The Addicted Brain

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The Addicted Brain

Why We Abuse Drugs, Alcohol, and Nicotine

Michael Kuhar

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This book is dedicated to those afflicted with brain disease, to their caregivers and supporters, and to the researchers who hope for a better future.

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About the Author

Michael Kuhar, Ph.D., is currently a professor at the Yerkes National Primate Research Center, Candler professor in the Emory University School of Medicine, and a Georgia Research Alliance Eminent Scholar. His general interests have been the structure and function of the brain, mental illness, and the drugs that affect the brain. Addiction has been his major focus for many years, and he is one of the most productive and highly cited scientists worldwide. He has trained a large cadre of students, fellows, and visitors, received a number of prestigious awards for his work, and remains involved in many aspects of addiction research and education. In June 2011, he received the Nathan B. Eddy lifetime achievement award from the College on Problems of Drug Dependence.

Introduction

Robert's friends convinced him to try crack cocaine at a senior party when he was still 17 years old. It took his head places he could only imagine, and he wanted more, more, more. Three years later, he could no longer hold a job. His teeth were loose and two had fallen out. He stole. He sold his body. He did anything for more! He had been to rehab twice and was back on the street again, and all he wanted was more.

This is a book about seduction, amazing pleasure, and a world inside your head that is both fantasy and real. This fantasy world is not easy to give up, and, like all fantasies, it can be trouble if you can't get back into the real world where you need to live, work, pay bills, and take care of loved ones. Drugs, the brain, and addiction create this dreamland of fantasy, but it can quickly turn into a hell, and it often does.

Research has taught us how drugs and other pleasures affect the brain. It turns out that drugs, gambling, Internet use, and chocolate all affect the brain in similar ways. The importance of this discovery extends well beyond knowing about drug abuse and pleasure; it impacts on ethics and morality, the nature of the brain as a survival organ, the evolution of the brain, and the good, the bad, and the ugly of human nature. Anything that reveals the vagaries and limitations of the human brain is useful and a service to us all. Understanding the brain and human behavior is a basic requirement for setting realistic goals for personal and societal improvement.

Aside from the amazing discoveries, a special glory of this book is the inclusion of wonderful techniques that help us examine the brains of drug users. For example, the development of brain imaging enables us to study how drugs affect the brain without any physical invasion of the head. This is something not even imagined decades

ago. There are many other striking techniques such as drug self-administration and biochemical analyses of tissues. When I say this is a glory, I realize that reveals something about me and my preferences, but you are invited to share in this. I'm lucky that I have spent more than four decades doing this science, watching its progress, and seeing its impact on public health. Within these pages is a fascinating story of science in the service of men.

Different drugs, some legal and others illegal, release powerful demons in our brains. Surprisingly, the demons—the chemicals and nerve cells in our brains—are already there, working in an important but much smaller way that is essential for our functioning. Drugs create the demons by disrupting the chemicals and nerve cells so that they get out of control and wreak havoc in many people. Decades of scientific research have revealed how this happens.

The demons behave as expected. Once unleashed and in power, they don't go away easily. Even after we stop taking drugs, they influence our actions for a long time, for many months or even years. They want you to continue to feed them by taking more and more drugs. Part of the power of the demons is that they reside in powerful brain systems. These brain systems *have* to be powerful because they have a big job, such as keeping us fit and surviving. The long life and the power of the demons make them formidable enemies, but we are not alone or helpless. Treatment and rehab centers help us regain control of our lives. The same demons seem to apply to other addictions—gambling, carbohydrates, sex, and the Internet. Studying one addiction—drugs—helps us understand other addictions.

Knowing the demons is helpful. Because we can understand them and what they do, we can develop medications and other treatments to thwart them and help drug users. In fact, the search for medications, although not yet complete, has been quite successful. We gain ground every day. Also, changing our behaviors and habits in constructive ways thwarts the demons.

Some of us are lucky and we either have no interest in drugs or can walk away from them at any time. Everybody's brains are different, at least to some degree, and have different vulnerabilities to drug use. Surprisingly, women and men respond differently to drugs, and so do adolescents and adults. Teens are a special concern because of their youth and increased sensitivity to drugs. Many studies have revealed why this is so and why some of us are more likely to get into trouble with drugs than others. Stress, involved in so many health problems, also feeds the demons of drug abuse. Our genetics also play a role, but not an overwhelming one; we can still fight back.

Drug abuse and addiction are costly, not the least because of the misery they bring. Because of this cost, society has invested in science to combat drug use. It is paying off. We have found the demons, and we can fight. But if you are new to the war itself, because of the addiction of a loved one, a patient, or yourself, then prepare to arm yourself to fight.

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1

What's in This Book, and Why Should I Read It?

"I'm only 14 years old and I'm in a drug counselor's office. I've been stealing, missing school, and failing most of my subjects. It seemed to start when I got involved with drugs. We got dope from older brothers and sisters, from parents' medicine cabinets, and on the streets. We never thought of it as 'doing drugs.' We were just having fun and hanging out, and we thought we could stop anytime. But we fooled ourselves. It caught up to us big time. Now I need to find out about what happened and what I can do to turn my life around. I need to know everything!"

Getting hooked on drugs is a sequence of attraction, seduction, compulsion, and pain. Drugs are dangerous and widespread, and dealing with them requires knowledge and help. This book is about alcohol, nicotine, and illegal drugs—how they work, what they do to the brain, and what can be done to stop using them. The book is especially about what happens inside the brain and why the brain just happens to be set up for drugs. Yes, the brain is set up for drugs; the brain is a co-conspirator, albeit an unwitting one!

When is someone a drug abuser or an addict?[1] If someone uses drugs casually and infrequently without significant problems and can take them or leave them, that person might best be called a *user*, which is still a dangerous situation. If taking drugs causes significant distress and problems in the person's life, then *abuser* might be the

best descriptor. If drugs are in control of a person's life, or if they can't stop, or if they do drugs in spite of personal distress and negative consequences, then they might be drug *dependent* or *addicted*. Even people who are not users, abusers, or addicts are very likely to gain from reading this book.

The text box that follows provides definitions of specific levels of drug use. Addiction is the most serious form of the disorder[2] and it can develop when drugs are taken repeatedly over a long period of time. Taking larger quantities of drugs more frequently is likely to result in addiction more quickly. However, there is no mathematical equation describing this process. It is not exact. Moreover, the process varies depending on the individual and his or her circumstances.

Definitions

DSM IV TR is the latest edition of the *Diagnostic and Statistical Manual of Mental Disorders* that is published through the American Psychiatric Association. It is the official manual for defining and diagnosing the spectrum of disorders that involve drug use. It is used by professionals to more precisely define the degree of drug abuse. Please see this manual for the official definitions.[3]

- **Drug use** can refer to any use of a drug, but more often, it refers to an occasional or recreational use of drugs. In this case, acute or immediate effects and toxicities can be significant. If the drug used is an illegal one, then there is the legal transgression to be concerned with, too. Also, there is the danger of continued use of drugs to where they become a more serious problem.
- **Drug abuse** is a more serious problem where there is a greater degree of drug use and a distressing or negative impact on the drug user's life. It can get further out of control.

- **Addiction** or **dependence** is yet more serious and includes more of a loss of control over drug seeking and drug taking in spite of distress and/or negative consequences. Note that both loss of control over behavior and distress or negative consequences are emphasized. But, there are additional characteristics of drug addiction that are well known. Considerable time may be spent getting and using the drug. More drug is taken than intended. Efforts to stop taking the drug often fail. Tolerance, which is the need to take larger quantities of the drug to get the same effect, develops. Also, perhaps there are withdrawal symptoms when the effect of the drug wears off. Thus, an individual might have a problem with drugs even though there are no distressing feelings or negative consequences that are evident. The words addiction or dependence are used to refer to more severe cases of drug seeking and taking.

The use of drugs is not simply a passing fad or the latest, cool thing. Drugs of one type or another have been with us for a long time, literally thousands of years. Opium has been used in China for centuries, and cocaine use in early Indian cultures goes back centuries. There is even a reference in the Bible about getting drunk on wine. There are things about both the nature of drugs and the human brain that make drug use enduring over the ages, and this reveals a special vulnerability in humans. For example, in 2006-2007 in the United States, there were more than 22 million people, 12 years of age and older, who were classified with drug abuse or drug dependence on illicit drugs[4] or alcohol.

What is it about addiction that grips certain individuals so firmly that they lose at least some control over their drug taking and sometimes over their lives? This book attempts to answer this question by examining research discoveries from the previous couple of decades. Extraordinary progress has been made in drug abuse research.

What Is a Drug?

When talking about drugs that can be abused, there are about seven different groups of substances. These are nicotine; sedatives such as alcohol, barbiturates, benzodiazepines, and inhalants such as fumes from glue; opiates such as heroin and morphine; psychostimulants such as cocaine, amphetamine, and methamphetamine; marijuana; hallucinogens; and caffeine. Prescription drugs that are abused comprise many of the previous classes and are shown in the following list:

- Club drugs, which includes:
  - GHB (Also known as Goop)
  - Ketamine (Also known as K)
  - MDMA (Also known as E)
  - Rohypnol (Also known as Roofies)
- Cocaine, which is also known as nose candy, C, and blow
- Crack (another form of cocaine, and also known as Freebase, Rooster, and Tornado)
- Hallucinogens, which includes:
  - LSD
  - Mescaline (cactus)
  - Psilocybin (Mexican mushrooms)
- Heroin (Also known as Big H, China White, and Smack)
- Inhalants, which include:
  - Air blast
  - Huffing
  - Moon gas
- Marijuana
- Methamphetamine (Also known as Crank, Ice, and Stove top)
- Prescription drugs, which include:
  - Methaqualone (Also known as Ludes)
  - Oxycontin (Also known as Hillbilly heroin)
  - Ritalin (Also known as Vitamin R)
- Steroids (Also known as Juice, Pumpers, and Weight trainers)

This list is composed of illicit drugs and doesn't include alcohol or nicotine. A much more detailed list of abused drugs can be found on the ONDCP (Office of National Control Drug Policy) website at http://www.whitehousedrugpolicy.gov/drugfact/crack/index.html.

Why are *these* groups of chemicals addicting? It is striking how they can have such different effects and uses; for example, opiates relieve pain, and sedatives produce sleep, yet both have the danger of addiction. What is it about these chemicals, and not others, that give them such power? A reasonable answer is that it is an *accident* that all these particular compounds are addicting. There are, perhaps, millions of chemical compounds on this earth, and it is, perhaps, just unfortunate that some of these chemicals can hook into the brain in such a way that they become addicting. Of course, some of these drugs are used more than others (see Figure 1-1).

It is useful and can eliminate confusion to make a distinction between the words *drugs* and *medications*. The word *drug* is used in this book to refer to a substance with the potential to cause harm, abuse, and addiction. Of course, there are other drugs that are therapeutic, cure diseases, and are employed by doctors to treat specific maladies. These latter substances are referred to herein as *medications*. Drugs of abuse can also have legitimate uses in medicine and be medications. Cocaine is a powerful vasoconstrictor in that it closes off blood vessels and can be used to reduce bleeding in surgery. Amphetamine is a stimulant and can be used to treat Attention Deficit Hyperactivity Disorder (ADHD). Opiates are indispensable in the treatment of pain, but they can cause addiction nonetheless. Depending on how and why they are used, many of the substances can be both drugs *and* medications. *Prescription drugs* are another example of this; they are medications that can be abused and therefore are also drugs.

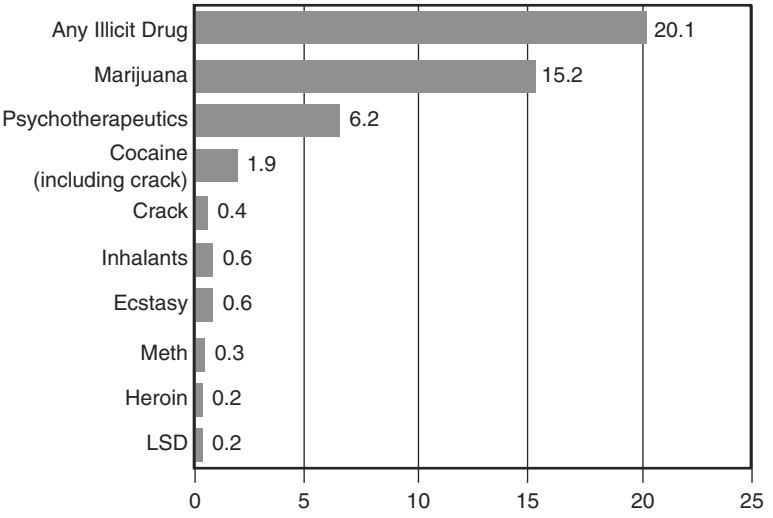

Figure 1-1 The number of individuals, ages 12 or older, who have used the indicated drug within the past 12 months (in millions). Psychotherapeutics refers to prescription drugs that were abused; these drugs include Oxycontin, Vicodin, amphetamines, Ritalin, and sedatives. These numbers of users, which range from 200,000 to over 15 million, are small compared to the number of individuals using the legal drugs, like alcohol and nicotine. More than 50 million people smoke, and an even larger number take alcohol regularly. The relatively larger use of alcohol and nicotine are probably due to the legality of these drugs and their greater availability. Legal drugs are used probably ten times more than illicit ones. (Source: SAMSHA, 2008, National Survey on Drug Use and Health, September 2009).

Why People Take Drugs

People take drugs for many reasons. They can produce a so-called rush of pleasurable sensations, which is a dramatic and memorable experience. Sometimes drugs are taken because of peer pressure or stress. Related to the latter, drugs are sometimes used to self-medicate unpleasant feelings such as pain, anxiety, or depression. When addicted, users may take drugs to avoid the negative symptoms of withdrawal. Withdrawal is a series of distressing feelings and physiologic reactions that occur when drug taking is stopped.

The Drug Experience

The drug experience usually fits a pattern among users. The first use of a drug, a critical occurrence, is often influenced by various factors that include curiosity, friends who may apply pressure to try a drug, availability of a drug, or even a permissive home where parents and siblings are users. Reactions to a drug can vary among individuals. Some people enjoy them and some don't. Perhaps someone begins taking a medication for a medical problem such as pain and then continues using.

The next phase is persistent drug use, in which there is more individual initiative and drive to find and take drugs. This can result in problems such as chronic intoxication, missing work or school, and perhaps stealing. There might be other missed obligations, arrests, or irresponsible behaviors such as unprotected sex. If drug taking continues, a state of addiction can result. Also, more and more of a drug may be taken to get the same effect, and efforts to stop drug use may fail. Other drug-related problems can occur in life, and good health can be threatened. Although some people can stop using drugs, others drift in and out of drug use for decades or for a lifetime. Someone might someday find that his or her life is gone, wasted by a brain disorder that he or she failed to understand and cope with.

Some drug abusers are lucky; they can quit by themselves or find a family member, friend, or counselor who can help them stop. They might get into treatment on their own or they might be forced into treatment by a judge. However it happens, treatment is effective, even for people forced into it. Sadly, because of ignorance, poverty, denial, or fear of the stigma of being labeled an addict, some never find treatment.

Drug Use Is Costly in Many Ways

Many individuals and families know from first-hand experience how hurtful addiction can be, not only to the drug users, but also to

individuals around them. The consequences of drug use include damaging families, relationships, or communities, and perhaps increasing the risks for serious illness or crime. Often, the drug user has vowed to stop and has tried to stop many times only to fall back and relapse into further drug use or dependence. The resulting feelings of helplessness, impotence, and failure can engulf and doom someone's entire world.

The personal and societal costs of drugs can be seen around us and in the media. Robert Downey Jr., a well known actor, producer, and singer, had a serious problem with drugs. He described to a judge how he couldn't stop using them even though he knew he was in trouble. He also said that while starring on the television series Ally McBeal, he was at a low point and didn't care if his acting career was over. But after five years of drug abuse, arrests, stints in rehab, and many relapses, he settled down to work on his problem. Ray Charles, the legendary performer, was addicted to heroin, but after his third drug bust, he went into rehab and gave up the drug. Fortunately, there are individuals who generously come forward, tell us their stories, and warn us about drugs. But not all drug users accept treatment or stop taking drugs, and that group generates great concern. There is even greater concern when our peers or the media glamorize drug use, which is quite dangerous.

Drug abuse is expensive. When we include additional health care costs, productivity losses, costs of crime, and so on, the dollar amount is great.[5] In 2002, for example, overall costs exceeded 180 billion dollars, and loss of productivity accounted for a large portion of that (see Figure 1-2). Costs increased more than 5 percent annually since 1992, with the most rapid increase in costs related to the criminal justice system. These dollar figures are comparable to those for heart disease, cancer, and mental illness. They reflect a major drain on society's resources. Of course, dollar amounts do not begin to reflect the *misery* that drug use can create for the individual, his or her friends, and family.

While the problems are great, they are not hopeless. Perhaps determination is wanting. Dr. Bertha Madras, a Harvard researcher in drug addiction and a former White House official, says, "When viewed from a national perspective, the drug abuse problem in this country is staggering. Yet I am certain that we can develop effective solutions and strategies if we overcome our biggest challenge—finding resolve."

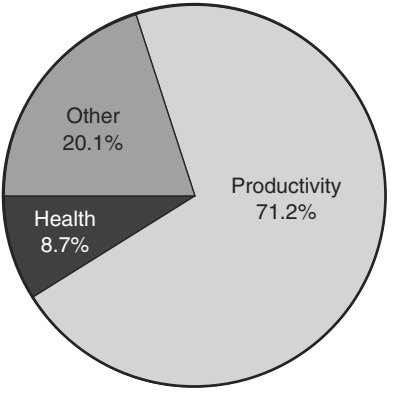

Figure 1-2 Distribution of illicit drug costs in 2002 by major components. The largest fraction of the cost of drug abuse is due to loss of productivity. "Other" costs primarily reflect the costs of the criminal justice system (incarceration, court costs, and so on) costs to victims of related crimes, and costs for social welfare. From source cited in note 5.

Other Addictions

Although this is a book about drugs and how people become hooked on drugs, it is also about *all* of our appetites; therefore, it can help us understand other potential addictions such as eating and gambling. For example, if someone overeats, craves carbohydrates every day, and has withdrawal symptoms when he stops cold turkey, then he may have a problem with carbohydrates. If such a person seeks help, then this book can help with understanding the problem and the needs for treatment. More is said later about food, gambling, and sexual drives.

Other Medications

Another point is that some therapeutically useful medicines (not addicting drugs), such as antidepressants, need to be taken over long periods of time and should not be stopped abruptly because of the danger of recurring disease. Studies of abused drugs, which also involve taking drugs over a long period of time, can inform us not only about how the useful medications produce their beneficial actions in the brain, but also about the problems in abruptly stopping their use.

Brain Structure and Functions

Before embarking on a study of the addicted brain, it is necessary to be aware of the brain and its organization. Different parts of the brain have different functions. Seventy-five percent of the human brain is made up of the wrinkled outer covering referred to as the cerebral cortex, which has different functional areas. Strokes or lesions of the motor cortex result in paralysis, the extent of which is dependent on the extent of the motor area involved. Patients with strokes in the association cortex have deficits of perception and attention. When the temporal lobe is damaged, the ability to recognize or name objects is impaired. Lesions or strokes of the frontal lobe result in personality changes, planning deficits, and inabilities to carry out complex behaviors. Strokes or tumors in other parts of the brain have many other effects as well (see Figure 1-3).

The brain is also the organ of awareness. When general anesthetics are administered, the electrical activity of the brain is reduced, and we lose awareness or go to sleep. If we stimulate the visual cortex, we might have visual images pop into our awareness. If the olfactory cortex is stimulated, then we might perceive odors. If we stimulate other parts of the brain, other events or sensations enter our awareness. Emotional behavior is also based in the brain. A group of brain regions collectively known as the limbic system controls emotional behavior and is partly responsible for feeling good. The following chapters link certain brain regions with feeling good and with drugs.

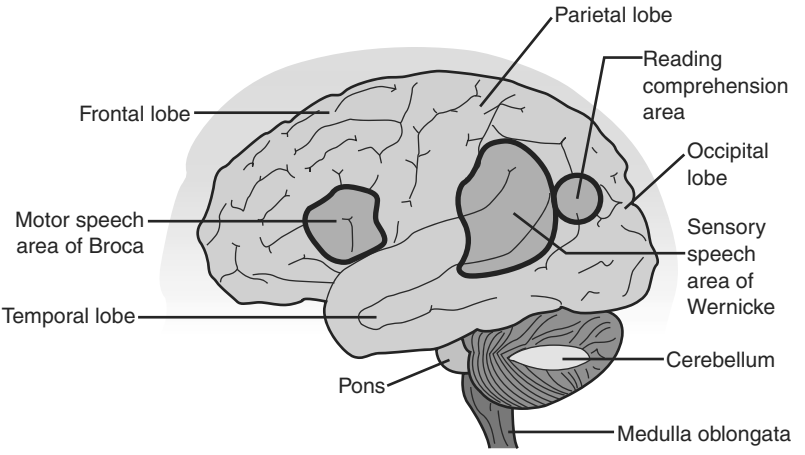

Figure 1-3 A lateral (sideways) surface view of the brain shows some of the more obvious regions, and each region has its own function. The specific functions of the various brain regions have become known after centuries of studies of patients with strokes, injuries, and tumors. Drug addiction also involves certain regions. (Adapted from http://medicalimages.allrefer.com/large/brain.jpg, accessed on December 20, 2010.)

The Tool Box

Science, like everything else in our lives, has become technology-driven, and there are marvelous new approaches and instruments that allow us to examine the tiniest parts of our chromosomes or peer into the depths of our brains without surgical invasion of the skull. These tools are powerful and interesting in and of themselves.

The science of genetics has advanced, and it is now possible, with a small sample of blood, to examine our genes. Because genes are the basis of heredity, and some aspects of drug addiction are heritable, studies of genes can be informative. The target of these studies is DNA, which is made up of four different chemicals called bases, and it is *the order of these chemicals in our DNA* that specifies our genes. These chemicals—abbreviated as the letters A, T, G, and C—are lined up in two parallel strands that comprise the structure of DNA. Again, it is the sequence of these bases, in groups of three, that

constitutes our genetic code, and certain parts of our genetic code can contribute to the likelihood of our becoming a drug user.

For looking inside our brains, noninvasive brain imaging techniques can be astonishing. Magnetic resonance imaging (or MRI) describes the structure of our brains, such that changes in the size of parts of our brains can be measured. Functional magnetic resonance imaging (fMRI) tells us about the functional activity of various brain regions. Positron emission tomography (PET) scanning is versatile. It can be used to reveal the activity of different brain regions or even the levels of certain brain chemicals and proteins. Overall, genetic and imaging studies are but two of the new tools that have become available over the past 25 to 35 years. These tools are out in front in the attack on drugs.

Questions to Be Answered

This book addresses many questions about drugs and the brain, including:

- Why is it said that addiction is a brain disorder rather than perhaps a moral failing?
- What happens in the brain of someone who uses drugs repeatedly?
- Can better medications for addicted individuals be expected in the future?
- Why is drug abuse chronic and relapsing, which is part of the essence of this disorder?
- Why are drugs so powerful that they can gain control of our behaviors, but we can't give up responsibility for our actions?
- Will *I* become drug dependent?
- Are there differences among, men, women, adolescents, and older adults in how they respond to and experience drugs?
- Can one recover from drug addiction and be cured?
- The stigma of being a drug abuser is a problem in that it often prevents searching for treatment or dealing with the problem openly.

Endnotes

[1] Throughout this book, we tend to refer to addiction as a disorder, but it is also often called a disease. The definition of addiction that is used in this book focuses on continued drug use in spite of distress and negative consequences. However, the official description is given in the Diagnostic and Statistical Manual of Mental Disorders produced by the American Psychiatric Association, and it includes more elements. The DSM IV TR is the current edition used by medical professionals for official diagnoses. The DSM is an evolving document and DSM V is due in the near future. Currently, the diagnosis of drug dependence requires the presence of three or more of several symptoms, and it is possible to have a diagnosis of substance dependence without the presence of distress or negative consequences. The official list of symptoms and diagnostic criteria for Substance Dependence and Substance Abuse can be found in an online version of the DSM IV TR. One possible site is http://www.psychiatryonline.com/content.aspx?aID=629, which was accessed on June 28, 2011. Only a qualified professional can make a diagnosis.

[2] Ibid.

[3] Ibid.

[4] An illicit drug is one that is not legal to produce, not legal to use or possess, or a medically useful therapeutic drug that is used non-medically.

[5] Office of National Drug Control Policy (2004). "The Economic Costs of Drug Abuse in the United States," 1992–2002. Washington, DC: Executive Office of the President (Publication No. 207303).

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