The Brain: Understanding Neurobiology Through the Study of Addiction

under a contract from the
National Institutes of Health

NIDA
NATIONAL INSTITUTE
ON DRUG ABUSE

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This material is based on work supported by the National Institutes of Health under Contract No: 263-98-C-0056. Any opinions, findings, conclusions, or recommendations expressed in this publication are those of the authors and do not necessarily reflect the view of the funding agency.

NIH Publication No. 00-4871

ISBN: #1-929614-05-5

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Special Thanks
BSCS and Videodiscovery thank the following individuals for providing resources or reviewing specific activities in this unit:
Dr. William Armstrong, University of Tennessee;
Dr. Richard Cannon, National Heart, Lung and Blood Institute;
Dr. Monica Skarulis, National Institute of Diabetes and Digestive and Kidney Diseases;
Dr. Michael Phelps, UCLA School of Medicine;
Dr. Johannes Czernin, UCLA School of Medicine;
David Twomey, UCLA School of Medicine; and
Jim Strommer, UCLA School of Medicine.

Cover Image Description
The cover shows a positron emission tomography (PET) image of a human brain. Blood flow to a particular brain area, the amygdala, increases when a cocaine addict experiences cravings for the drug. The image, when compared to those taken of non-addicts, reveals that just eliciting memories of drug abuse in a cocaine addict is sufficient to cause changes in brain activity.

Contents

Foreword

This curriculum supplement, from *The NIH Curriculum Supplements Series*, brings cutting-edge medical science and basic research discoveries from the laboratories of the National Institutes of Health (NIH) into classrooms. As the largest medical research institution in the United States, NIH plays a vital role in the health of all Americans, and seeks to foster interest in research, science, and medicine related careers for future generations. NIH's Office of Science Education (OSE) is dedicated to promoting science education and scientific literacy.

We designed this curriculum supplement to complement existing life science curricula at both the state and local levels and to be consistent with the *National Science Education Standards*.[1] It was developed and tested by a team composed of teachers from across the country, scientists, medical experts, and other professionals with relevant subject-area expertise from institutes and medical schools across the country, an NIH scientist or representative from each of the 25 institutes, and curriculum design experts from Biological Sciences Curriculum Study (BSCS) and Videodiscovery. The authors incorporated real scientific data and actual case studies into classroom activities. A three-year development process included geographically dispersed field tests by teachers and students.

The structure of this module enables teachers to effectively facilitate learning and stimulate student interest by applying scientific concepts to real-life scenarios. Design elements include a conceptual flow of lessons based on BSCS's 5E Instructional Model of Learning, multi-subject-integration emphasizing cutting-edge science content, and built-in assessment tools. Activities promote active and collaborative learning and are inquiry-based to help students develop problem-solving strategies and critical thinking.

NIH will release new supplements each year targeting students between grades K–12. Each curriculum supplement comes with a complete set of materials for both teachers and students including printed materials, extensive background and resource information, and a CD-ROM with videos and interactive activities. These supplements are distributed at no cost to teachers across the United States. All materials may be copied for classroom use, but may not be sold. We welcome feedback from our users. For a complete list of curriculum supplements, updates, availability and ordering information, or to submit feedback, please visit our Web site at: *http://science-education.nih.gov* or write to:

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We appreciate the valuable contributions of the talented staff at Biological Sciences Curriculum Study (BSCS) and Videodiscovery, Inc. We are also grateful to the NIH scientists, advisors, and all other participating professionals for their work and dedication. Finally, we thank the teachers and students who participated in focus groups and field tests to ensure that these supplements are both engaging and effective. I hope you find our series a valuable addition to your classroom and wish you a productive school year.

Bruce A. Fuchs, Ph.D.
Director
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[1] The National Academy of Sciences released the *National Science Education Standards* in December 1995 outlining what all citizens should understand about science by the time they graduate from high school. The *Standards* encourages teachers to select major science concepts that empower students to use information to solve problems rather than stressing memorization of unrelated information.

About the National Institutes of Health

The National Institutes of Health (NIH), the world's top medical research center, is charged with addressing the health concerns of the nation. The NIH is the largest U.S. governmental sponsor of health studies conducted nationwide.

Simply described, the NIH's goal is to acquire new knowledge to help prevent, detect, diagnose, and treat disease and disability, from the rarest genetic disorder to the common cold. The NIH works toward that goal by conducting research in its own laboratories in Bethesda, Maryland and at several other locations throughout the United States; supporting the research of nonfederal scientists throughout the country and abroad; helping to train research investigators; and fostering communication of medical information to the public.

The NIH Supports Research

A principal concern of the NIH is to invest wisely the tax dollars entrusted to it for the support and conduct of medical research. Approximately 82 percent of the investment is made through grants and contracts supporting research and training in more than 2,000 universities, medical schools, hospitals, and research institutions throughout the United States and abroad.

Approximately 10 percent of the budget goes to more than 2,000 projects conducted mainly in NIH laboratories. About 80 percent covers support costs of research conducted both within and outside the NIH.

NIH Research Grants

To apply for a research grant, an individual scientist must submit an idea in a written application. Each application undergoes a peer review process. A panel of scientific experts, who are active researchers in the medical sciences, first evaluates the scientific merit of the application. Then, a national advisory council or board, composed of eminent scientists as well as members of the public who are interested in health issues or the medical sciences, determines the project's overall merit and priority. Because funds are limited, the process is very competitive.

The Nobelists

The rosters of those who have conducted research, or who have received NIH support over the years, include some of the world's most illustrious scientists and physicians. Among them are 101 scientists who have won Nobel Prizes for achievements as diverse as deciphering the genetic code and learning what causes hepatitis.

Five Nobelists made their prize-winning discoveries in NIH laboratories: Doctors Christian B. Anfinsen, Julius Axelrod, D. Carleton Gajdusek, Marshall W. Nirenberg, and Martin Rodbell.

Impact of the NIH on the Nation's Health

The research programs of the NIH have been remarkably successful during the past 50 years. NIH-funded scientists have made substantial progress in understanding the basic mechanisms of disease and have vastly improved the preventive, diagnostic, and therapeutic options available.

During the past few decades, NIH research played a major role in making possible achievements like these:

- Mortality from heart disease, the number one killer in the United States, dropped by 36 percent between 1977 and 1999.
- Improved treatments and detection methods increased the relative five-year survival rate for people with cancer to 60 percent.
- With effective medications and psychotherapy, the 19 million Americans who suffer from depression can now look forward to a better, more productive future.
- Vaccines protect against infectious diseases that once killed and disabled millions of children and adults.
- In 1990, NIH researchers performed the first trial of gene therapy in humans. Scientists are increasingly able to locate, identify, and describe the functions of many of the genes in the human genome. The ultimate goal is to develop screening tools and gene therapies for the general population for cancer and many other diseases.

Educational and Training Opportunities at the NIH

The NIH offers myriad opportunities including summer research positions for students. For details, visit *http://science-education.nih.gov/students.*

For more information about the NIH, visit *http://www.nih.gov.*

The NIH Office of Science Education

The NIH Office of Science Education (OSE) is bringing exciting new resources free of charge to science teachers of grades kindergarten through 12. OSE learning tools support teachers in training the next generation of scientists and scientifically literate citizens. These materials cover information not available in standard textbooks and allow students to explore biological concepts by using real world examples. In addition to the curriculum supplements, OSE provides a host of valuable resources accessible through the OSE Web site (*http://science-education.nih.gov),* such as

- **Snapshots of Science and Medicine**.[2] This online magazine—plus interactive learning tools—is designed for ease of use in high school science classrooms. Three issues, available for free, are published during the school year. Each focuses on a new area of research and includes four professionally written articles on findings, historical background, related ethical questions, and profiles of people working in the field. Also included are a teaching guide, classroom activities, handouts, and more. (*http://science-education.nih. gov/snapshots*)
- **Women Are Scientists Video and Poster Series**.[3] This series provides teachers and guidance counselors with free tools to encourage young women to pursue careers in the medical field. The informative, full-color video and poster sets focus on some of the careers in which women are currently underrepresented. Three video and poster sets are now available: *Women are Surgeons*, *Women are Pathologists*, and *Women are Researchers*. (*http:// science-education.nih.gov/women*)
- **Internship Programs**. Visit the OSE Web site to obtain information on a variety of NIH programs open to teachers and students. (*http://science-education.nih.gov/students*)
- **National Science Teacher Conferences**. Thousands of copies of NIH materials are distributed to teachers for free at the OSE exhibit booth at conferences of the National Science Teachers Association and the National Association of Biology Teachers. OSE also offers teacher-training workshops at many conferences. (*http://science-education.nih.gov/exhibits*)

In the development of learning tools, OSE supports science education reform as outlined in the *National Science Education Standards* and related guidelines.

We welcome your comments about existing resources and suggestions about how we may best meet your needs. Feel free to send your comments to us at *http://science-education.nih.gov/feedback.*

[2,3] These projects are collaborative efforts between OSE and NIH Office of Research on Women's Health.

About the National Institute on Drug Abuse

The National Institute on Drug Abuse (NIDA), one of the research institutes that comprise the National Institutes of Health, was established in 1974 as the Federal focal point for research, treatment, prevention and training services, and data collection on the nature and extent of drug abuse. NIDA's mission is to lead the Nation in bringing the power of science to bear on drug abuse and addiction. This charge has two critical components. First, NIDA supports and conducts research across a broad range of disciplines to explore the biomedical and behavioral foundations of drug abuse. Second, NIDA ensures that the results of research are rapidly and effectively disseminated so that the scientific findings can be used to improve drug abuse and addiction prevention, treatment, and policy.

NIDA is the world's leading supporter of research on the health aspects of drug abuse and addiction. NIDA-supported science addresses the most fundamental and essential questions about drug abuse, ranging from the molecule to managed care, and from DNA to community outreach research. When NIDA was founded, many people incorrectly viewed drug abuse as a problem of people with character flaws and weak wills. Today, thanks to the research accomplishments of hundreds of scientists, those simplistic ideologies are being replaced by a better understanding of the complex biological, behavioral, social, and public health aspects of drug abuse. Scientists have shown that while initial experimentation with drugs may be voluntary, continuing drug abuse changes the brain in fundamental and long-lasting ways. These brain changes trigger the compulsive drug-seeking and drug-taking behaviors that are the hallmarks of drug addiction. NIDA's scientists have clearly shown that drug abuse is a preventable behavior and drug addiction is a treatable brain disease. Among the many and diverse accomplishments over the past three decades, NIDA-supported research has:

- identified the molecular sites in the brain where every major drug of abuse—opiates, cocaine, PCP, and THC (the active ingredient in marijuana)—has its initial effect. These discoveries, together with computer-aided drug design, are paving the way to development of novel medications to break the cycle of addiction.
- produced a neurobehavioral model to explain drug-taking behavior to improve treatment and rehabilitation methods.
- supported the development of two medications, LAAM and naltrexone, through the approval process by the FDA for the treatment of opiate addiction.
- supported the development and evaluation of pharmacologic treatment for newborns withdrawing from exposure to narcotics.
- defined nicotine addiction and the scientific basis for therapy using nicotine gum and skin patches.
- pioneered innovative community-based research on AIDS prevention efforts that showed that drug users will change AIDS risk behaviors, which can reduce their susceptibility to HIV infection and AIDS.
- demonstrated that participation in methadone treatment significantly reduces HIV seroconversion rates and decreases high-risk behaviors.
- demonstrated that successful drug abuse treatment reduces criminality as well as relapse to addiction.
- demonstrated the value of treating drug abusers' depression and other mental disorders to improve the results of addiction therapy.
- measured the positive impact of comprehensive research-based community drug prevention strategies that involve the media, schools, families, neighborhoods, and the workplace.
- used advanced imaging techniques to identify in awake humans the specific brain circuits that are involved in craving, euphoria, and other sequelae of drug addiction. These exciting studies will provide the foundation for the development of new, targeted medications to block individual aspects of drugs.
- used molecular genetic technologies to clone the genes for the major receptors for virtually

every abusable drug, thus providing scientists with the tools necessary to study in fine detail how drugs of abuse exert their many behavioral effects.
- produced genetically engineered animals in which a particular drug receptor had been eliminated or "knocked out." These animals are providing unprecedented insight into how drugs exert their many effects in the brain and produce addiction.
- demonstrated that prenatal exposure to cigarettes and marijuana have long-term effects on cognitive performance.
- successfully immunized rats against the psychostimulant effects of cocaine, thus opening up the possibility of developing a vaccination against cocaine addiction.

The results of these and other achievements through NIDA-funded research offer this country's best hope for solving the medical, social, and public health problems of drug abuse and addiction.

The need for greater knowledge of drug abuse continues to grow. Ever-changing drug use patterns, the continuing transmission of HIV infection among drug abusers, and the need to develop new and effective treatment and prevention methods underscore the importance of research in finding new and better ways to alleviate the pain and devastation of addiction. NIDA's goals for the future include:

- to design and develop new medications for opioid and cocaine addiction, especially for use during pregnancy, by building on the recent molecular discoveries that have uncovered the basis for addiction in the brain.
- to develop techniques to detect subtle effects of drug exposure in children of drug-using parents to provide opportunities for early preventive or clinical intervention.
- to broaden research on women and addiction to determine the biological and behavioral differences that need to be addressed in effective drug abuse prevention and treatment.
- to reduce the spread of HIV infection through improved drug abuse interventions and better understanding of the interactions of drugs of abuse and the body's immune system.
- to apply state-of-the-art neuroimaging techniques to the problems of drug abuse prevention and treatment.
- to design, develop, and test new behavioral therapies and promote their use for appropriate patient populations.
- to study the treatment of special clinical problems presented by drug abusers with HIV, tuberculosis, hepatitis, and other infections.
- to understand the organization and financing of drug abuse treatment and its benefits to the larger health care system.
- to identify the protective and resiliency factors that prevent drug use in those individuals with multiple risk factors so more effective prevention techniques can be developed.
- to strengthen the research infrastructure, by providing additional opportunities for research training and career development for clinical researchers and improved mechanisms for training and mentoring of minority researchers.
- to expand the use of scientific information to educate the public about the real nature of drug abuse and addiction and the hope and promise for more effective prevention and treatment.
- to broaden the dissemination of research findings and improve drug abuse prevention and treatment practice and policy.

The Essence of Drug Addiction

By Alan I. Leshner, Ph.D., Director, National Institute on Drug Abuse

(NAPS)-The word "addiction" calls up many different images and strong emotions. But what are we reacting to? Too often we focus on the wrong aspects of addiction so our efforts to deal with this difficult issue can be badly misguided.

Any discussion about psychoactive drugs, particularly drugs like nicotine and marijuana, inevitably moves to the question "but is it really addicting?" The conversation then shifts to the so-called types of addiction—whether the drug is "physically" or "psychologically" addicting. This issue revolves around whether or not dramatic physical withdrawal symptoms occur when an individual stops taking the drug, what we in the field call "physical" dependence.

The assumption that follows then is that the more dramatic the physical withdrawal symptoms, the more serious or dangerous the drug must be. Indeed, people always seem relieved to hear that a substance "just" produces psychological addiction, or has only minimal physical withdrawal symptoms. Then they discount its dangers. They are wrong. Marijuana is a case in point here, and I will come back to it shortly.

Defining Addiction

Three decades of scientific research, coupled with even longer clinical experience, has taught us that focusing on this physical vs. psychological distinction is off the mark, and a distraction from the real issue. From both clinical and policy perspectives, it does not matter much what physical withdrawal symptoms occur. Other aspects of addiction are far more important.

Physical dependence is not that important because, first, even the florid withdrawal symptoms of heroin and alcohol addiction can be managed with appropriate medications. Therefore, physical withdrawal symptoms should not be at the core of our concerns about these substances.

Second, and more important, many of the most addicting and dangerous drugs do not even produce very severe physical symptoms upon withdrawal. Crack cocaine and methamphetamine are clear examples. Both are highly addicting, but stopping their use produces very few physical withdrawal symptoms, certainly nothing like the physical symptoms of alcohol or heroin withdrawal.

What does matter tremendously is whether or not a drug causes what we now know to be the essence of addiction: **uncontrollable, compulsive drug seeking and use, even in the face of negative health and social consequences**. This is the crux of how many professional organizations all define addiction, and how we all should use the term. It is really only this expression of addiction—**uncontrollable, compulsive craving, seeking and use of drugs**—that matters to the addict and to his or her family, and that should matter to society as a whole. These are the elements responsible for the massive health and social problems caused by drug addiction.

Essence of Addiction

Drug craving and the other compulsive behaviors are the essence of addiction. They are extremely difficult to control, much more difficult than any physical dependence. They are the principal target symptoms for most drug treatment programs. For an addict, there is no motivation more powerful than drug craving. As the movie "Trainspotting" showed us so well, the addict's entire life becomes centered on getting and using the drug. Virtually nothing seems to outweigh drug craving as a motivator. People have committed all kinds of crimes and even abandoned their children just to get drugs.

Rethinking Addiction

Focusing on addiction as compulsive, uncontrollable drug use should help clarify everyone's perception of the nature of addiction and of potentially addicting drugs. For the addict and the clinician, this more accurate definition forces the focus of treatment away from simply managing physical withdrawal symptoms and toward dealing with the more meaningful, and powerful, concept of *uncontrollable* drug seeking and use. The task of treatment is to regain control over drug craving, seeking and use.

Rethinking addiction also affects which drugs we worry about and the nature of our concerns. The message from modern science is that in deciding which drugs are addicting and require what kind of societal attention, we should focus primarily on whether taking them causes uncontrollable drug seeking and use. One important example is the use of opiates, like morphine, to treat cancer pain. In most circumstances, opiates are addicting. However, when administered for pain, although morphine treatment can produce physical dependence—which now can be easily managed after stopping use—it typically does not cause compulsive, uncontrollable morphine seeking and use, addiction as defined here. This is why so many cancer physicians find it acceptable to prescribe opiates for cancer pain.

An opposite example is marijuana, and whether it is addicting. There are some signs of physical dependence or withdrawal in heavy users, and withdrawal has been demonstrated in studies on animals. But what matters much more is that every year more than 100,000 people, most of them adolescents, seek treatment for their inability to control their marijuana use. They suffer from compulsive, uncontrollable marijuana craving, seeking and use. That makes it addicting, certainly for a large number of people.

Treating Addiction: Follow the Science

It is important to emphasize that addiction, as defined here, can be treated, both behaviorally and, in some cases, with medications, but it is not simple. We have a range of effective addiction treatments in our clinical toolbox although admittedly not enough. This is why we continue to invest in research, to improve existing treatments and to develop new approaches to help people deal with their compulsive drug use.

Our national attitudes and the ways we deal with addiction and addicting drugs should follow the science and reflect the new, modern understanding of what matters in addiction. We certainly will do a better job of serving everyone affected by addiction—addicts, their families and their communities—if we focus on what really matters to them. As a society, the success of our efforts to deal with the drug problem depends on an accurate understanding of the problem.

Further information on drug abuse and addiction can be found on the NIDA homepage at *www.nida.nih.gov*. Free publications can be ordered from the National Clearinghouse for Alcohol and Drug Information by calling 1-800-729-6686.

Source: *http://www.nida.nih.gov/Published_Articles/Essence.html*.

Introduction to the Module

What Are the Objectives of the Module?

The Brain: Understanding Neurobiology Through the Study of Addiction has several objectives. The first is to help students understand major concepts in neurobiology. The brain controls everything a person does, including regulating breathing and heart rate, movement, cognitive thought, and emotions. The module seeks to provide students with a fundamental knowledge of how the neurons in the brain convey information to regulate these diverse functions.

The second objective is to provide students with factual information on how drugs of abuse alter the function of the brain. Drugs of abuse exert their effects by altering the communication between neurons. Some of the changes resulting from drug abuse are short-term while others are long-term, and potentially permanent. At some point in drug abuse, the brain changes and the abuser becomes an addict. The drug addict has a compulsive need to continue to take drugs despite adverse physical, social, and emotional consequences. At this time, scientists continue to investigate what changes occur in the brain when a person becomes addicted to drugs.

Science plays an important role in assisting individuals as they make choices about enhancing personal and public welfare. In this module, students see that science provides evidence that can be used to support ways of understanding and treating human disease. In addition to being the world's largest supporter of research into drug abuse and addiction, the National Institute on Drug Abuse also is committed to ensuring the rapid and effective dissemination of research findings to improve drug abuse and addiction prevention, treatment, and policy. This module is one method of providing this information to the public. The lessons in this module encourage students to think about the relationships among knowledge, choice, behavior, and enhanced human health in this way:

knowledge (what is known and not known) + choice = power

power + behavior = enhanced human health

An additional objective of this module is to encourage students to think in terms of these relationships now and as they grow older.

Why Teach the Module?

One challenge for science teachers is to make science meaningful to high school students. Students at this age want to see the relevance of the material to their lives. This module presents fundamental principles of neurobiology in relation to drugs of abuse. This link to drugs grabs students' attention because, in today's world, drugs affect virtually all students either directly or indirectly. This real-life context engages students and makes neurobiology something more than just another topic to memorize for biology class. They can apply the information to make decisions about their lives.

"Excellent information on drug actions and neurobiology presented in an inquiry format. Students handled difficult concepts because of the way they were presented."

—Field-test Teacher

"It appears that students really did learn the material on neurotransmission and drug addiction. I actually heard one student kidding another about their dopamine levels! Another student was in my room after school explaining to an underclassman how information gets from one part of the body to the other—complete with diagrams on the board."

—Field-test Teacher

"The topic is of interest to students. The information is current and goes beyond what is available in textbooks."
—Field-test Teacher

What's In It for the Teacher?

The Brain: Understanding Neurobiology Through the Study of Addiction meets many of the criteria used to assess teachers and their programs.

- The module is **standards based** and meets science content, teaching, and assessment standards as expressed in the *National Science Education Standards*. It pays particular attention to the standards that describe what students should know and be able to do with respect to **scientific inquiry**.
- The module includes a computer-based **technology component** that uses a CD-ROM on which there are mini-documentaries, animations, and interactive activities.
- It is an **integrated** module, drawing most heavily from the subjects of science, mathematics, health, and language arts.
- Finally, the module includes built-in **assessment** tools, indicated by an assessment icon in the lessons.

In addition, the module provides a means for **professional development**. Teachers can engage in new and different teaching practices like those described in this module without completely overhauling their entire yearlong program. In *Designing Professional Development for Teachers of Science and Mathematics*[1], Susan Loucks-Horsley *et al.* write that replacement modules, such as *The Brain: Understanding Neurobiology Through the Study of Addiction*, can "offer a window through which teachers can get a glimpse of what new teaching strategies look like in action." By experiencing a short-term unit like this one, teachers can "change how they think about teaching and embrace new approaches that stimulate students to problem solve, reason, investigate, and construct their own meaning for the content." The use of a replacement unit like this can encourage reflection and discussion and stimulate teachers to improve their practices by focusing on student learning through inquiry.

The following table correlates topics often included in the high school curriculum with the lessons presented in this module. This information is presented to help teachers make decisions about incorporating this material into their curriculum.

Major Topics Presented in *The Brain: Understanding Neurobiology Through the Study of Addiction*

Topics	Lesson 1	Lesson 2	Lesson 3	Lesson 4	Lesson 5
Localization of brain function	•				
General functions of specific brain areas	•				
Anatomy of the neuron		•			
Neurotransmission		•	•		
Mechanism of drug action on neurons			•	•	
Environmental, behavioral, and genetic influences on addiction				•	•
Addiction as a chronic disease				•	•

Implementing the Module

The five lessons in this module are designed to be taught either in sequence for approximately two weeks (as a replacement for a part of the standard curriculum) or as individual lessons that support or enhance your treatment of specific concepts in high school biology. The following pages offer general suggestions about using these materials in the classroom; you will find specific suggestions in the procedures provided for each lesson.

What Are the Goals of the Module?

The Brain: Understanding Neurobiology Through the Study of Addiction is designed to help students develop the following major goals associated with scientific literacy:

- to understand some basic fundamentals about neurobiology and how drugs of abuse change the brain;
- to recognize that drug addiction is a treatable, chronic brain disease;
- to experience the process of scientific inquiry and develop an enhanced understanding of the nature and methods of science; and
- to appreciate the role of science in society and the relationship between basic science and human health.

What Are the Science Concepts and How Are They Connected?

The lessons presented in this module form a conceptual whole that will provide students with a fundamental knowledge of neurobiology, drug abuse, and drug addiction. Students begin by learning how different areas of the brain regulate specific functions, including feeling pleasure (*The Brain: What's Going On in There?*).

Conceptual Flow of the Lessons

Lesson	Learning Focus*	Major Concept
Lesson 1 *The Brain: What's Going On in There?*	Engage/ Explore	Specific brain regions control specific brain functions.
Lesson 2 *Neurons, Brain Chemistry, and Neurotransmission*	Explore/ Explain	Neurons convey information using electrical and chemical signals.
Lesson 3 *Drugs Change the Way Neurons Communicate*	Explain/ Elaborate	Drugs affect the biology and chemistry of the brain.
Lesson 4 *Drug Abuse and Addiction*	Explain/ Elaborate	Addiction is a brain disease.
Lesson 5 *Drug Addiction Is a Disease —So What Do We Do about It?*	Elaborate/ Evaluate	Drug addiction is a recurring chronic disease that can be treated effectively similar to other chronic diseases.

*See *How Does the 5E Instructional Model Promote Active, Collaborative, Inquiry-based Learning?* on page 4.

Students extend their understanding of the brain by learning how neurons in the brain relay information through electrical and chemical signals (*Neurons, Brain Chemistry, and Neurotransmission*). Once students understand how neurons communicate, they explore how drugs of abuse alter the function of the brain by disrupting the signaling process between neurons (*Drugs Change the Way Neurons Communicate*). Students can then apply their knowledge of how drugs act at the cellular level to understand that drug addiction is a brain disease that is signified by changes in the brain, some of which may persist a long time or may be permanent (*Drug Abuse and Addiction*). Finally, students consider how treatment for the disease of drug addiction compares with that for other chronic diseases (*Drug Addiction Is a Disease—So What Do We Do about It?*). The chart, *Conceptual Flow of the Lessons*, on page 3, illustrates the sequence of major concepts addressed by the five lessons.

How Does the Module Correlate with the *National Science Education Standards?*

The Brain: Understanding Neurobiology Through the Study of Addiction supports teachers in their efforts to reform science education in the spirit of the National Research Council's 1996 *National Science Education Standards (NSES)*. The content of the module is explicitly standards based: Each time a standard is addressed in a lesson, an icon appears in the margin and the applicable standard is identified. The chart, *Content Standards: Grades 9–12*, on pages 5–6, lists the specific content standards that this module addresses.

Teaching Standards

The suggested teaching strategies in all the lessons support teachers as they work to meet the teaching standards outlined in the *National Science Education Standards*. The module helps teachers of science plan an inquiry-based science program by providing short-term objectives for students. It also includes planning tools such as the *Conceptual Flow of the Lessons* chart and the *Suggested Timeline* for teaching the module. Teachers can use this module to update their curriculum in response to their students' interest in this topic. The focus on active, collaborative, and inquiry-based learning helps teachers support the development of student understanding and nurture a community of science learners.

The structure of the lessons in this module enables teachers to guide and facilitate learning. All the activities encourage and support student inquiry, promote discourse among students, and challenge students to accept and share responsibility for their learning. The use of the 5E Instructional Model, combined with active, collaborative learning, allows teachers to respond effectively to the diversity of student backgrounds and learning styles. The module is fully annotated, with suggestions for how teachers can encourage and model the skills of scientific inquiry, as well as the curiosity, openness to new ideas and data, and skepticism that characterize science.

Assessment Standards

Teachers can engage in ongoing assessment of their teaching and of student learning using the variety of assessment components embedded within the module's structure. The assessment tasks are authentic: They are similar in form to tasks in which students will engage in their lives outside the classroom or in which scientists participate. Annotations guide teachers to these opportunities for assessment and provide answers to questions that can help teachers analyze student feedback.

How Does the 5E Instructional Model Promote Active, Collaborative, Inquiry-based Learning?

Because learning does not occur through a process of passive absorption, the lessons in this module promote active learning: Students are involved in more than listening and reading. They are developing skills, analyzing and evaluating evidence, experiencing and discussing, and talking to their peers about their own understandings. Students work collaboratively with others to solve problems and plan investigations. Many students find that they learn better when they work with others in a collaborative environment than they can when they work alone in a competitive environment. When all this active,

Content Standards: Grades 9–12	
Standard A: As a result of activities in grades 9–12, all students should develop	**Correlation to *The Brain: Understanding Neurobiology Through the Study of Addiction***
• Abilities necessary to do scientific inquiry	
* Identify questions and concepts that guide scientific investigations.	Lessons 1, 2, 3, 4, and 5
* Design and conduct scientific investigations.	Lesson 3
* Use technology and mathematics to improve investigations and communications.	Lessons 1, 2, 3, 4, and 5
* Formulate and revise scientific explanations and models using logic and evidence.	Lessons 2, 3, 4, and 5
* Recognize and analyze alternative explanations and models.	Lessons 1, 2, 3, and 4
* Communicate and defend a scientific argument.	Lessons 1, 2, and 3
* Use mathematics in all aspects of scientific inquiry.	Lesson 4
• Understandings about scientific inquiry	
* Scientists rely on technology to enhance the gathering and manipulation of data.	Lessons 1 and 4
* Mathematics is essential in scientific inquiry.	Lessons 3 and 4
Standard C: As a result of their activities in grades 9–12, all students should develop understanding of	
• The cell	
* Cells have particular structures that underlie their functions.	Lesson 2
* Most cell functions involve chemical reactions.	Lesson 2
* Cell functions are regulated.	Lessons 2 and 3
* Cells can differentiate, and complex multicellular organisms are formed as a highly organized arrangement of differentiated cells.	Lessons 1 and 2
• Behavior of organisms	
* Multicellular animals have nervous systems that generate behavior.	Lessons 1, 2, and 3
* Organisms have behavioral responses to internal changes and to external stimuli.	Lessons 1, 2, and 3
* Behavioral biology has implications for humans, as it provides links to psychology, sociology, and anthropology.	Lessons 4 and 5
Standard E: As a result of their activities in grades 9–12, all students should develop	
• Understandings about science and technology	
* Science often advances with the introduction of new technologies.	Lessons 1 and 4

Content Standards: Grades 9–12 (continued)	
Standard F: As a result of their activities in grades 9–12, all students should develop understanding of	
• Personal and community health	
* The severity of disease symptoms is dependent on many factors, such as human resistance and the virulence of the disease-producing organism.	Lessons 4 and 5
* Personal choice concerning fitness and health involves multiple factors.	Lessons 4 and 5
* An individual's mood and behavior may be modified by substances.	Lessons 1, 4, and 5
* Families serve basic health needs, especially for young children.	Lesson 5
Standard G: As a result of their activities in grades 9–12, all students should develop understanding of	
• Nature of scientific knowledge	
* Because all scientific ideas depend on experimental and observational confirmation, all scientific knowledge is, in principle, subject to change as new evidence becomes available.	Lessons 1, 2, 3, 4, and 5
Historical perspectives	
* Usually, changes in science occur as small modifications in extant knowledge.	Lesson 1

collaborative learning is directed toward inquiry science, students succeed in making their own discoveries. They ask questions, observe, analyze, explain, draw conclusions, and ask new questions. These inquiry experiences include both those that involve students in direct experimentation and those in which students develop explanations through critical and logical thinking.

This view of students as active thinkers who construct their own understanding out of interactions with phenomena, the environment, and other individuals is based on the theory of **constructivism**. A constructivist view of learning recognizes that students need time to

- express their current thinking;
- interact with objects, organisms, substances, and equipment to develop a range of experiences on which to base their thinking;
- reflect on their thinking by writing and expressing themselves and comparing what they think with what others think; and
- make connections between their learning experiences and the real world.

This module provides a built-in structure for creating a constructivist classroom: The 5E Instructional Model. This model sequences the learning experiences so that students have the opportunity to construct their understanding of a concept over time. The model takes students through five phases of learning that are easily described using five words that begin with the letter "E": Engage, Explore, Explain, Elaborate, and Evaluate. The following paragraphs illustrate how the 5Es are implemented across the lessons in this module.

Engage

Students come to learning situations with prior knowledge. This knowledge may or may not be congruent with the concepts presented in this module. The Engage lesson provides the opportunity for teachers to find out what students already know or what they think they know about the topic and concepts to be developed.

The Engage lesson in this module, Lesson 1: *The Brain: What's Going On in There?*, is designed to

- pique students' curiosity and generate interest,

- initiate students' thinking about the function of the brain,
- encourage students to compare their ideas with the ideas of others, and
- allow teachers to assess what students do or do not understand about the stated outcomes of the lesson.

Explore

In the Explore phase of the module, Lesson 1, *The Brain: What's Going On in There?*, and Lesson 2, *Neurons, Brain Chemistry, and Neurotransmission*, students explore the function of the brain both as a body organ and as a collection of interacting cells. The lessons provide a common set of experiences within which students can compare what they think about what they are observing and experiencing.

During the Explore phase of the lessons, students

- use their skills of observation, logic, and deduction to gain an understanding of the process by which neurons relay information;
- acquire a common set of experiences with their classmates so they can compare results and ideas; and
- observe, describe, record, compare, and share their ideas and experiences.

Explain

The Explain components of Lesson 2, *Neurons, Brain Chemistry, and Neurotransmission*, and Lesson 3, *Drugs Change the Way Neurons Communicate*, provide opportunities for students to connect their previous experiences and to begin to make conceptual sense of the main ideas of the module. This stage also allows for the introduction of formal language, scientific terms, and content information that might make students' previous experiences easier to describe and explain.

In the Explain lessons in this module, students

- explain concepts and ideas about neurotransmission;
- incorporate the correct scientific terminology into their explanations;
- add new information about the actions of drugs to their understanding of neurotransmission;
- revise their ideas;
- compare their current thinking with what they previously thought;
- listen to and compare other's explanations of their results with their own; and
- become involved in student-to-student discourse in which they explain their thinking to others and debate their ideas.

Elaborate

In Elaborate lessons, students apply or extend the concepts in new situations and relate their previous experiences to new ones.

In the Elaborate lessons in this module, parts of Lessons 3 and 4, *Drug Abuse and Addiction*, students

- add information about the effects of drugs to increase their understanding of neurotransmission;
- consider the factors, including physical, environmental, and social, that influence the outcome of an individual's drug abuse;
- connect ideas, solve problems, and apply their understanding in these new situations;
- draw reasonable conclusions from evidence and data;
- add depth to their understanding of concepts and processes; and
- communicate their understanding to others.

Evaluate

The Evaluate lesson is the final stage of the instructional model, but it only provides a "snapshot" of what the students understand and how far they have come from where they began. In reality, the evaluation of students' conceptual understanding and ability to use skills begins with the Engage lesson and continues throughout each stage of the model, as described in the following section. Combined with the students' written work and performance of tasks throughout the module, however, the Evaluate lesson can serve as a summative assessment of what students know and can do.

The Evaluate lesson in this module, Lesson 5, *Drug Addiction Is a Disease—So What Do We Do about It?*, provides opportunities for students to

- demonstrate what they understand about the function of the brain and the effects of drugs on that function;

- integrate information from the previous lessons to form a deeper understanding of both neurobiology and drug abuse;
- assess their own progress by comparing their current understanding with their prior knowledge;
- apply their knowledge to situations in the real world; and
- ask new questions that take them deeper into a concept or topic area.

To review the relationship of the 5E Instructional Model to the concepts presented in the module, see the chart, *Conceptual Flow of the Lessons*, on page 3.

When a teacher uses the 5E Instructional Model, he or she engages in practices that are very different from those of a traditional teacher. In response, students also participate in their learning in ways that are different from those seen in a traditional classroom. The charts, *What the Teacher Does* and *What the Students Do*, on pages 9 and 10, outline those differences.

How Does the Module Support Ongoing Assessment?

Because teachers will use this module in a variety of ways and at a variety of points in their curriculum, the most appropriate mechanism for assessing student learning is one that occurs informally at various points within the five lessons, rather than something that happens more formally just once at the end of the module. Accordingly, integrated within the lessons in the module are specific assessment components. These "embedded" assessment opportunities include one or more of the following strategies:

- performance-based activities (for example, participating in discussions of how drugs affect brain function or constructing graphs);
- oral presentation to the class (for example, explaining analysis of data); and
- written assignments (for example, answering questions or writing about demonstrations).

These strategies allow the teacher to assess a variety of aspects of the learning process, such as students' prior knowledge and current understanding, problem-solving and critical-thinking skills, level of understanding of new information, communication skills, and ability to synthesize ideas and apply understanding to a new situation. An assessment icon and an annotation that describes the aspect of learning that teachers can assess appear in the margin beside the step in which each embedded assessment occurs.

How Can Teachers Promote Safety in the Science Classroom?

Even simple science demonstrations and investigations can be hazardous unless teachers and students know and follow safety precautions. Teachers are responsible for providing students with active instruction concerning their conduct and safety in the classroom: Posting rules in a classroom is not enough. They also need to provide adequate supervision and advance warning if there are dangers involved in the science investigation. By maintaining equipment in proper working order, teachers ensure a safe environment for students.

The following are important ways to implement and maintain a safety program.

- Provide eye protection for students, teachers, and visitors. Require that everyone participating wear regulation goggles in any situation where there might be splashes, spills, or spattering. Teachers should always wear goggles in such situations.
- Know and follow the state and district safety rules and policies. Be sure to fully explain to the students the safety rules they should use in the classroom.
- At the beginning of the school year, establish consequences for students who behave in an unsafe manner. Make these consequences clear to students.
- Do not overlook any violation of a safety practice, no matter how minor. If a rule is broken, take steps to ensure that the infraction will not occur a second time.
- Set a good example by observing all safety practices. This includes wearing eye protection during all investigations when eye protection is required for the students.

What the Teacher Does		
Stage of the Instructional Model	**That Is *Consistent* with the 5E Instructional Model**	**That Is *Inconsistent* with the 5E Instructional Model**
Engage	• Piques students' curiosity and generates interest • Determines students' current understanding (prior knowledge) of a concept or idea • Invites students to express what they think • Invites students to raise their own questions	• Introduces vocabulary • Explains concepts • Provides definitions and answers • Provides closure • Discourages students' ideas and questions
Explore	• Encourages student-to-student interaction • Observes and listens to the students as they interact • Asks probing questions to redirect the students' investigations when necessary • Asks questions to help students make sense of their experiences • Provides time for students to puzzle through problems	• Provides answers • Proceeds too rapidly for students to make sense of their experiences • Provides closure • Tells the students that they are wrong • Gives information and facts that solve the problem • Leads the students step-by-step to a solution
Explain	• Encourages students to use their common experiences and data from the Engage and Explore lessons to develop explanations • Asks questions that help students express understanding and explanations • Requests justification (evidence) for students' explanations • Provides time for students to compare their ideas with those of others and perhaps to revise their thinking • Introduces terminology and alternative explanations after students express their ideas	• Neglects to solicit students' explanations • Ignores data and information students gathered from previous lessons • Dismisses students' ideas • Accepts explanations that are not supported by evidence • Introduces unrelated concepts or skills
Elaborate	• Focuses students' attention on conceptual connections between new and former experiences • Encourages students to use what they have learned to explain a new event or idea • Reinforces students' use of scientific terms and descriptions previously introduced • Asks questions that help students draw reasonable conclusions from evidence and data	• Neglects to help students connect new and former experiences • Provides definitive answers • Tells the students that they are wrong • Leads students step-by-step to a solution
Evaluate	• Observes and records as students demonstrate their understanding of concept(s) and performance of skills • Provides time for students to compare their ideas with those of others and perhaps to revise their thinking • Interviews students as a means of assessing their developing understanding • Encourages students to assess their own progress	• Tests vocabulary words, terms, and isolated facts • Introduces new ideas or concepts • Creates ambiguity • Promotes open-ended discussion unrelated to the concept or skill

What the Students Do		
Stage of the Instructional Model	**That Is *Consistent* with the 5E Instructional Model**	**That Is *Inconsistent* with the 5E Instructional Model**
Engage	• Become interested in and curious about the concept/topic • Express current understanding of a concept or idea • Raise questions such as, What do I already know about this? What do I want to know about this? How could I find out?	• Ask for the "right" answer • Offer the "right" answer • Insist on answers or explanations • Seek closure
Explore	• "Mess around" with materials and ideas • Conduct investigations in which they observe, describe, and record data • Try different ways to solve a problem or answer a question • Acquire a common set of experiences so they can compare results and ideas • Compare their ideas with those of others	• Let others do the thinking and exploring (passive involvement) • Work quietly with little or no interaction with others (only appropriate when exploring ideas or feelings) • Stop with one solution • Demand or seek closure
Explain	• Explain concepts and ideas in their own words • Base their explanations on evidence acquired during previous investigations • Become involved in student-to-student conversations in which they debate their ideas • Record their ideas and current understanding • Reflect on and perhaps revise their ideas • Express their ideas using appropriate scientific language • Compare their ideas with what scientists know and understand	• Propose explanations from "thin air" with no relationship to previous experiences • Bring up irrelevant experiences and examples • Accept explanations without justification • Ignore or dismiss other plausible explanations • Propose explanations without evidence to support their ideas
Elaborate	• Make conceptual connections between new and former experiences • Use what they have learned to explain a new object, event, organism, or idea • Use scientific terms and descriptions • Draw reasonable conclusions from evidence and data • Communicate their understanding to others	• Ignore previous information or evidence • Draw conclusions from "thin air" • Use terminology inappropriately and without understanding
Evaluate	• Demonstrate what they understand about the concept(s) and how well they can implement a skill • Compare their current thinking with that of others and perhaps revise their ideas • Assess their own progress by comparing their current understanding with their prior knowledge • Ask new questions that take them deeper into a concept or topic area	• Disregard evidence or previously accepted explanations in drawing conclusions • Offer only yes-or-no answers or memorized definitions or explanations as answers • Fail to express satisfactory explanations in their own words • Introduce new, irrelevant topics

- Know and follow waste disposal regulations.
- Be aware of students who have allergies or other medical conditions that might limit their ability to participate in activities. Consult with the school nurse or school administrator.
- Anticipate potential problems. When planning teacher demonstrations or student investigations, identify potential hazards and safety concerns. Be aware of what might go wrong and what can be done to prevent the worst-case scenario. Before each activity, alert the students to the potential hazards verbally and distribute specific safety instructions as well.
- Supervise students at all times during a hands-on activity.
- Provide sufficient time for students to set up the equipment, perform the investigation, and properly clean up and store the materials after use.
- Never assume that students know or remember safety rules or practices from their previous science classes.

How Can Controversial Topics Be Handled in the Classroom?

Teachers sometimes feel that the discussion of values is inappropriate in the science classroom or that it detracts from the learning of "real" science. The lessons in this module, however, are based upon the conviction that there is much to be gained by involving students in analyzing issues of science, technology, and society. Society expects all citizens to participate in the democratic process, and our educational system must provide opportunities for students to learn to deal with contentious issues with civility, objectivity, and fairness. Likewise, students need to learn that science intersects with life in many ways.

In this module, students have a variety of opportunities to discuss, interpret, and evaluate basic science and health issues, some in the light of values and ethics. As students encounter issues about which they feel strongly, some discussions might become controversial. How much controversy develops will depend on many factors, such as how similar the students are with respect to socioeconomic status, perspectives, value systems, and religious preferences. In addition, the language and attitude of the teacher factor into the flow of ideas and the quality of exchange among the students.

The following guidelines may help teachers facilitate discussions that balance factual information with feelings.

- Remain neutral. Neutrality may be the single most important characteristic of a successful discussion facilitator.
- Encourage students to discover as much information about the issue as possible.
- Keep the discussion relevant and moving forward by questioning or posing appropriate problems or hypothetical situations. Encourage everyone to contribute, but do not force reluctant students into the discussion.
- Emphasize that everyone must be open to hearing and considering diverse views.
- Use unbiased questioning to help the students critically examine all views presented.
- Allow for the discussion of all feelings and opinions.
- Avoid seeking consensus on all issues. The multifaceted issues that the students discuss result in the presentation of divergent views, and students should learn that this is acceptable.
- Acknowledge all contributions in the same evenhanded manner. If a student seems to be saying something for its shock value, see whether other students recognize the inappropriate comment and invite them to respond.
- Create a sense of freedom in the classroom. Remind students, however, that freedom implies the responsibility to exercise that freedom in ways that generate positive results for all.
- Insist upon a nonhostile environment in the classroom. Remind students to respond to ideas instead of to the individuals presenting those ideas.

- Respect silence. Reflective discussions often are slow. If a teacher breaks the silence, students may allow the teacher to dominate the discussion.
- At the end of the discussion, ask the students to summarize the points that they and their classmates have made. Respect students regardless of their opinion about any controversial issue.

Using the CD-ROM

The CD-ROM component of *The Brain: Understanding Neurobiology Through the Study of Addiction* is a tool like an overhead projector or a textbook that can help you organize your use of the module, engage student interest in learning, and orchestrate and individualize instruction. The CD-ROM contains the following major resources:

- introductions to the National Institutes of Health and the National Institute on Drug Abuse;
- mini-documentaries, animations, and simulations required to teach various activities within the lessons;
- supplemental video clips and animations that can enhance students' understanding of concepts presented in the print material; and
- printable files of this module.

Installation Instructions

The CD-ROM runs on Apple Macintosh and IBM-compatible personal computers.

The minimum requirements for a Macintosh computer are the following: OS 8.5 operating system or higher, Power PC processor, 256-color monitor or higher, 32 megabytes RAM, QuickTime 4 or 5 for Macintosh, and a 2x CD-ROM. Mac users can download QuickTime from Apple Computers at *http:// www.apple.com/quicktime/download/*.

The minimum requirements for IBM-compatible computers are the following: Windows 95 operating system or higher, Pentium 100 processor or higher, 256-color monitor or higher, 32 megabytes RAM, Soundblaster or Windows Sound System–compatible card, Windows Media Player, and a 2x CD-ROM. Windows users can download

Loading Instructions for the CD-ROM

IBM-Compatible Computers

Place the CD in the CD-ROM drive and close the door. The CD should automatically launch the program.
If you have turned off the autorun feature on your CD-ROM drive or if you want to run the software without ejecting and re-inserting the disk each time you use the program, do one of the following:

- Click Start / Run and type the following in the dialog box: d:\nida.exe (change "d:\" if necessary). Click OK.

Macintosh Computers

Place the CD in the CD-ROM drive and close the door.
Open the CD-ROM, then click on the NIH icon.

Network Installation

A network installation of the entire program requires up to 450 to 650 megabytes of disk space. Performance of the videos will depend on the network speed and the processor speed of client stations. Each client computer must have QuickTime 4 or higher installed.

1. Place the disk in the CD-ROM drive and click on Quit if program opens automatically.
2. Create a folder on the network or local drive where you want to install the application and name it *The Brain*.
3. Copy all the folders and files in the root directory of the CD-ROM into the new folder. Note: Macintosh users cannot see files from the PC format on the CD-ROM and vice versa. If you run both platforms from your network, you will need to copy files from the CD to the network twice, once from a network PC and once from a network Mac. If you have room, create two complete copies of the software in different folders, one for each platform. Because users will see both Mac and PC files on the network, be sure that Mac users open only the Mac files and PC users open only the PC files.
4. To run the application, follow the procedures described here for IBM-compatible or Macintosh computers by locating the local or network copy of the desired program files.

the latest version of this player from Microsoft at *http://www.microsoft.com/windows/windowsmedia/en/Download/default.asp.*

To use the CD-ROM, load it into the CD-ROM drive as you would any other CD. Then, follow the installation instructions shown in the chart on page 13.

Note: If you have trouble running the CD-ROM, please make sure you have the correct plug-ins loaded on your computer(s). For more information, please consult the Readme file on the CD-ROM.

Getting the Most Out of the CD-ROM

Before you use this CD-ROM or any other piece of instructional software in your classroom, it may be valuable to identify some of the benefits you expect software to provide. Well-designed instructional multimedia software can:

- motivate students by helping them enjoy learning and want to learn more because it enlivens content that students otherwise might find dull and uninteresting;
- offer unique instructional capabilities that allow students to explore topics in greater depth and in ways that are closer to actual field experiences than print-based resources can offer;
- provide teachers with support for experimenting with new instructional approaches that allow students to work independently or in small teams and that give teachers increased credibility among today's technology-literate students; and
- increase teacher productivity by helping teachers with assessment, record keeping, and classroom planning and management; this module offers teachers the convenience of several weeks of instruction stored in the space of a single CD and this teacher's guide.

The ideal use of the CD-ROM requires one computer for each student team; the installation instructions explain how to make the information available over a network. However, if you have only one computer and CD-ROM drive available, you still can use the CD (for example, by using a suitable display device to show animations or videos to the whole class or by rotating teams through a computer station to access CD-ROM–based resources). If you do not have the facilities for using the CD-ROM in your classroom, a print-based alternative for each activity that requires the CD is included in this module.

Collaborative Groups

Many of the activities in this module are designed to be completed by groups of students working together. Although individual students working alone can complete many of the specific steps, this strategy will not stimulate the types of student-student interactions that are one of the goals of active, collaborative, inquiry-based learning. Therefore, we recommend that you organize collaborative groups of two or three students, depending on the number of computers equipped with CD-ROM drives you have available. If necessary, up to six students may work as a group, although the students may not be as involved in the activity. Students in groups larger than this will have difficulty organizing the student-computer interactions equitably, which can lead to one or two students assuming the primary responsibility for the computer-based work. Although this type of arrangement can be efficient, it means that some students do not get the opportunity to experience the in-depth discovery and analysis that the enclosed CD-ROM was designed to stimulate.

If you are teaching all five lessons as a unit, we recommend that you keep your students in the same collaborative groups for all of the activities in the lessons. This will allow each group to develop a shared experience with the software and with the ideas and issues that the activities present. A shared experience also will enhance your students' perceptions of the lessons as a conceptual whole.

If your student-to-computer ratio is greater than six students to one computer, you will need to change the way you teach the module from the instructions in the lessons. For example, if you have only one computer available, you may want students to complete the CD-based work across an extended time period. You can do this in several ways. The most practical way is to use your computer as a center along with several other centers at which students complete other activities. In this strategy,

students would rotate through the computer center, eventually completing the CD-based work that you have assigned.

A second way to structure the lessons if you have only one computer available is to use a projection system to display the computer monitor onto a screen for the whole class to see simultaneously. Giving selected students in the class the opportunity to manipulate the program in response to class suggestions and requests can give students some of the same type of autonomy in their learning that they would gain if they were working with the CD in small teams.

Using the Student Lessons

The heart of this module is the set of five lessons that follow. These lessons are the vehicles that we hope will carry important concepts related to neurobiology and drug addiction to your students. To review the concepts in detail, refer to the chart, *Conceptual Flow of the Lessons* on page 3.

Format of the Lessons

As you scan the lessons, you will find that each contains several major features.

At a Glance gives the teacher a convenient overview of the lesson.

- The **Overview** provides a short summary of student activities.
- The **Major Concept** section lists the central idea the lesson is designed to convey.
- **Objectives** lists two to four specific understandings or abilities students should have after completing the lesson.
- The **Basic Science-Health Connection** describes how the material in the lesson illustrates the relationship between basic science and personal and public health. The mission of the NIH is to "uncover new knowledge that will lead to better health for everyone." This mission statement recognizes that basic science and personal and public health are inextricably linked and form a powerful whole. Research into the basic processes of life leads inevitably to strategies for improving health, and questions about health trigger research into basic processes.

Background Information provides the teacher with the science content that underlies the key concepts of the lessons. The information provided here is *not* intended to form the basis of lectures to students. Instead, it is designed to enhance the teacher's understanding of the content so that the teacher can more accurately facilitate class discussions, answer student questions, and provide additional examples.

In Advance provides instructions for collecting and preparing the materials required to complete the activities in the lesson.

- **CD-ROM Activities** tells the teacher which of the lesson's activities make use of segments on the CD-ROM.
- **Photocopies** lists the paper copies or transparencies that need to be made from masters, which follow the student lessons.
- **Materials** lists all the materials other than photocopies needed for each of the activities in the lesson.
- **Preparation** outlines the things the teacher needs to do to be ready to teach each of the activities in the lesson.

Procedure outlines the steps for each activity in the lesson. It provides implementation suggestions and answers to questions.

Within the procedures, annotations provide additional commentary.

- **Tip from the Field Test** includes actual field-test teachers' suggestions for teaching strategies, class management, and module implementation.
- **Notes** give information about special points to remember as you are teaching the activity.
- **Assessment** provides the teacher with strategies for assessing student progress throughout the module and is identified by an assessment icon (see below).
- **Icons** identify specific annotations:

This icon identifies teaching strategies that address specific science content standards as defined by the *National Science Education Standards.*

This icon identifies when to use the CD-ROM as part of the teaching strategies. An annotation instructs the teacher how to find the appropriate segment on the CD-ROM. Information about using the CD-ROM can be found in the section, *Using the CD-ROM*. A print-based alternative is provided in each lesson for all CD-ROM activities in the event that a computer with a CD-ROM drive is not available.

This icon identifies when assessment is embedded in the module's structure. An annotation suggests strategies for assessment.

This icon identifies a print-based alternative to a CD-ROM activity to use if computers are not available.

The **Masters** required to teach the lessons are located in a separate section at the end of the module.

Timeline for Teaching the Module

There are several ways to complete the five lessons in this module.

The suggested timeline (on pages 18–19) outlines the optimal plan for completing the five lessons in this module. The plan assumes you will teach the

Suggested Timeline	
Timeline	**Activity**
3 weeks ahead	Reserve computers Check CD-ROM performance
1 week ahead	Copy masters Make transparencies
Day 1	**Lesson 1** Activity 1: *What Does the Brain Do?* Activity 2: *Positron Emission Tomography and Brain Function*
Day 2	**Lesson 1 (Continued)** Activity 3: *Parts of the Brain* Activity 4: *Who Was Phineas Gage?* Activity 5: *Where Do Drugs Act?*
Day 3	**Lesson 2** Activity 1: *Anatomy of a Neuron* Activity 2: *How Do Neurons Communicate?*
Day 4	**Lesson 2 (Continued)** Activity 3: *Do All Neurotransmitters Have the Same Effect?* Activity 4: *One Neuron Signals Another*
Day 5	**Lesson 3** Activity 1: *Drugs Alter Neurotransmission*
Day 6	**Lesson 3 (Continued)** Activity 2: *How Does Caffeine Affect You?* Activity 3: *Routes of Administration*
Day 7	**Lesson 4** Activity 1: *How Does Drug Abuse Begin?* Activity 2: *Drug Abuse Is Voluntary; Addiction Is Compulsive*
Day 8	**Lesson 4 (Continued)** Activity 3: *When Does Abuse Become Addiction?* Activity 4: *Environmental, Behavioral, and Social Influences on Drug Abuse and Addiction* Activity 5: *Long-term Effects of Drug Abuse and Addiction*

Suggested Timeline (continued)	
Timeline	**Activity**
Day 9	**Lesson 5** Activity 1: *How Effective is Treatment?* Activity 2: *Evaluating the Case Studies* Activity 3: *Success Rates for Treating Chronic Illness* Activity 4: *Addiction Is a Brain Disease*

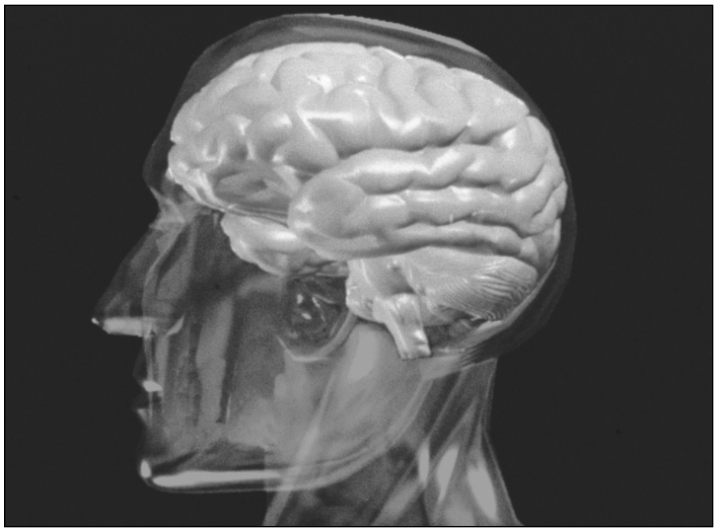
Abbreviated Timeline	
Timeline	**Activity**
3 weeks ahead	Reserve computers Check CD-ROM performance
1 week ahead	Copy masters Make transparencies
Day 1	**Lesson 1** Activity 1: *What Does the Brain Do?* Activity 2: *Positron Emission Tomography and Brain Function* Activity 3: Omit Activity 4 (assign as homework): *Who Was Phineas Gage?* Activity 5: *Where Do Drugs Act?*
Day 2	**Lesson 2** Activity 1: *Anatomy of a Neuron* Activity 2: *How Do Neurons Communicate?* Activity 3: Omit Activity 4: Omit
Day 3	**Lesson 3** Activity 1: *Drugs Alter Neurotransmission* Activity 2: Omit Activity 3: Omit
Day 4	**Lesson 4** Activity 1: *How Does Drug Abuse Begin?* Activity 2: *Drug Abuse Is Voluntary; Addiction Is Compulsive* Activity 3: Omit Activity 4 (assign as homework): *Environmental, Behavioral, and Social Influences on Drug Abuse and Addiction* Activity 5 (have students watch the CD-ROM mini-documentary independently during free time or assign Master 4.6 as homework): *Long-term Effects of Drug Abuse and Addiction*
Day 5	**Lesson 5** Activity 1: *How Effective is Treatment?* Activity 2: *Evaluating the Case Studies* Activity 3: *Success Rates for Treating Chronic Illness* Activity 4 (assign as homework): *Addiction Is a Brain Disease*

activities on consecutive days. If your class requires more time to complete the activities, discuss issues raised in this module, or complete the activities on the CD-ROM, adjust your timeline accordingly.

The second timeline on page 19 outlines an abbreviated timeline for completing the lessons in the curriculum supplement in one week. By this timeline, students skip some activities and focus on ones that convey the most important concepts. Students will complete other activities as homework assignments. Students will miss a great deal of the richness of the unit and the details that add interest to the material, but they can still benefit from learning many new concepts.

Lesson 1
Engage/ Explore

The Brain: What's Going On in There?



Source: National Institute on Drug Abuse (1996) The Brain & the Actions of Cocaine, Opiates, and Marijuana. Slide Teaching Packet for Scientists.

At a Glance

Overview
Students examine images of human brains that illustrate that specific regions of the brain regulate specific functions. They extend that knowledge to learn that drugs of abuse activate an area of the brain called the reward system. The same brain region is stimulated in response to basic survival needs to produce feelings of pleasure.

Major Concept
Specific brain regions control specific brain functions.

Objectives
By the end of these activities, students will

- understand that particular functions are localized to specific areas of the brain,
- appreciate that imaging techniques allow scientists to study activity in the brain, and
- recognize that normal behaviors can activate the reward system in the brain and that drugs of abuse affect those same reward circuits.

Basic Science–Health Connection
The brain controls virtually everything humans experience, including movement, sensing our environment, regulating our involuntary body processes such as breathing, as well as controlling our emotions. Ongoing scientific research into the organization and function of the brain has led, and will continue to lead, to new treatments of diseases such as Parkinson's disease, epilepsy, stroke, and mental illnesses (including depression and schizophrenia).

Background Information

The brain is the organ of behavior. It is also the organ of our mind. Both overt behavior and consciousness are manifestations of the work of our brains. Other people can see an individual's overt behaviors, whereas consciousness is apparent only in our individual minds. The field of neuroscience studies how people control their behaviors, thoughts, and feelings, and how these actions sometimes get out of control.

The brain processes a huge amount of information in a remarkably efficient manner. Think about driving a car. It is something most of us do without much difficulty. But to do it properly, we must perform a remarkable number of tasks. First we have to make sure that our body is in working order. Heart rate and breathing have to be properly regulated, body temperature held steady, and we certainly have to be sure we don't fall asleep. Despite the complexity of these tasks, we carry them out with no conscious involvement on our part. Then, there are the things we are aware of. We have to see the road and hear the traffic (or the radio), use information from our feet, legs, hands, and arms to know where the gas pedal and steering wheel are, and then generate the body movements to control the direction and speed of the car. All of this often takes place while we are talking to someone else in the car, or even while talking on the phone (although this may not be the best idea). The magnitude and speed of data processing needed to do this are stunning, but most of us consider driving to be an easy task.

Different Regions of the Brain Regulate Different Functions

How does the brain carry out multiple tasks at one time? The answer is that the brain splits the larger task—driving, in our example—into smaller ones: seeing, hearing, moving, and so forth. Even those tasks are split into their component parts. One part of the human brain analyzes the movement of objects that we

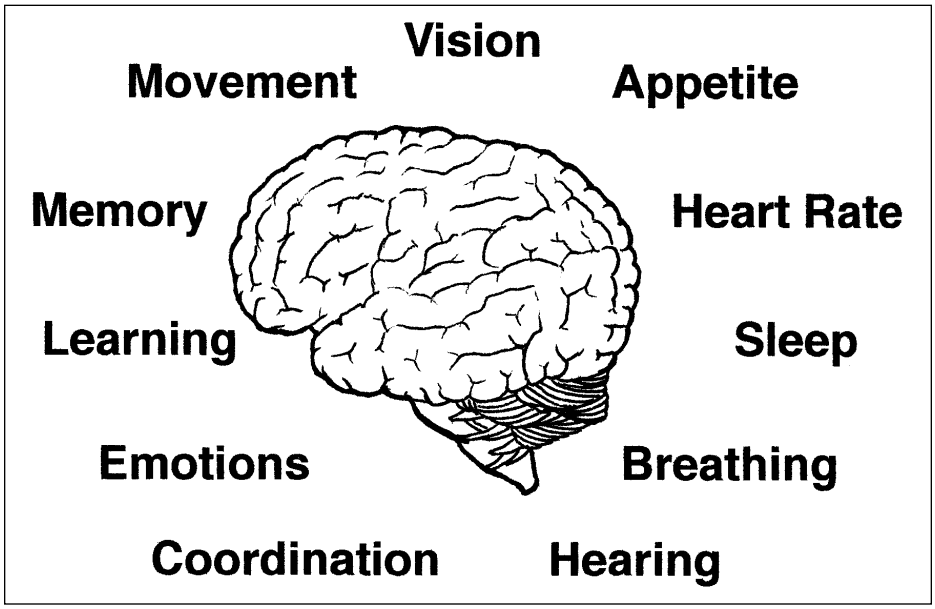


Figure 1.1: The human brain regulates everything a person does.

see, while another part is responsible for actually recognizing them. In short, specific parts of the brain carry out specific tasks. Not only that, but each part of the brain specializes in a specific kind of task. This means that whenever that task needs to be done, the appropriate information is processed by that part of the brain.

The flip side of this organizational scheme is that if a part of the brain is damaged, then the job it used to undertake cannot be done. For example, damage to the occipital lobe at the back of the brain can cause blindness, but it has no effect on a person's ability to hear or move. Because the job of seeing is highly compartmentalized, individuals who have lost one aspect of sight, such as the ability to see colors or to recognize faces, may still be able to do other visual tasks. Imagine being able to recognize someone by hearing his or her voice, but not being able to recognize his or her face when you see it.

The advantage of this localization of function is when larger jobs are parceled out throughout the brain, they all can be done at once. This "division of labor" adds great speed to our ability to perceive what is happening in the world around us, to analyze it, and then to generate appropriate responses. Dealing with information in this way is called **parallel processing**.[1] Computer scientists have used this concept in the development of computers.

The human brain consists of several large regions each of which is responsible for some of the activities necessary for life. These include the brainstem, cerebellum, limbic system, diencephalon, and cerebral cortex.[2,3]

The **brainstem** is the part of the brain that connects the brain and spinal cord.

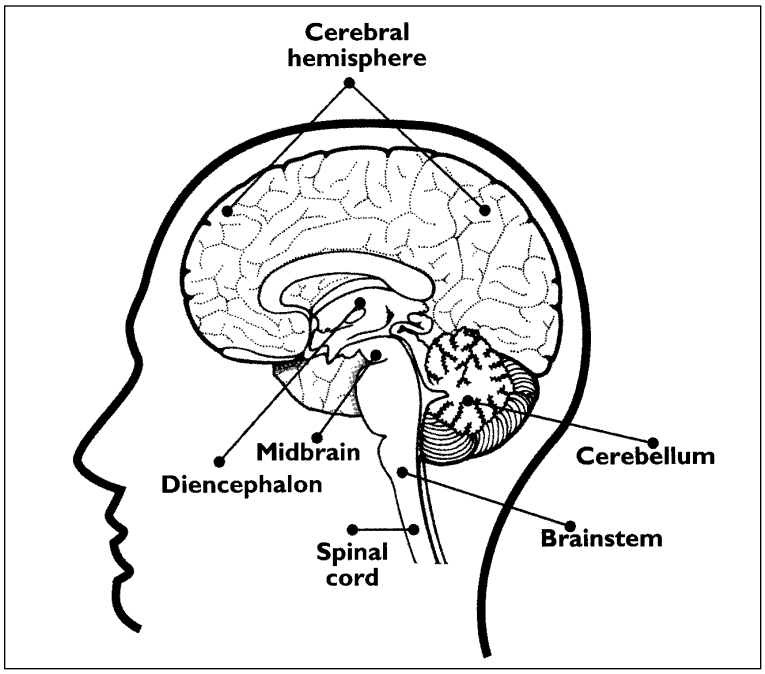


Figure 1.2: This drawing of a brain cut in half illustrates some of the major regions of the brain. Source: National Institute on Drug Abuse (1997) Mind Over Matter: The Brain's Response to Drugs, Teacher's Guide.

This part of the brain is involved in coordinating many basic functions such as heart rate, breathing, eating, and sleeping.

The **cerebellum** coordinates the brain's instructions for skilled repetitive movements and for maintaining balance and posture.

The **limbic system**, as discussed in the next section, is involved in regulating emotions and motivations. In addition, parts of the limbic system, the amygdala and hippocampus, are important for memory functions.

The **diencephalon** contains the thalamus and hypothalamus. The thalamus is involved in sensory perception and the regulation of movement. The hypothalamus is an important regulator of the pituitary gland.

The **cerebral cortex** makes up the largest part of the brain mass and lies over and around most of the other brain structures. It is the part of the brain that is responsible for thinking, perceiving, and producing and understanding language. The cortex can be divided into areas that are involved in vision, hearing, touch, movement, smell, and thinking and reasoning.

Drugs Act On the Reward System in the Brain

Just as specific areas of the brain control seeing and hearing, specific brain areas also regulate emotions and motivations. These functions are carried out by a part of the brain called the **limbic system**. The limbic system, similar to other regions in the brain, influences how we respond to the world around us. Imag-

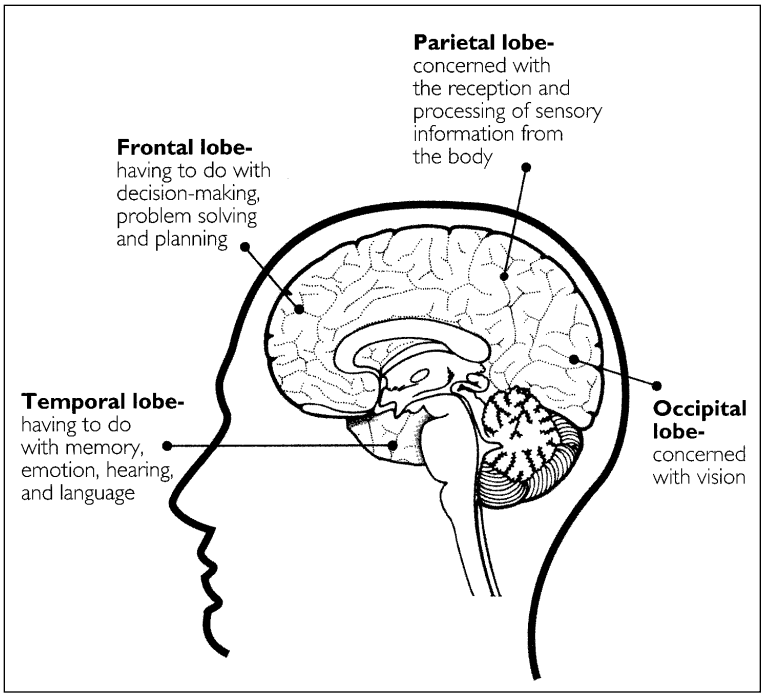


Figure 1.3: This drawing of a brain cut in half illustrates the lobes of the cerebral cortex and describes their main functions. Source: National Institute on Drug Abuse (1997) Mind Over Matter: The Brain's Response to Drugs, Teacher's Guide.

ine a cool sunny day. You finish your work early and head to your favorite park for a leisurely walk with your dog. You are feeling so mellow that you merely scratch the dog behind the ears when he slobbers on your clean shirt. You might have a very different reaction on another day when you have to work late, traffic is backed up, and the dog runs away instead of coming to welcome you home. This time when the dog slobbers on you (after he finds his way home again), you shove him away and scold him.

The feelings you have in those two different situations are a result of your limbic system at work. The limbic system uses memories, information about how your body is working, and current sensory input to generate your emotional responses to current situations.

The limbic system is involved in many of our emotions and motivations, particularly those related to survival, such as fear and anger. The limbic system also regulates feelings of pleasure related to our survival, such as those experienced from eating and sex. The feelings of pleasure, which scientists call reward, are very powerful. If something is pleasurable or rewarding, you want to do it again. Life-sustaining activities such as eating and sex activate a circuit of specialized nerve cells that are devoted to producing and regulating pleasure. These cells are located at the top of the brainstem in the **ventral tegmental area (VTA)**. These neurons relay their messages through their axons to nerve cells in a limbic system structure called the **nucleus accumbens**. Additional nerve fibers reach part of the frontal region of the cerebral cortex. This circuit of neurons is called the **reward system**.[1,2]

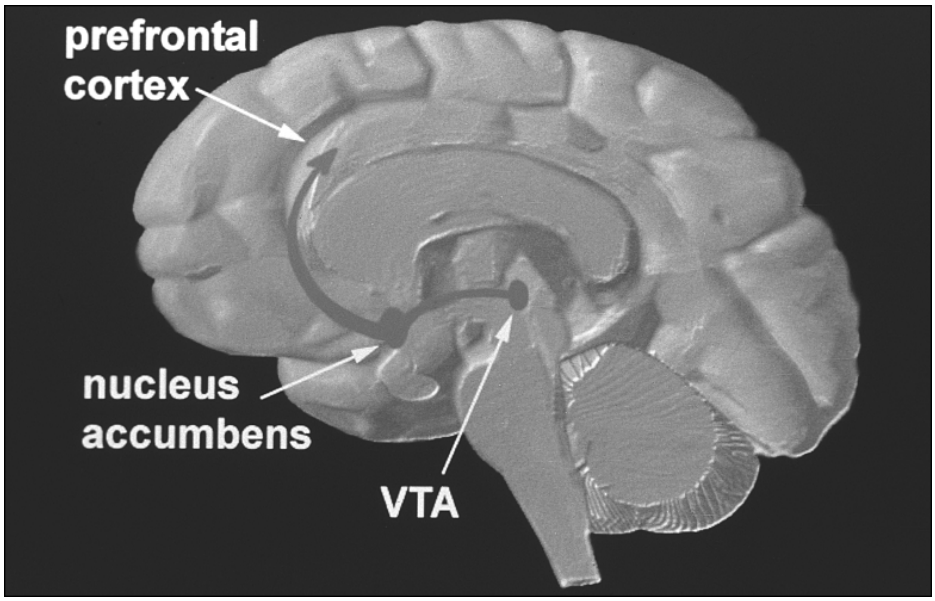


Figure 1.4: This drawing of a brain cut in half illustrates the brain areas and systems involved in the reward system, or pleasure circuit. Neurons in the ventral tegmental area (VTA) extend axons to the nucleus accumbens and part of the prefrontal cortex. Source: National Institute on Drug Abuse (1996) The Brain & the Actions of Cocaine, Opiates, and Marijuana. Slide Teaching Packet for Scientists.

Drugs of abuse activate these same VTA and nucleus accumbens neurons; that is why drugs produce pleasurable feelings to the drug user. And, because the feelings are pleasurable, the user wants to continue to experience the pleasure that he or she felt during previous drug use. One of the reasons that drugs of abuse can exert such powerful control over our behavior is that they act directly on the more evolutionarily primitive brainstem and limbic structures, which can override the cortex in controlling our behavior.

Different drugs of abuse affect the neurons of the reward system in different ways. The activities in Lesson 3 in this module will elucidate the mechanisms by which drugs of abuse exert their effects.

Imaging the Brain

Scientists increasingly use newer technologies to learn more about how the brain works and how drugs of abuse change how the brain works. Historically, scientists could examine brains only after death, but new imaging procedures enable scientists to study the brain in living animals, including humans.

One of the most extensively used techniques to study brain activity and the effects of drugs on the brain is **positron emission tomography** (**PET**). PET measures the spatial distribution and movement of radioisotopes in tissues of living subjects. Because the patient is awake, the technique can be used to investigate the relationship between behavioral and physiological effects and changes in brain activity. PET scans can detect nanomolar concentrations of tracer molecules and achieve spatial resolution of about 4 millimeters. In addition, computers can reconstruct images obtained from a PET scan in two or three dimensions.

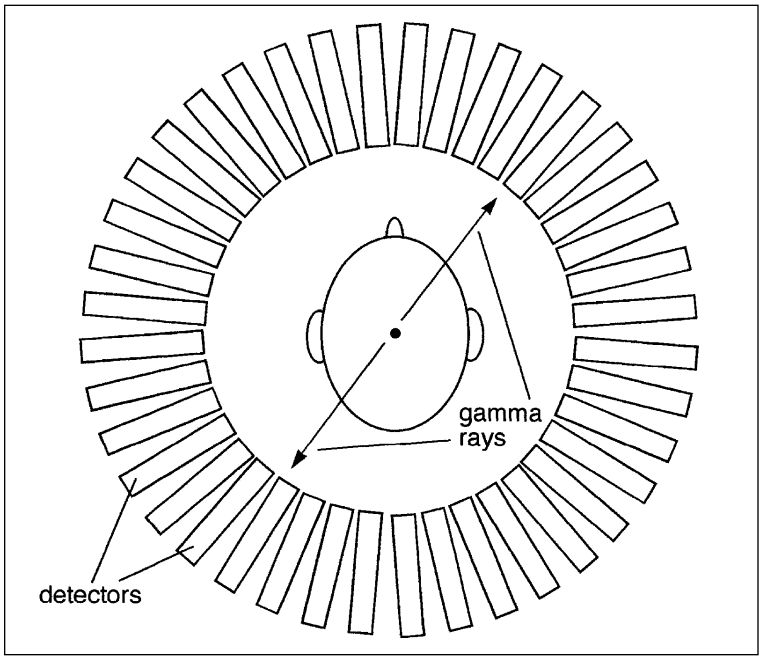


Figure 1.5: When an unstable positron collides with an electron, the particles are annihilated and two gamma rays are emitted at 180° from each other. Detectors record gamma ray emission to localize the site of positron annihilation.

PET requires the use of compounds that are labeled with positron-emitting isotopes.[4,5] A cyclotron accelerates protons into the nucleus of nitrogen, carbon, oxygen, or fluorine to generate these isotopes. The additional proton makes the isotope unstable. To become stable again, the proton must break down into a neutron and a positron. The unstable positron travels away from the site of generation and dissipates energy along the way. Eventually, the positron collides with an electron leading to the emission of two gamma rays at 180 degrees from one another. The gamma rays reach a pair of detectors that record the event. Because the detectors respond only to simultaneous emissions, scientists can precisely map the location where the gamma rays were generated. The labeled radioisotopes

are very short-lived. The half-life (the time for half of the radioactive label to disintegrate) of the commonly used radioisotopes ranges from approximately two minutes to less than two hours, depending on the specific compound. Because a PET scan requires only small amounts (a few micrograms) of short-lived radioisotopes, negative pharmacological effects are imperceptible.

PET scans can answer a variety of questions about brain function, including the activity of neurons. Scientists use different radiolabeled compounds to investigate different biological questions. For example, radiolabeled glucose can identify parts of the brain that become more active in response to a specific stimulus. Active neurons metabolize more glucose than inactive neurons. Active neurons will emit more positrons. This will show as red or yellow on PET scans compared to blue or purple in areas where the neurons are not highly active. PET also helps scientists investigate how drugs affect the brain by enabling them to:

- determine the distribution of a drug in the body,
- measure the local concentration of a drug at binding sites,
- estimate receptor occupancy based on competitive binding assays,
- evaluate the effects of drugs on other neurotransmitter systems, and
- investigate the activity of enzymes that metabolize the drug.[6]

In addition to its uses in research, PET also is a powerful tool for diagnosing

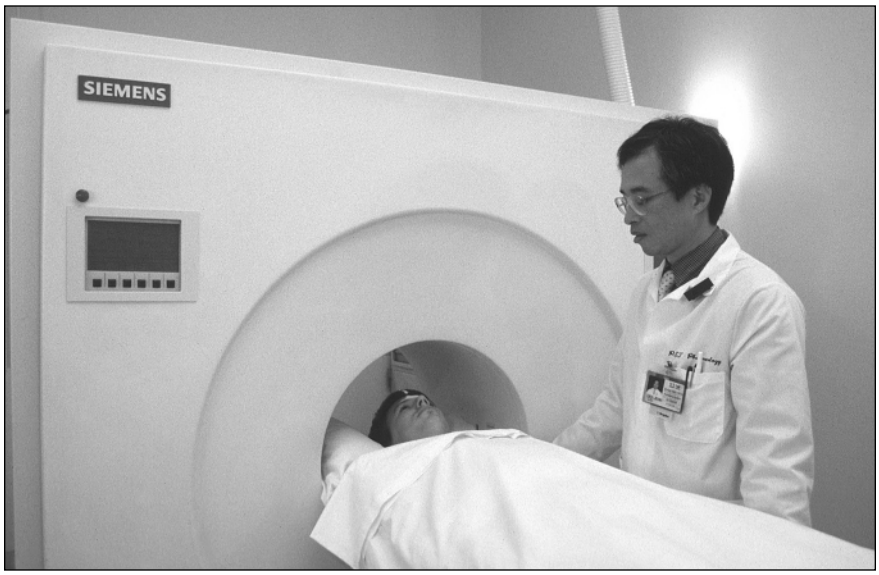


Figure 1.6: Photograph of PET imaging equipment. Photo courtesy of UCLA School of Medicine.

Different Neuroimaging Techniques Provide Different Information About the Brain

PET scanning is a major neuroimaging technique used in drug abuse research. However, researchers also use other techniques when they better answer a scientific question. Similar to PET, single photon emission computed tomography (SPECT), magnetic resonance imaging (MRI), and electroencephalography (EEG) are noninvasive procedures that can measure biological activity through the skull and reveal the living brain at work.[4,8] Each technique has its own advantages and each provides different information about brain structure and function. Scientists often use more than one technique when conducting their research studies.

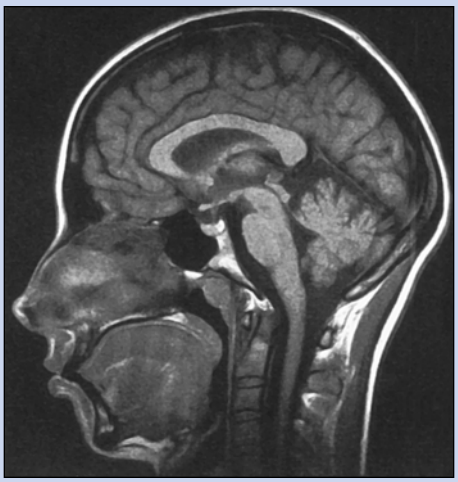


Figure 1.7: MRI image of human brain. Photo courtesy of Penrad Imaging, Colorado Springs, CO.

Similar to PET, SPECT imaging uses radioactive tracers and a scanner to record data that a computer constructs into two- or three-dimensional images of active brain regions. Because the tracers used in SPECT take longer to deteriorate than those for PET, longer periods of time between tests are required for SPECT. While PET is more versatile than SPECT and produces more detailed images with a higher degree of resolution, SPECT is much less expensive than PET and can address many of the same drug abuse research questions.

MRI uses magnetic fields and radio waves to produce high-quality two- or three-dimensional images of brain structures without injecting radioactive tracers. In this procedure, a large cylindrical magnet creates a magnetic field around the research volunteer's head, and radio waves are sent through the magnetic field. Sensors read the signals and a computer uses the information to construct an image. Using MRI, scientists can image both surface and deep brain structures with a high degree of anatomical detail, and they can detect minute changes in these structures over time. A modification of this technique, called functional MRI (fMRI), enables scientists to see images of blood flow in the brain as it occurs. fMRI provides superior image clarity along with the ability to assess blood flow and brain functions in just a few seconds. However, PET retains the advantage of being able to identify which brain receptors are being activated by neurotransmitters, abused drugs, and potential treatment compounds.

EEG uses electrodes placed on the scalp to detect and measure patterns of electrical activity in the brain. The greatest advantage of EEG is speed: it can record complex patterns of neural activity occurring within fractions of a second after a stimulus has been administered. The drawback to EEG is that it does not provide the spatial resolution of fMRI or PET. Researchers often combine EEG images of brain electrical activity with MRI scans to localize brain activity more precisely.

and monitoring certain diseases.[7] For example, PET scans may be used to locate tumors in cancer patients, monitor the spread of cancer, and evaluate the effectiveness of cancer treatment. PET scans are able to reveal the presence of tumors because of the rapid metabolism characteristic of cancerous cells. PET images reveal this increased glucose utilization by cells that have high metabolic rates. PET is an accurate test for coronary heart disease because it can detect areas of diminished blood flow to the heart. Doctors also employ PET to reveal changes in the brain that occur with Alzheimer's disease, Parkinson's disease, or seizure disorders. PET is a valuable tool because it:

- is safe,
- replaces multiple testing procedures with a single exam,
- can detect diseases before they show up on other tests,
- can show the progress of disease, and
- reduces or eliminates the need for invasive procedures such as surgery.[7]

In Advance

CD-ROM Activities	
Activity Number	**CD-ROM**
Activity 1	no
Activity 2	yes
Activity 3	yes
Activity 4	no
Activity 5	no

Photocopies		
For the class	**For each group of 3 students**	**For each student**
1 transparency of Master 1.3, *PET Image Tasks* 1 transparency of Master 1.4, *Major Regions of the Brain* 1 transparency of Master 1.5, *Areas of the Cerebral Cortex and Their Functions* 1 transparency of Master 1.7, *The Reward System*	1 copy of Master 1.1, *Positron Emission Tomography (PET) Images* [a] 1 copy of Master 1.2, *Interpreting PET Images*	1 copy of Master 1.6, *What Happened to Phineas Gage?*

[a] The CD-ROM version of Activity 2 is the preferred approach. Copies of Master 1.1, *Positron Emission Tomography (PET) Images*, are needed only if the CD-ROM is unavailable for classroom use. If needed, make one set of color photocopies for each team of 3 students. Several field-test teachers laminated the color copies to help preserve them.

Materials	
Activity 1	6 to 8 index cards (3” x 5” or 4” x 6”)
Activity 2	overhead projector
Activity 3	overhead projector
Activity 4	none
Activity 5	overhead projector

Preparation

Prepare task cards for Activity 1, Step 1 (see page 30). Decide which tasks you wish students to do. Write the instructions for each task on an index card.

Arrange for the class to use the computer lab for Activities 2 and 3.

Procedure

This activity is designed to engage students in learning about the brain and to help the teacher assess the students' prior knowledge of the scope of functions regulated by the human brain.

ACTIVITY 1: WHAT DOES THE BRAIN DO?

1. **Ask for 6-8 volunteers (one for each task) to participate in an activity. Ask them to come to the front of the room, and give each volunteer one of the prepared task cards. Then ask each volunteer, one at a time, to perform the task listed on his or her task card.**

   The specific tasks can and should be very diverse. The following list suggests some appropriate tasks:

   - wave hands in the air
   - eat
   - hop up and down on the right foot
   - walk around the classroom
   - look out the window
   - recite the Pledge of Allegiance
   - sing "Mary Had a Little Lamb"
   - do an algebra problem (e.g., Solve the following problem: 5x +14 = 34. What is the value of x?)
   - recall and describe the way to get from the classroom to the cafeteria (e.g., Give directions to walk from this classroom to the cafeteria.)
   - read a sentence aloud (e.g., Read the following sentence aloud: "Four score and seven years ago our fathers brought forth on this continent, a new nation, conceived in Liberty, and dedicated to the proposition that all men are created equal."[9])

2. **After the volunteers perform the tasks, ask the students to identify the part of the body that is involved in *all* of the tasks.**

   The goal for this question is for students to acknowledge that the brain is involved in regulating all human physiological, behavioral, and emotional functions. For example, point out that all students are breathing. When most people think about breathing, they think about the lungs, but not the involvement of the brain. Also, point out that each student's heart is beating. Although the heart is actually pumping the blood, the brain fulfills an important role in regulating the heartbeat. The involvement of the brain will be more obvious for some of the tasks than for others.

3. **After students deduce that the brain is involved in all of these activities, ask students to suggest how they think scientists investigate what happens in the human brain.**

   Students will provide a variety of answers, including watching a person's behavior, electrical shocks, various imaging techniques (such as PET scans, CT scans, or MRI), using animals (either living or dead) for research, and so forth.

ACTIVITY 2: POSITRON EMISSION TOMOGRAPHY AND BRAIN FUNCTION

The following procedures describe how to conduct the CD-ROM version of this activity, which is the preferred method of instruction. Instructions for conducting the alternative print version follow.

Content Standard A: Formulate and revise scientific explanations and models using logic and evidence.
Content Standard A: Scientists rely on technology to enhance the gathering and manipulation of data.
Content Standard C: Organisms have behavioral responses to internal changes and to external stimuli.

1. **Before starting the computer-based activity, inform students that they will be analyzing positron emission tomography (PET) images. Scientists use PET to investigate the function of the living human brain. The PET images that the students will examine use radioactive glucose to identify parts of the brain that are active. Active brain areas use more glucose than less active areas and thus more of the labeled glucose is taken up into the active areas. PET images are color-coded by a computer. The most active brain areas are shown in red. Areas in yellow are less active than the areas in red, but are more active than the areas in green. The least active areas are shown in blue or purple.**

   PET images are color-coded by computer to show activity in the brain. Students will see a color scale on the screen with the PET images for reference.

   Students may have seen color-coded computer images on television weather reports. In weather radar images, areas encountering heavy storms appear in red and yellow, and areas experiencing milder weather disturbances appear in green or blue.

2. **Divide the class into groups of three students. Arrange for each group to work at a computer to complete the CD-ROM activity, *Analyzing Brain Images*. Give each group a copy of Master 1.2, *Interpreting PET Images.***

   Load the CD-ROM on the computers. From the main menu on the CD-ROM, select *The Brain: What's Going on In There?* and then click on *Analyzing Brain Images.*

3. **Instruct students to work with their group members to analyze the PET images and to answer the questions on Master 1.2. When students reach question #5, display a transparency of Master 1.3, *PET Image Tasks,* to provide the needed information.**

4. **After the groups complete the activity and write their answers to the questions on Master 1.2, discuss the answers to the questions as a class.**

Content Standard A: Abilities Necessary to do Scientific Inquiry. Communicate and defend a scientific argument.

SAMPLE ANSWERS TO QUESTIONS ON MASTER 1.2

Question 1. When you look at the images that make up Set #1, how do the four images differ from each other?

The brain images are different sizes. The images show variation in the amount and pattern of the different colors.

Question 2. Why are four images shown in each set of PET images? Why would scientists need to examine more than one PET image taken of a subject's brain?

The four PET images in each set show the activity at different levels of the brain. If a scientist examines only a single image, he or she could miss important information.

Question 3. When comparing the images in Set #1 to the images in Sets #2, 3, 4, 5, and 6, how is the activity of the brain in each of these sets different from Set #1?

Set Number	Identify the image that shows the greatest change (a, b, c, or d)	Describe the change in brain activity
2	b	There is more red on the right side of the brain, mainly near the center in terms of front-to-back direction. There is also red on the left side, but it is not as strong as on the right side.
3	b	The main activation is in the back of the brain on both sides of the midline.
4	c	The main activation is at the front of the brain near the periphery on both sides of the midline.
5	d	The main activation is in four areas, two on each side of the brain. Two are very near the back of the brain, and two are farther forward.
6	a	The main areas of activation are a spot on the left side of the brain and a smaller spot near the front of the brain on the midline.

Question 4. The PET images shown in Set #1 show brain activity in a resting brain. The images in Sets #2-6 show activity in the brains of humans who are doing different tasks. When you look at the PET scans and the chart in question #3, what generalizations can you make about the activity of the brain when different tasks are performed?

The key points of this exercise are different brain areas are activated during different tasks, and different brain functions are localized to different brain areas.

Question 5. Compare the tasks that the subject performed during each of the PET scans (as shown on the overhead transparency) to the individual's brain activity. Use the information from the overhead and from the PET images to complete the following chart.

Set Number	Name of the brain region that is more active in the PET image	This part of the brain is involved in processing information related to
2	auditory cortex	hearing
3	primary visual cortex	vision, sight
4	frontal cortex	thinking
5	hippocampus	memory
6	motor cortex	movement

5. Instruct students to watch the CD-ROM video *How PET Works*.

From the Main Menu, select *The Brain: What's Going On In There?* Then click on *How is PET Done?*

This video expands students' understanding of PET. A scientist explains how PET imaging is done.

After students have completed the activity, you may wish to challenge them by asking them to propose an explanation for why functions are localized to specific brain areas. Why would this be beneficial from an evolutionary standpoint? (See Background Information on pages 22–23.)

Content Standard E: Understandings about Science and Technology. Science often advances with the introduction of new technology.

ALTERNATE VERSION OF ACTIVITY 2
FOR CLASSES WITHOUT ACCESS TO COMPUTERS

The following procedure provides instruction for completing Activity 2 without the use of the computer. Use this version if your students do not have access to computers equipped with a CD-ROM drive.

1. Tell students that one of the ways that scientists investigate the function of the living human brain is by using positron emission tomography (PET). The PET images that the students will examine use radioactive glucose to identify parts of the brain that are active. Active brain areas use more glucose than less active areas and thus more of the labeled glucose is taken up into the active areas. PET scans are color-coded. The scale bar shown on Master 1.1, *Positron Emission Tomography (PET) Images*, with the PET images provides a reference. The most active brain areas are shown in red. Areas in yellow are less active than the areas in red, but are more active than the areas in green. The least active areas are shown in blue or purple.

PET images are color-coded by computer to show activity in the brain. This is similar to color-coded images students may have seen on television weather reports. In weather radar images, areas encountering heavy storms appear in red and yellow, and areas experiencing milder weather disturbances appear in green or blue.

Content Standard A: Formulate and revise scientific explanations and models using logic and evidence.
Content Standard A: Scientists rely on technology to enhance the gathering and manipulation of data.
Content Standard C: Organisms have behavioral responses to internal changes and to external stimuli.

2. Divide the class into groups of three students. Give each group a copy of Master 1.1, *Positron Emission Tomography (PET) Images* and a copy of Master 1.2, *Analyzing Positron Emission Tomography (PET) Images*.

3. Help students understand how the PET images correlate to the orientation of the brain in the body.

The PET images show a cross-section of the brain. The four images in each set show four different levels of the brain. In these images, the front of the brain is toward the top (the subject's face is toward the top of the image.) Have the students examine the PET scans and identify the regions that become active in response to each stimulus.

Content Standard A: Abilities Necessary to do Scientific Inquiry. Communicate and defend a scientific argument.

Content Standard C: Cells can differentiate and complex multicellular organisms are formed as a highly organized arrangement of differentiated cells.

Remember, the names of the parts of the brain are not the important concepts that students need to learn. Rather, this is a way for students to relate what they have learned about localization of brain function to other activities and thus reinforce the concept that different brain regions control different functions.

4. **Instruct students to work with their group members to answer the questions on Master 1.2. When students reach question #5, display a transparency of Master 1.3, *PET Image Tasks*, to provide the needed information.**

5. **Discuss the answers to the questions on Master 1.2 as a class.**

   Answers for the questions on Master 1.2 are listed in the procedure for the CD-ROM version of Activity 2 on pages 31–32.

ACTIVITY 3: PARTS OF THE BRAIN

Note to teachers: This activity is intended for classes that want more information about the anatomy of the brain. Learning the names and functions of brain lobes and regions is *not* a major focus and could distract some students from the main concept that brain functions are localized to specific brain areas. Understanding the main concept is critical for understanding how neurons communicate and how drugs of abuse affect neuronal function. These topics are covered in Lessons 2 and 3.

1. **Have students continue in their groups to conduct the segment of the CD-ROM titled, *What Does This Part of the Brain Do?***

   To access this CD-ROM piece, on the main menu, select *The Brain: What's Going On In There?* Then click on *What Does This Part of the Brain Do?*

ALTERNATE VERSION OF ACTIVITY 3 FOR CLASSES WITHOUT ACCESS TO COMPUTERS

1. **Display a transparency of Master 1.4, *Major Regions of the Brain,* that shows major brain regions and Master 1.5, *Areas of the Cerebral Cortex and Their Function,* that shows the lobes of the cerebral cortex and their general functions.**

2. **Ask students to take out their completed worksheet on Master 1.2. Review the tasks that the students performed in Step 1 of Activity 1 and ask students to identify the part of the brain that was active in each case.**

   From the information in question #5 on Master 1.2, students should be able to identify the brain area involved in some of the tasks performed in Step 1, but others were not covered in that question. Also, for some of the activities listed more than one function is involved. For example, reciting the Pledge of Allegiance requires both memory and speech. Be aware that this chart is very simplified. Virtually all mental functions involve more than one brain area.

Activity	General Functions Involved	Brain Area(s) Involved*
breathing		brainstem (medulla)
heart rate		brainstem (medulla)
waving hands in the air	movement	cerebrum—frontal lobe (motor cortex) cerebellum
hopping up and down on the right foot	movement	cerebrum—frontal lobe (motor cortex) cerebellum
walking around the classroom	movement	cerebrum—frontal lobe (motor cortex) cerebellum
looking out the window	vision	cerebrum—occipital lobe (primary visual cortex)
reciting the Pledge of Allegiance	speech/memory	cerebrum—frontal lobe hippocampus
doing an algebra problem	thinking	cerebrum—frontal lobe
remembering directions to get from the classroom to the school cafeteria	memory	hippocampus
reading a sentence	speech	cerebrum—parietal lobe and frontal lobe

*This is very simplified. Most mental functions involve more than one area of the brain.

ACTIVITY 4: WHO WAS PHINEAS GAGE?

1. Give each student a copy of Master 1.6, *What Happened to Phineas Gage?* Instruct students to read the story and answer the questions.

Phineas Gage was injured in an accident in the 1800s. His recovery from the injury and the resulting change in personality and behavior gave scientists new insight into brain function.[10, 11]

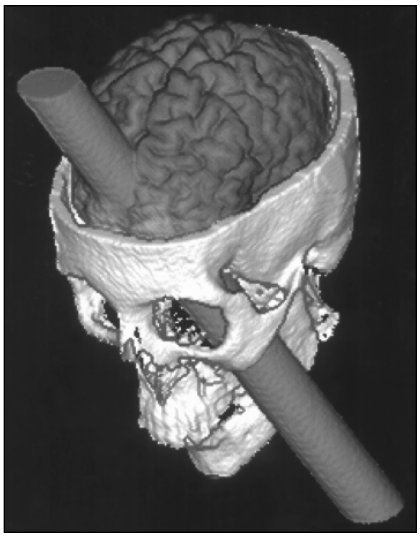


Figure 1.8: Computer reconstruction of the skull of Phineas Gage illustrating the projection of the tamping rod through the brain. Reprinted with permission from Damasio H, Grabowski T, Frank R, Galaburda AM, Damasio AR: The return of Phineas Gage: Clues about the brain from a famous patient. *Science* 264: 1102-1105. Department of Neurology and Image Analysis Facility, University of Iowa. Copyrighted 1994 *American Association for the Advancement of Science.*

Content Standard A: Scientists rely on technology to enhance the gathering and manipulation of data.
Content Standard C: Multicellular animals have nervous systems that generate behavior.
Content Standard G: Usually, changes in scientific knowledge occur as small modifications in extant knowledge.

SAMPLE ANSWERS TO QUESTIONS ON MASTER 1.6

Question 1. How did Phineas Gage change after the accident?

After the accident, Gage's personality changed. He was no longer the likeable and responsible person he was prior to the accident. Instead he was irresponsible and used profanity.

Question 2. How did Phineas Gage's accident change scientists' understanding of the brain?

Scientists learned that the brain does more than control language and movement. It also controls emotions and social behaviors. Equally important, scientists learned that the brain processes information for specific functions in specific brain areas.

Content Standard C: Multicellular organisms have nervous systems that generate behavior.
Content Standard F: An individual's mood and behavior may be modified by substances.

ACTIVITY 5: WHERE DO DRUGS ACT?

1. **Now that students understand that different areas in the brain process specific types of stimuli, ask students to consider things that make them feel good, or are pleasurable. How might doing something pleasurable change brain activity?**

   If students understand, from Activity 2 of this lesson, that brain functions are localized to specific brain areas, they should suspect that things that make them feel pleasure will stimulate a specific brain region.

2. **Display the transparency of Master 1.7, *The Reward System*. Tell students that part of the brain produces and regulates feelings of pleasure, which scientists call reward. This brain region is called the reward system. The parts of the brain that make up the reward system are the ventral tegmental area (VTA), nucleus accumbens, and part of the frontal region of the cerebral cortex. This brain region responds to life-sustaining activities such as eating and drinking, as well as species-sustaining sexual activity.**

If students understand that PET images reveal changes in brain activity and that drugs activate the reward system in the brain, students should predict that the reward system (the VTA and nucleus accumbens) should be more active after an individual takes drugs. These brain areas should appear red or yellow in PET scans taken after drug use whereas they would be purple or blue in PET images taken before drug use.

3. **Introduce students to the idea that drugs of abuse activate the brain's reward system, or pleasure circuit. Drugs alter the way in which the reward system functions. Drugs also act on other regions of the brain, but their action in the reward system makes the drug abuser feel pleasure and want to continue taking drugs.**

   Students will learn more about how drugs exert these effects in the remaining lessons in this curriculum supplement.

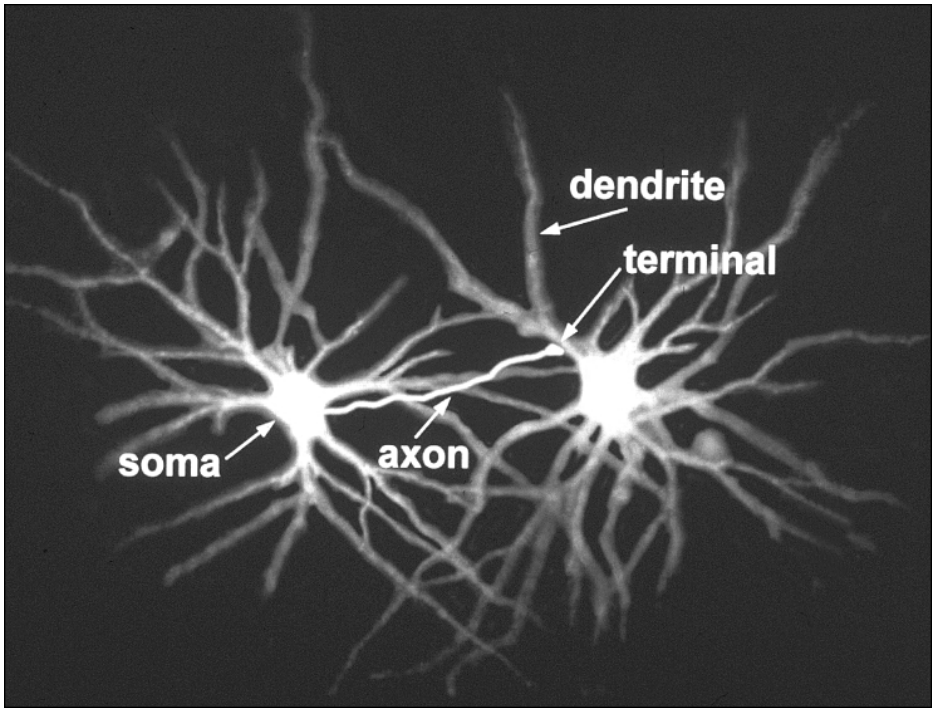
4. **Ask students to hypothesize how PET images of a person's brain would change after taking drugs of abuse.**

   Currently, PET technology is not sensitive enough to allow scientists to visualize this reward system activation. The VTA and nucleus accumbens are too small for PET images to detect significant activity changes. Scientists have relied on other technologies to learn that drugs of abuse do activate these brain regions.

Some students may hypothesize that PET images of the brain after drug abuse would also show changes in other regions of the brain. This is correct. Drugs do affect other regions of the brain, but it is the reward system that gives the pleasurable feelings associated with drug use. More information on the more widespread effects of drugs on the brain is presented in Lesson 4.

Lesson 2
Explore/ Explain

Neurons, Brain Chemistry, and Neurotransmission



Source: National Institute on Drug Abuse (1996) The Brain & the Actions of Cocaine, Opiates, and Marijuana. Slide Teaching Packet for Scientists.

At a Glance

Overview

Students learn that the neuron is the functional unit of the brain. To learn how neurons convey information, students analyze a sequence of illustrations and watch an animation. They see that neurons communicate using electrical signals and chemical messengers called neurotransmitters that either stimulate or inhibit the activity of a responding neuron. Students then use the information they have gained to deduce how one neuron influences the action of another.

Major Concept

Neurons convey information using electrical and chemical signals.

Objectives

By the end of these activities, the students will

- understand the hierarchical organization of the brain, neuron, and synapse;
- understand the sequence of events involved in communication at the synapse; and
- understand that synaptic transmission involves neurotransmitters that may be either excitatory or inhibitory.

Basic Science–Health Connection

Communication between neurons is the foundation for brain function. Understanding how neurotransmission occurs is crucial to understanding how the brain processes and integrates information. Interruption of neural communication causes changes in cognitive processes and behavior.

Background Information

The Brain Is Made Up of Nerve Cells and Glial Cells

The brain of an adult human weighs about three pounds and contains billions of cells. The two distinct classes of cells in the nervous system are **neurons** (nerve cells) and **glia** (glial cells).

The basic signaling unit of the nervous system is the neuron. The brain contains billions of neurons; the best estimates are that the adult human brain contains 10^{11} neurons. The interactions between neurons enable people to think, move, maintain homeostasis, and feel emotions. A neuron is a specialized cell that can produce different actions because of its precise connections with other neurons, sensory receptors, and muscle cells. A typical neuron has four morphologically defined regions: the cell body, dendrites, axons, and presynaptic terminals.[1, 2, 3]

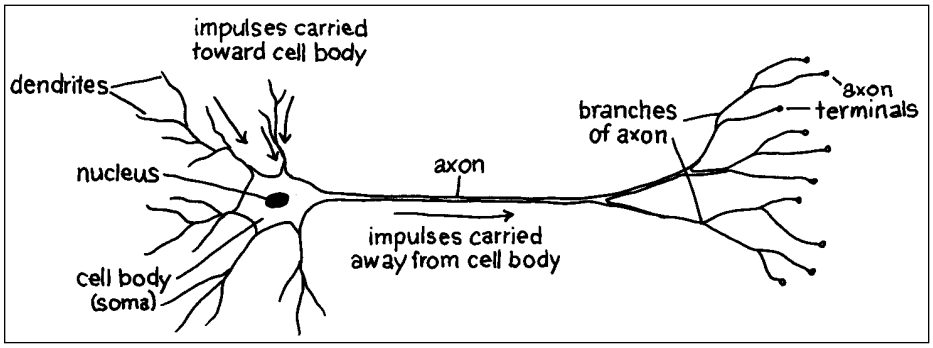


Figure 2.1: The neuron, or nerve cell, is the functional unit of the nervous system. The neuron has processes called dendrites that receive signals and an axon that transmits signals to another neuron.

The **cell body**, also called the **soma**, is the metabolic center of the neuron. The nucleus is located in the cell body and most of the cell's protein synthesis occurs in the cell body.

A neuron usually has multiple processes, or fibers, called **dendrites** that extend from the cell body. These processes usually branch out somewhat like tree branches and serve as the main apparatus for receiving input into the neuron from other nerve cells.

The cell body also gives rise to the **axon**. Axons can be very long processes; in some cases, they may be up to one meter in length. The axon is the part of the neuron that is specialized to carry messages away from the cell body and to relay messages to other cells. Some large axons are surrounded by a fatty insulating material called myelin, which enables the electrical signals to travel down the axon at higher speeds.

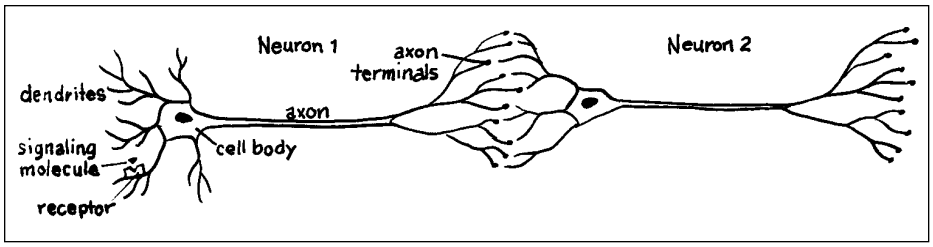


Figure 2.2: Neurons transmit information to other neurons. Information passes from the axon of the presynaptic neuron to the dendrites of the postsynaptic neuron.

Near its end, the axon divides into many fine branches that have specialized swellings called presynaptic terminals. These presynaptic terminals end in close proximity to the dendrites of another neuron. The dendrite of one neuron receives the message sent from the presynaptic terminal of another neuron.

The site where a presynaptic terminal ends in close proximity to a receiving dendrite is called the **synapse**. The cell that sends out information is called the **presynaptic** neuron, and the cell that receives the information is called the **postsynaptic** neuron. It is important to note that the synapse is *not* a physical connection between the two neurons; there is no cytoplasmic continuity between the two neurons. The intercellular space between the presynaptic and postsynaptic neurons is called the **synaptic space** or **synaptic cleft**. An average neuron forms approximately 1,000 synapses with other neurons. It has been estimated that there are more synapses in the human brain than there are stars in our galaxy. Furthermore, synaptic connections are not static. Neurons form new synapses or strengthen synaptic connections in response to life experiences. This dynamic change in neuronal connections is the basis of learning.

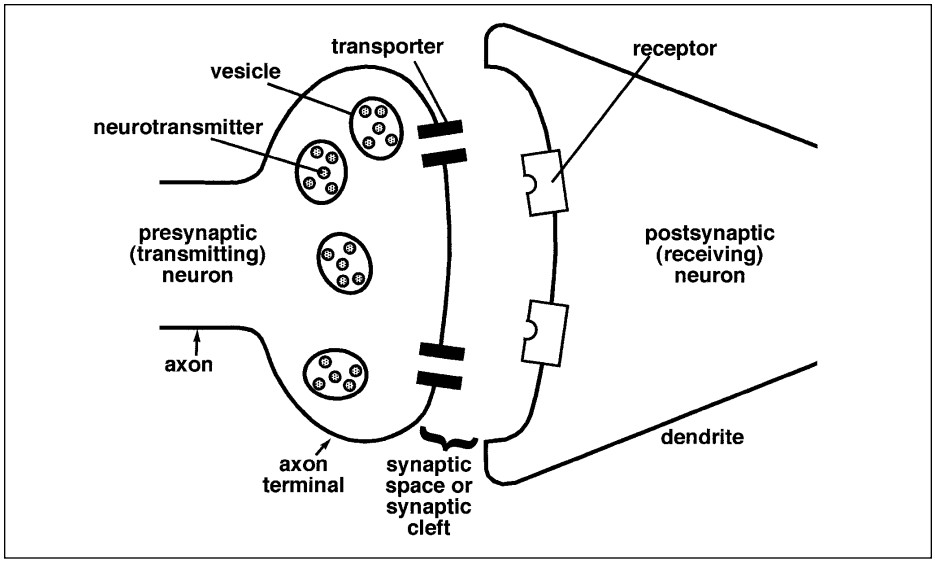


Figure 2.3: The synapse is the site where chemical signals pass between neurons. Neurotransmitter is released from the presynaptic neuron terminals into the extracellular space, the synaptic cleft or synaptic space. The released neurotransmitter molecules can then bind to specific receptors on the postsynaptic neuron membrane to elicit a response.

The brain contains another class of cells called glia. There are as many as ten to fifty times more glial cells than neurons in the central nervous system. Glial cells are categorized as microglia or macroglia. Microglia are phagocytic cells that are mobilized after injury, infection or disease. They are derived from macrophages and are unrelated to other cell types in the nervous system. The three types of macroglia are oligodendrocytes, astrocytes, and Schwann cells. The oligodendrocytes and Schwann cells form the myelin sheaths that insulate axons and enhance conduction of electrical signals along the axons.

Scientists know less about the functions of glial cells than they do about the functions of neurons. Glial cells fulfill a variety of functions including:

- Glial cells function as supporting elements in the nervous system to provide structure and to separate and insulate groups of neurons.
- Oligodendrocytes in the central nervous system and Schwann cells in the peripheral nervous system form myelin, the sheath that wraps around certain axons.
- Some glial cells are scavengers that remove debris after injury or neuronal death.
- Some glial cells buffer the potassium ion (K^+) concentration in the extracellular space, and some glial cells take up and remove chemical neurotransmitters from the extracellular space after synaptic transmission.
- Some glial cells guide the migration of neurons and direct the outgrowth of axons during development.
- Some glial cells induce formation of impermeable tight junctions in endothelial cells that line the capillaries and venules of the brain to form the blood-brain barrier.
- Glial cells may serve nutritive functions for nerve cells.[3]

The Blood-Brain Barrier

The blood-brain barrier protects the neurons and glial cells in the brain from substances that could harm the cells. Endothelial cells that form the capillaries and venules make this barrier forming impermeable tight junctions. Astrocytes surround the endothelial cells and induce them to form these junctions. Unlike blood vessels in other parts of the body that are relatively leaky to a variety of molecules, the blood-brain barrier keeps many substances, including toxins, away from the neurons and glia.

Blood gases, such as oxygen, and small nutritional molecules do get into the brain.[3,4] In addition, drugs of abuse can penetrate the blood-brain barrier. Because most drugs are fat-soluble they can pass through the barrier to reach the brain cells.

The blood-brain barrier is important for maintaining the environment of neurons in the brain, but it also presents problems for scientists who are investigating new treatments for brain disorders. If a medication cannot get into the brain to the neurons, it cannot be effective. Researchers attempt to circumvent the problems in different ways. Some techniques attach potential therapeutic agents to molecules that pass through the blood-brain barrier while others attempt to open the blood-brain barrier so that the therapeutic compounds can reach the brain's neurons.[5]

Neurons Use Electrical and Chemical Signals to Transmit Information
The billions of neurons that make up the brain coordinate thought, behavior, homeostasis, and more. How do all these neurons pass and receive information?

Neurons convey information by transmitting messages to other neurons or other types of cells, such as muscles. The following discussion focuses on how one neuron communicates with another neuron. Neurons employ electrical signals to relay information from one part of the neuron to another. The neuron converts the electrical signal to a chemical signal in order to pass the information to another neuron. The target neuron then converts the message back to an electrical impulse to continue the process.

Within a single neuron, information is conducted via electrical signaling. When a neuron is stimulated, an electrical impulse, called an **action potential**, moves along the neuron axon or dendrite.[6] Action potentials enable signals to travel very rapidly along the neuron fiber. Action potentials last less than 2 milliseconds (1 millisecond = 0.001 second) and the fastest action potentials can travel the length of a football field in one second. Action potentials result from the flow of ions across the neuronal cell membrane. Neurons, like all cells, maintain a balance of ions inside the cell that differs from the balance outside of the cell. This uneven distribution of ions creates an electrical potential across the cell membrane. This is called the **resting membrane potential**. In humans, the resting membrane potential ranges from -40 millivolts (mV) to -80 mV with –65 mV as an average resting membrane potential. The resting membrane potential is, by convention, assigned a negative number because the inside of the neuron is more negatively charged than the outside environment of the neuron. This negative charge results from the unequal distribution of sodium ions (Na^+), potassium ions (K^+), chloride ions (Cl^-), and other organic ions. The resting membrane potential is maintained by an energy-dependent Na^+-K^+ pump that keeps Na^+ levels low inside the neuron and K^+ levels high inside the neuron. In addition, the neuronal membrane is more permeable to K^+ than it is to Na^+, so that K^+ tends to leak out of the cell more readily than Na^+ diffuses into the cell.

A stimulus occurring at the end of a nerve fiber starts an electrical change that travels like a wave over the length of the neuron. This electrical change, the action potential, results from a change in the permeability of the neuronal membrane. Sodium ions rush into the neuron, and the inside of the cell becomes more positive. The Na^+-K^+ pump then restores the balance of sodium and potassium to resting levels. However, the influx of Na^+ ions in one area of the neuron fiber starts a similar change in the adjoining segment and the impulse moves from one end of the neuronal fiber to the other. Action potentials are an **all-or-none phenomenon**. Regardless of the stimuli, the amplitude and duration of an action potential are the same. The action potential either occurs or it doesn't. The response of the neuron to an action potential depends on how many action potentials it transmits and the time interval between them.

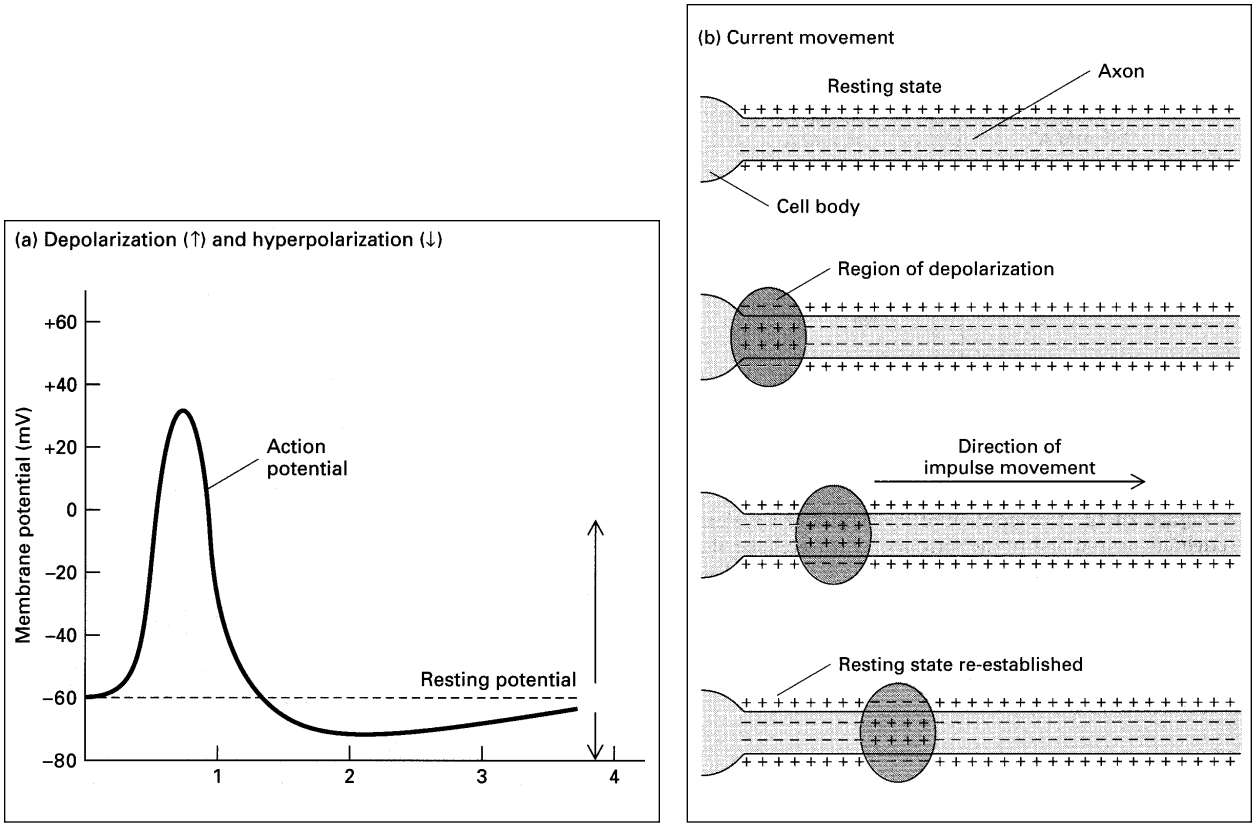


Figure 2.4: (a) Recording of an action potential in an axon following stimulation at time 0 due to changes in the permeability of the cell membrane to sodium and potassium ions. (b) The cell membrane of a resting neuron is more negative on the inside of the cell than on the outside. When the neuron is stimulated, the permeability of the membrane changes allowing Na^{+} to rush into the cell. This causes the inside of the cell to become more positive. This local change starts a similar change in the adjoining segment of the neuron's membrane. In this manner, the electrical impulse moves along the neuron. From: Molecular Cell Biology by Lodish et al. 1986, 1990 by Scientific American Books, Inc. Used with permission by W.H. Freeman and Company.

Electrical signals carry information *within* a single neuron. Communication *between* neurons (with a few exceptions in mammals) is a chemical process. When the neuron is stimulated, the electrical signal (action potential) travels down the axon to the axon terminals. When the electrical signal reaches the end of the axon, it triggers a series of chemical changes in the neuron. Calcium ions (Ca^{++}) flow into the neuron. The increased Ca^{++} in the axon terminal then initiates the release of neurotransmitter. A **neurotransmitter** is a molecule that is released from a neuron to relay information to another cell. Neurotransmitter molecules are stored in membranous sacs called **vesicles** in the axon terminal. Each vesicle contains thousands of molecules of a neurotransmitter. For neurons to release their neurotransmitter, the vesicles fuse with the neuronal membrane and then release their contents, the neurotransmitter, via exocytosis. The neurotransmitter molecules are released into the synaptic space and diffuse across the synaptic space to the postsynaptic neuron. A neurotransmitter molecule can then bind to a special receptor on the membrane of the postsynaptic neuron. **Receptors** are membrane proteins that

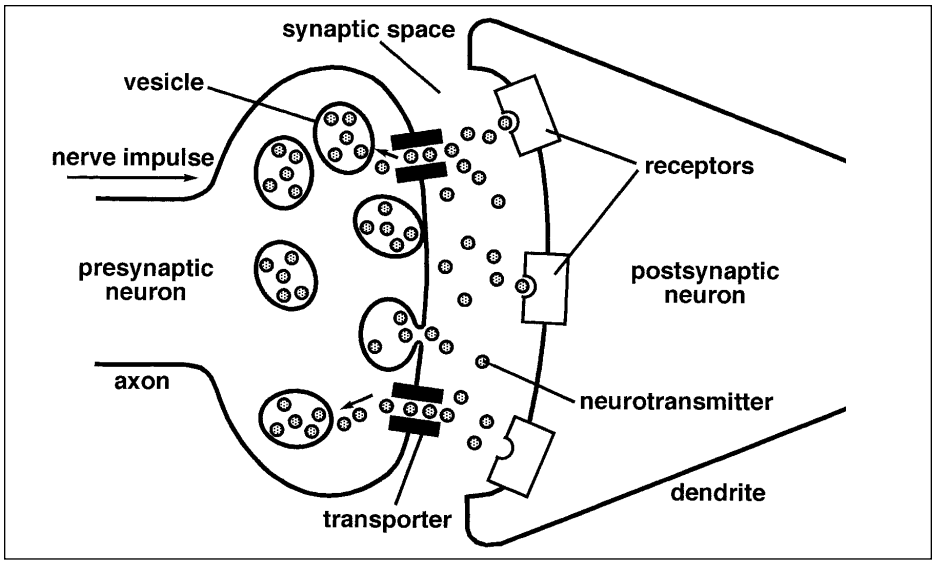


Figure 2.5: Schematic diagram of a synapse. In response to an electrical impulse, neurotransmitter molecules released from the presynaptic axon terminal bind to the specific receptors for that neurotransmitter on the postsynaptic neuron. After binding to the receptor, the neurotransmitter molecules either may be taken back up into the presynaptic neuron through the transporter molecules for repackaging into vesicles or may be degraded by enzymes present in the synaptic cleft.

are able to bind a specific chemical substance, such as a neurotransmitter. For example, the dopamine receptor binds the neurotransmitter dopamine, but does not bind other neurotransmitters such as serotonin. The interaction of a receptor and neurotransmitter can be thought of as a lock-and-key for regulating neuronal function. Just as a key fits only a specific lock, a neurotransmitter binds only to a specific receptor. The chemical binding of neurotransmitter and receptor initiates changes in the postsynaptic neuron that may generate an action potential in the postsynaptic neuron. If it does trigger an action potential, the communication process continues. After a neurotransmitter molecule binds to its receptor on the postsynaptic neuron, it comes off of (releases from) the receptor and diffuses back into the synaptic space. The released neurotransmitter, as well as any neurotransmitter that did not bind to a receptor, is either degraded by enzymes in the synaptic cleft or it may be

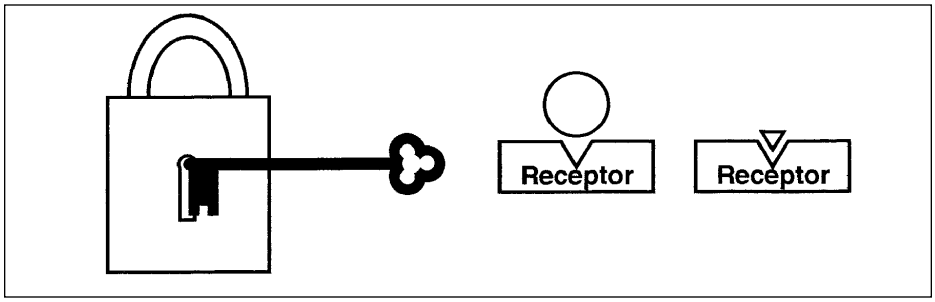


Figure 2.6: Like a lock that will open only if the right key is used, a receptor will bind only a molecule that has the right chemical shape. Molecules that do not have the right “fit” will not bind to the receptor and will not cause a response.

taken back up into the presynaptic axon terminal by active transport through a **transporter** or **reuptake pump**. Once the neurotransmitter is back inside the axon terminal, it is either destroyed or repackaged into new vesicles that may be released the next time the neuron is stimulated. Different neurotransmitters are inactivated in different ways.

Neurotransmitters Can Be Excitatory or Inhibitory

Different neurotransmitters fulfill different functions in the brain. Some neurotransmitters act to stimulate the firing of a postsynaptic neuron. Neurotransmitters that act this way are called **excitatory** neurotransmitters because they lead to changes that generate an action potential in the responding neuron.[1, 7] Other neurotransmitters, called **inhibitory** neurotransmitters, tend to block the changes that cause an action potential to be generated in the responding cell. Table 2.1 lists some of the major neurotransmitters used in the body and their major functions. Each neuron generally synthesizes and releases a single type of neurotransmitter. (Neurons may contain other signaling chemicals, such as neurohormones, in addition to their neurotransmitter.)

The postsynaptic neuron often receives both excitatory and inhibitory messages. The response of the postsynaptic cell depends on which message is stronger. Keep in mind that a single neurotransmitter molecule cannot cause an action potential in the responding neuron. An action potential occurs when many neurotransmitter molecules bind to and activate their receptors. Each interaction contributes to the membrane permeability changes that generate the resultant action potential.

Table 2.1: Major Neurotransmitters in the Body [1, 7, 8]

Neurotransmitter	Role in the body
Acetylcholine	A neurotransmitter used by spinal cord neurons to control muscles and by many neurons in the brain to regulate memory. In most instances, acetylcholine is excitatory.
Dopamine	The neurotransmitter that produces feelings of pleasure when released by the brain reward system. Dopamine has multiple functions depending on where in the brain it acts. It is usually inhibitory.
GABA (gamma-aminobutyric acid)	The major inhibitory neurotransmitter in the brain.
Glutamate	The most common excitatory neurotransmitter in the brain.
Glycine	A neurotransmitter used mainly by neurons in the spinal cord. It probably always acts as an inhibitory neurotransmitter.
Norepinephrine	Norepinephrine acts as a neurotransmitter and a hormone. In the peripheral nervous system, it is part of the fight-or-flight response. In the brain, it acts as a neurotransmitter regulating normal brain processes. Norepinephrine is usually excitatory, but is inhibitory in a few brain areas.
Serotonin	A neurotransmitter involved in many functions including mood, appetite, and sensory perception. In the spinal cord, serotonin is inhibitory in pain pathways.

In Advance

CD-ROM Activities	
Activity Number	**CD-ROM**
Activity 1	no
Activity 2	yes
Activity 3	yes
Activity 4	optional

Photocopies		
For the class	**For each group of 3 students**	**For each student**
1 transparency of Master 2.1, *Anatomy of a Neuron* 1 transparency of Master 2.2, *Neurons Interact with Other Neurons Through Synapses* 1 transparency of Master 2.4, *Neurons Communicate by Neurotransmission* 1 transparency of Master 2.6, *Recording the Activity of a Neuron* 1 transparency of Master 1.7, *The Reward System* (from Lesson 1)	1 copy of Master 2.3, *How Do Neurons Communicate?*	1 copy of Master 2.5, *Neurotransmission* 1 copy of Master 2.7, *Neurotransmitter Actions* 1 copy of Master 2.8, *Neurons in Series*

Materials	
Activity 1	overhead projector
Activity 2	overhead projector (if using the version without the CD-ROM)
Activity 3	none
Activity 4	none

Preparation

Arrange for students to have access to computers for Activities 2, 3, and 4.

Procedure

ACTIVITY 1: ANATOMY OF A NEURON

1. Remind students of the PET scans they examined in Activity 2 of Lesson 1. Ask students to think about the areas shown in red or yellow on a PET scan in response to a stimulus. What specifically composes those areas?

Students may respond correctly that the areas shown in red or yellow on the PET images are made up of *brain cells* that are more active than the cells

Content Standard C: Cells have particular structures that underlie their functions.
Content Standard C: Cells can differentiate, and complex multicellular organisms are formed as a highly organized arrangement of differentiated cells.

in other regions. Students may even be able to say that the areas represent *neurons* in the brain that are activated. The goal is to reinforce that the brain is made up of millions of individual cells. The areas shown in the PET images are not just large amorphous masses.

2. **Display a transparency of Master 2.1, *Anatomy of a Neuron*. Explain to students that the basic functional unit of the brain and nervous system is the neuron. Point out the parts of a neuron and discuss their functions.**

   The cell body of the neuron is the metabolic center of the neuron. The nucleus is in the cell body. Most of the proteins are made in the cell body.

   Neurons have specialized cell processes, or fibers, that extend from the cell body. The dendrites are branched fibrous processes specialized to receive input and carry information *toward* the cell body.

   The axon is usually larger in diameter than the dendrites and is specialized to carry information *away* from the cell body. An axon may be very long. Some axons are over one meter in length.

3. **Display the top half of a transparency of Master 2.2, *Neurons Interact With Other Neurons Through Synapses*. Point out that the axon terminals of one neuron end near the dendrites of another neuron.**

4. **Reveal the lower portion of Master 2.2 showing the synapse. Inform students that the connection between the two neurons is called a *synapse*. Explain the terms presynaptic and postsynaptic.**

   The *presynaptic* neuron is the neuron whose axon forms a synapse with the dendrite of another neuron. The presynaptic neuron sends out information.

   The *postsynaptic* neuron is the neuron whose dendrite forms a synapse with the axon of the presynaptic neuron. The postsynaptic neuron receives information.

   Note: Help students understand that there is no *physical* connection between the two neurons.

5. **When students understand that the brain is composed of neurons and neurons interact with other neurons, display the transparency of Master 1.7, *The Reward System* (used in Lesson 1), again and discuss the reward pathway in terms of the neurons.**

   The cell bodies of the neurons that drugs affect are located in the ventral tegmental area (VTA). Those cells extend their axons to nerve cells in an area of the brain called the nucleus accumbens. Some nerve fibers extend to part of the frontal region of the cerebral cortex.

ACTIVITY 2: HOW DO NEURONS COMMUNICATE?

Before doing this activity, students need to have a good understanding of the difference between an axon and a dendrite and the direction of information flow along these neuronal fibers. Remember that dendrites carry information toward the cell body and axons carry information away from the cell body. Also, students need to understand the terms presynaptic and postsynaptic.

Content Standard A: Formulate and revise scientific explanations and models using logic and evidence.
Content Standard A: Communicate and defend a scientific argument.
Content Standard C: Cell functions are regulated.

In this activity, students will use the CD-ROM to enhance what they deduce from a print-based activity. If computers are not available for viewing the CD-ROM, a print modification of the activity is also provided. The procedures for each version of the activity are the same except for Step #4. When you reach that point in the activity, select the appropriate step.

1. **Ask students to consider what purpose synapses serve.**

   Some students are likely to respond correctly that synapses serve to connect neurons (synapses do not connect neurons physically, but they do connect them functionally). This enables neurons to communicate by passing signals between them.

2. **Remind students that the brain is an organ that regulates body functions, behaviors, and emotions. Neurons are the cells that fulfill these functions. How do neurons do this?**

   Neurons control these functions by passing signals across the synapse from one neuron to the next that dictate whether the receiving neuron is activated.

3. **Divide the class into groups of three students. Give each group a copy of Master 2.3, *How Do Neurons Communicate?* Ask students to look at and discuss the diagrams and, as a group, write a summary of how they believe the neurons are interacting at each step.**

   At this point, students will not know the correct terminology for the structures and molecules involved in neurotransmission. Encourage students to use whatever terms they wish to describe what is represented in the diagrams. The main point of this activity is for students to begin to understand that specific events happen both within a neuron and between neurons during neurotransmission.

SAMPLE ANSWERS TO MASTER 2.3

Students are likely to use a variety of terms in their responses. Although at this point the use of correct vocabulary is not the critical issue, some students will use the terms axon, dendrite, presynaptic, and postsynaptic that they learned in Activity 1.

Diagram #1 The presynaptic neuron ending has large circles in it. The large circles have smaller circles inside. There are two sets of bars that cross the end (membrane) of the presynaptic neuron. The postsynaptic neuron has two rectangular-shaped boxes on the end (membrane) of the neuron.

Diagram #2 Nothing has changed except that there is a lightning bolt (electrical signal) and an arrow indicating that the lightning bolt is moving toward the end of the presynaptic neuron.

Diagram #3 One of the larger circles is now in contact with the end of the presynaptic neuron. Another circle is now releasing the small circles into the space between the neurons.

Diagram #4 The small circles are in the space between the neurons and one small circle is now attached to the box-shaped figures on the end of the postsynaptic neuron.

Diagram #5 The lightning bolt symbol (electrical signal) is at the postsynaptic neuron now. The arrow indicates that it is moving away from the neuron ending.

Diagram #6 The small circles are no longer attached to the box-shaped figures on the postsynaptic neurons. The arrows seem to indicate that the small circles are now moving back into the presynaptic neuron and going back into the larger circles.

4. Have the students watch the neurotransmission animation on the CD-ROM. They may wish to view the animation several times.

Students can access the animation by clicking on *Neurons, Brain Chemistry, and Neurotransmission* on the main menu and then clicking on the button, *How Neurotransmission Works.*

Now that students have explored neurotransmission by completing Master 2.3, the animation will help them incorporate the proper terminology and clarify any misunderstandings.

If computers are not available to view the CD-ROM animation of neurotransmission, display a copy of Master 2.4, *Neurons Communicate by Neurotransmission.* Read through the material with the students.

Students should **not** copy the information on Master 2.4. The goal is for students to listen to the reading to help them learn the proper terminology and clarify their understanding of neurotransmission.

5. After the students have been introduced to the proper terminology by the animation or the reading, give each student a copy of Master 2.5, *Neurotransmission.* Ask them to revise their summary of neurotransmission using the appropriate terminology. Encourage students to discuss their answers with the other members of their group.

Students may wish to watch the animation or review the reading again while doing this step. The goal is not to have students copy the explanation from the CD-ROM, but to revise their understanding of neurotransmission, incorporate the appropriate terminology, and correct any misconceptions they had from Master 2.3.

SAMPLE ANSWERS TO MASTER 2.5

Diagram #1 This diagram shows the component parts of the neurotransmission process between electrical impulses.

Diagram #2 An electrical impulse travels down the axon toward the presynaptic nerve terminals.

Diagram #3 The vesicles containing neurotransmitter move toward the neuron cell membrane at the end of the axon. The vesicles fuse to the membrane and then release their contents (neurotransmitter molecules) into the synaptic cleft.

Diagram #4 The neurotransmitter is in the synaptic cleft and binds to the receptor on the postsynaptic neuron's membrane.

Diagram #5 Neurotransmitter molecules are still bound to the receptors and an electrical signal passes along the postsynaptic neuron away from the neuron's ending.

Diagram #6 Neurotransmitter molecules are released from the receptors. Neurotransmitter molecules are taken back up into the presynaptic neuron through the transporter. Once inside the presynaptic neuron terminal, the neurotransmitter molecules are repackaged into vesicles.

6. **Once the groups have finished revising their summaries, hold a class discussion and put together a summary of how neurotransmission occurs. Inform students that the diagrams and CD-ROM animation are simplified models of neurotransmission. Many hundreds or thousands of receptors that can bind neurotransmitter are present in the dendrites of a postsynaptic neuron.**

7. **Remind students of the reward system. The neurons that make up the reward system use a neurotransmitter called *dopamine*. Dopamine neurotransmission occurs as the students learned in Masters 2.3, 2.4 (print alternative), 2.5, and the CD-ROM animation.**

ACTIVITY 3: DO ALL NEUROTRANSMITTERS HAVE THE SAME EFFECT?

Now that students understand that neurotransmitters are the chemical messengers involved in communication between neurons, students will learn that different neurotransmitters can affect neurotransmission differently.

Content Standard C: Cell functions are regulated.

1. **Show an overhead transparency of Master 2.6, *Recording the Activity of a Neuron*. Explain that scientists study the activity of neurons by recording the electrical impulses that neurons generate when they are activated, or fire. These electrical impulses are called action potentials.**

   Master 2.6 shows a diagram of a microelectrode recording the electrical activity of a neuron in the brain. The action potentials are amplified, and then analyzed by a computer that counts the number of spikes that occur during a period of time. The action potentials appear as vertical lines, or spikes, on the oscilloscope. If the recording were slowed down,

the action potentials would appear similar to that shown in Figure 2.4 (see Background Information section). A signal is also sent to an audio amplifier that produces a click sound each time an action potential is generated in the neuron. The more frequently the spikes appear on the screen with accompanying audible clicks, the more frequently the neuron is firing.

2. **Divide the class into groups of three. Give each group a copy of Master 2.7, *Neurotransmitter Actions*. Tell students that they will analyze the effects of different neurotransmitters on the activity of a neuron. Have the groups answer the questions that follow the data analysis.**

   After the groups have completed the questions, discuss their answers to make sure that students understand that different neurotransmitters have different effects on neurons.

SAMPLE ANSWERS TO MASTER 2.7

Question 1. Why is saline applied to the resting neuron?

The resting neuron is the control for the experiment. If a scientist wants to determine what effect applying a neurotransmitter has on a neuron, he or she must have a control. The neurotransmitter applied to the other neurons would be in a saline solution, so applying saline to the resting neuron provides information about how a neuron responds to the solvent solution. If the control neuron does not respond in the same way as the experimental neurons, this indicates that the neurotransmitter applied to those neurons is the cause for the response, not the saline itself, or the act of applying a solution to the neuron.

Question 2. When the neurotransmitter glutamate is applied to the neuron, how does its activity change?

Glutamate stimulates the neuron and causes it to generate more electrical impulses.

Question 3. How does the application of the two neurotransmitters, glutamate and GABA, change the activity of the neuron?

The application of glutamate and GABA to the neuron inhibits the neuron so that it generates few electrical impulses.

Question 4. Predict how the activity of the neuron would change if only GABA was applied to the neuron.

If GABA can inhibit a neuron even when glutamate is added, GABA by itself should inhibit the neuron's activity.

Question 5. Do all neurotransmitters affect a neuron in the same way?

No, the neurotransmitters glutamate and GABA have opposite effects on the neuron's activity.

Question 6. How would the application of glutamate to a neuron change the amount of neurotransmitter that is released from that neuron? How would the application of GABA to a neuron change the amount of neurotransmitter that is released from that neuron?

If glutamate is applied to a neuron, it causes the neuron to generate more electrical impulses. This would increase the amount of neurotransmitter that the neuron releases from its axon terminals.

If GABA is applied to a neuron, it reduces the number of electrical impulses generated by that neuron. The decreased activity in the neuron would decrease the amount of neurotransmitter that the neuron releases from its axon terminals.

3. Students can continue this activity using the CD-ROM simulation of applying neurotransmitters to a neuron.

From the main menu on the CD-ROM, click on *Neurons, Brain Chemistry, and Neurotransmission* and then select *Neurotransmitter Actions.*

ACTIVITY 4: ONE NEURON SIGNALS ANOTHER

This activity is the most challenging one in the lesson. It requires students to integrate what they learned in Activities 2 and 3. If students successfully complete this activity, they will have a good understanding of how neurons communicate.

Content Standard A: Formulate and revise scientific explanations and models using logic and evidence.
Content Standard A: Communicate and defend a scientific argument.
Content Standard C: Cell functions are regulated.

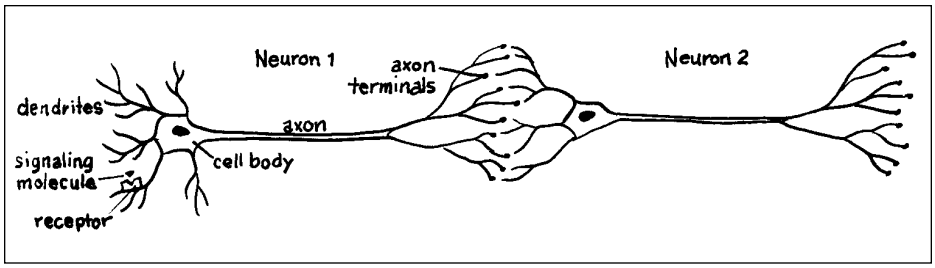
1. **Copy the chart from Master 2.8, *Neurons in Series*, onto the board.**

2. **Now that students understand that neurotransmitters can either stimulate or inhibit the generation of action potentials in a neuron, they will continue to examine how one neuron signals another in a series. Give each student a copy of Master 2.8. As a class, work through Case A on the master to determine how the stimulatory and inhibitory neurotransmitter effects alter dopamine release from the last neuron in the series. Fill in the answers on the chart.**

   You may wish to use an ↑ or ↓ arrow to indicate an increase or decrease in the activity of the neuron or the amount of neurotransmitter released from a neuron. Students may find it helpful to refer to their work on Master 2.5.

Case A

The signal molecule that affects Neuron #1 in this case is inhibitory. It reduces the chances that Neuron #1 will fire. Thus, it acts to decrease the activity of Neuron #1. If Neuron #1 is less active, it releases less neurotransmitter. Neuron #1 produces glutamate, an excitatory neurotransmitter. The decreased level of neurotransmitter release from Neuron #1 leads to a decreased level of activity of Neuron #2. If Neuron #2 is less active, it will release less dopamine.



Case	Does the signal molecule excite or inhibit Neuron #1?	Does the activity of Neuron #1 increase or decrease?	Does the amount of neurotransmitter released from Neuron #1 increase or decrease?	What is the name of the neurotransmitter released from Neuron #1?	Is the neurotransmitter released from Neuron #1 excitatory or inhibitory?	Does the activity of Neuron #2 increase or decrease?	Does the amount of dopamine released from Neuron #2 increase or decrease?
A	inhibit	↓	↓	glutamate	excitatory	↓	↓

Tip from the field test: Students sometimes became confused by the multiple neurotransmitters involved in each case. A common misconception was the same neurotransmitter that acted to stimulate or inhibit a neuron then passed through the neuron and was released from the axon terminals at the other end. Remind students what they learned in Activity 2 regarding the fate of a neurotransmitter after it binds to, and then comes off of, its receptor. The released neurotransmitter is either degraded or taken back up into the axon terminal that released it.

For the purpose of this activity, the signal molecule is a neurotransmitter. In Lesson 3, students will learn that drugs of abuse can also act in a similar way to alter neurotransmission.

3. **After the students have worked through the first example as a class, ask them to work in their small groups to complete the chart for Cases B-D. Students will determine how inhibitory and excitatory inputs contribute to the activity of a neuron that is part of a series.**

As a student group finishes one of the cases (B-D), have a group member come to the board and fill in the blanks for that problem. When all of the groups are finished, ask the group that completed each line on the board to explain its answers to the rest of the class. If another group disagrees with the answer, have that group explain its reasoning. As a class, resolve the discrepancies and reach a consensus explanation. In this way, students practice critical thinking and communication skills.

SAMPLE ANSWERS FOR MASTER 2.8

Case A. The signaling molecule is inhibitory. Neuron #1 releases glutamate as its neurotransmitter. Neuron #2 releases dopamine as its neurotransmitter.

The inhibitory signal molecule decreases the activity of Neuron #1. If Neuron #1 is less active, it releases less neurotransmitter. Neuron #1 produces glutamate, an excitatory neurotransmitter. The decreased amount of neurotransmitter released from Neuron #1 leads to a decreased level of activity of Neuron #2. If Neuron #2 is less active, it will release less dopamine.

Listening to students explain their answers, defend their reasoning, and modify their responses after listening to other students explain their logic will help you assess students' understanding of neurotransmission.

Case B. The signaling molecule is excitatory. Neuron #1 releases glutamate as its neurotransmitter. Neuron #2 releases dopamine as its neurotransmitter.

The excitatory signal molecule increases the activity of Neuron #1. If Neuron #1 is more active, it releases more neurotransmitter. Neuron #1 produces glutamate, an excitatory neurotransmitter. The increased amount of neurotransmitter released from Neuron #1 leads to an increase in the activity level of Neuron #2. If Neuron #2 is more active, it will release more dopamine.

Case C. The signaling molecule is inhibitory. Neuron #1 releases GABA as its neurotransmitter. Neuron #2 releases dopamine as its neurotransmitter.

The inhibitory signal molecule decreases the activity of Neuron #1. If Neuron #1 is less active, it releases less neurotransmitter. Neuron #1 produces GABA, an inhibitory neurotransmitter. The decreased amount of neurotransmitter released from Neuron #1 leads to an increase in the activity level of Neuron #2 (less GABA = less inhibition of Neuron #2). If Neuron #2 is more active, it will release more dopamine.

Case D. The signaling molecule is excitatory. Neuron #1 releases GABA as its neurotransmitter. Neuron #2 releases dopamine as its neurotransmitter.

The excitatory signal molecule increases the activity of Neuron #1. If Neuron #1 is more active, it releases more neurotransmitter. Neuron #1 produces GABA, an inhibitory neurotransmitter. The increased amount of neurotransmitter released from Neuron #1 leads to a decrease in the activity level of Neuron #2 (more GABA = stronger inhibition of Neuron #2). If Neuron #2 is less active, it will release less dopamine.

Case	Does the signal molecule excite or inhibit Neuron #1?	Does the activity of Neuron #1 increase or decrease?	Does the amount of neurotrans-mitter released from Neuron #1 increase or decrease?	What is the name of the neuro-transmitter released from Neuron #1?	Is the neuro-transmitter released from Neuron #1 excitatory or inhibitory?	Does the activity of Neuron #2 increase or decrease?	Does the amount of dopamine released from Neuron #2 increase or decrease?
A	inhibit	↓	↓	glutamate	excitatory	↓	↓
B	excite	↑	↑	glutamate	excitatory	↑	↑
C	inhibit	↓	↓	GABA	inhibitory	↑	↑
D	excite	↑	↑	GABA	inhibitory	↓	↓

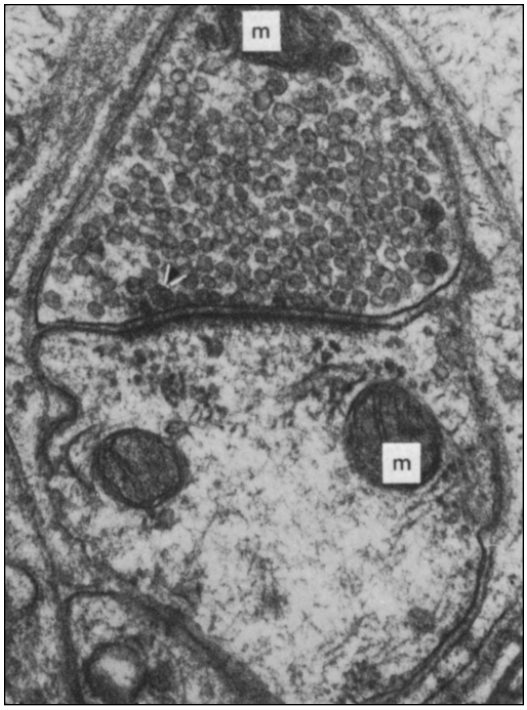
4. Ask students to keep their completed worksheets, Master 2.5 and 2.8. Students will refer to these when they do activities in Lesson 3.

5. Students may continue to explore how signals from one neuron influence the target neuron by doing the CD-ROM activity, *Neurons in Series*.

To access the *Neurons in Series* activity, click on *Neurons, Brain Chemistry, and Neurotransmission* on the main menu. Then select the *Neurons in Series* option from the submenu.

Lesson 3
Explain/ Elaborate

Drugs Change the Way - Neurons Communicate-



From: *Principles of Neural Science*, Third edition, Eric R. Kandel, James H. Schwartz, Thomas M. Jessell ©The McGraw-Hill Companies. (m = mitochondria)

At a Glance

Overview
Students build upon their understanding of neurotransmission by learning how different drugs of abuse disrupt communication between neurons. Students then conduct an activity investigating the effect of caffeine on their heart rate. Finally, students analyze data on how the way a drug is taken into the body influences its effect.

Major Concept
Drugs affect the biology and chemistry of the brain.

Objectives
By the end of these activities, the students will

- understand that certain drugs interfere selectively with neurotransmission, and
- realize that the effect of a drug is dependent upon dosage and route of administration.

Basic Science–Health Connection
Drugs of abuse are valuable tools for investigations of brain function because they can mimic or block actions of neurotransmitters, and thus exert effects on homeostasis and behavior.

Background Information

Drugs Disrupt Neurotransmission

How do drugs cause their effects on the brain and behavior? Lesson 1 introduced students to the idea that a specific brain region, the reward system (part of the limbic system), regulates feelings of pleasure and that this region is activated by drugs of abuse. But what do drugs actually do in that brain region? Drugs interfere with neurotransmission. More specifically, drugs of abuse produce feelings of pleasure by altering neurotransmission by neurons in the reward system that release the neurotransmitter dopamine.[1,2] Thus, drugs of abuse alter the communication between neurons that is mediated by dopamine. Because the synapse is so complex, there are a variety of sites at which drugs may affect synaptic transmission. One way to affect synaptic transmission is to increase the amount of neurotransmitter that is released into the synaptic space. Drugs like alcohol, heroin, and nicotine excite the dopamine-containing neurons in the ventral tegmental area (VTA) so that they produce more action potentials.[1,2] As the number of action potentials increases, so does the amount of dopamine released into the synapse. Amphetamines (e.g., methamphetamine, crystal, crank) actually cause the release of dopamine from the vesicles. This is independent of the rate of action potentials and, depending on dose, can cause a relatively quick and prolonged rise of extracellular dopamine levels.

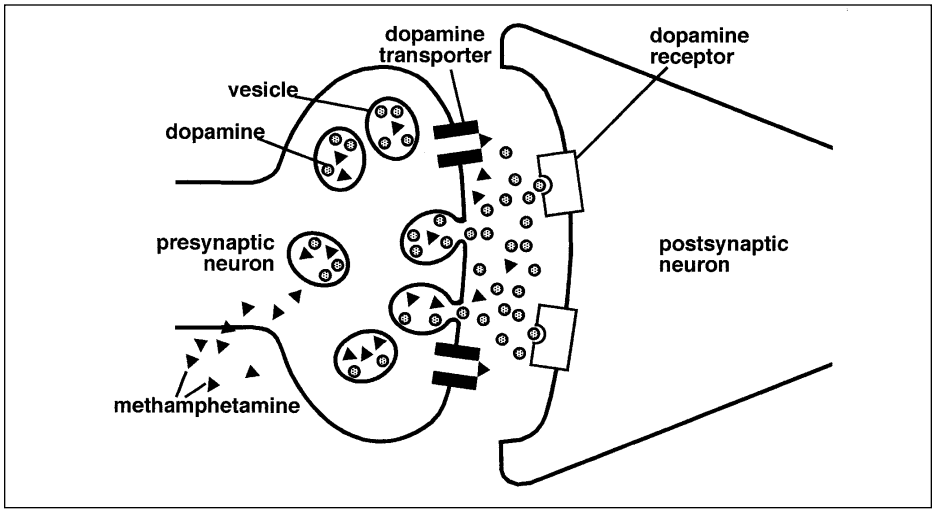


Figure 3.1: Methamphetamine alters dopamine neurotransmission in two ways. Methamphetamine enters the neuron by passing directly through nerve cell membranes. It is carried to the nerve cell terminals by transporter molecules that normally carry dopamine or norepinephrine. In the nerve terminal, methamphetamine enters the dopamine- or norepinephrine-containing vesicles and causes the release of neurotransmitter. Methamphetamine also blocks the dopamine transporter from pumping dopamine back into the transmitting neuron. Methamphetamine acts similarly to cocaine in this way.

Nicotine not only acts at the cell body in the VTA to increase the number of action potentials and number of vesicles released from a neuron, but it also acts by another mechanism to alter dopamine release. When nicotine binds to nicotine receptors on the dopamine-containing axon terminals in the nucleus accumbens, more dopamine is released with each action potential.[1]

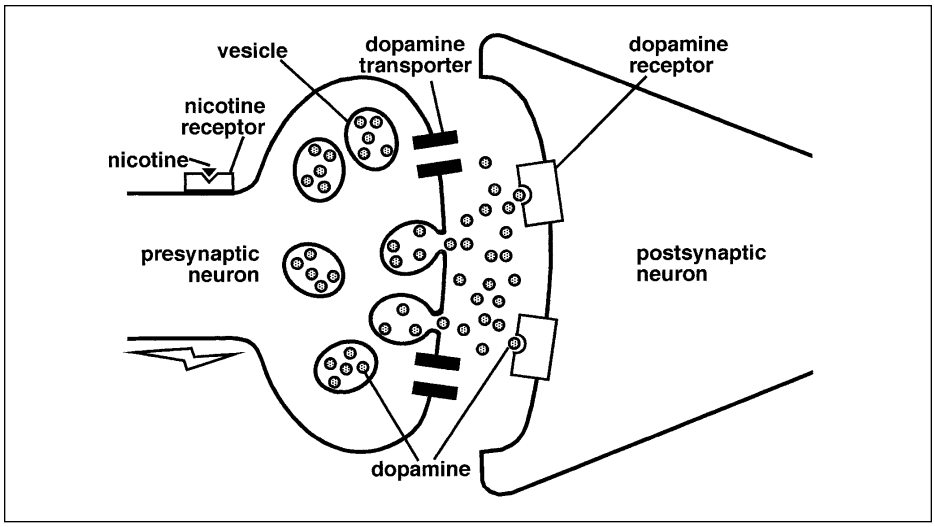


Figure 3.2: Nicotine binds to specific receptors on the presynaptic neuron. When nicotine binds to receptors at the cell body, it excites the neuron so that it fires more action potentials (electrical signals) that move toward the synapse causing more dopamine release (not shown in figure). When nicotine binds to nicotine receptors at the nerve terminal (shown above), the amount of dopamine released in response to an action potential is increased.

Drugs may also alter synaptic transmission by directly affecting the postsynaptic receptors. Some drugs activate receptors and others block them.

While THC (the main psychoactive chemical in marijuana) and morphine activate their specific receptors, other drugs block specific receptors. Caffeine, the mild stimulant found in coffee and some soft drinks, exerts its effects by preventing a neurotransmitter / neuromodulator called adenosine from binding to its receptor. Normally, the binding of adenosine to its receptor causes sedation; it is a natural sleep-inducer. Instead of causing sedation, the blocking of the adenosine receptors with caffeine leads to an increase in activity and arousal levels.[1, 3]

The actions of some drugs are very complex. LSD, for example, acts on serotonin receptors. Serotonin, an important neurotransmitter in many brain regions, is involved in regulating a wide variety of functions, including mood and basic survival functions such as sleep and eating. Scientists continue to study how hallucinogens act, but apparently LSD activates some serotonin receptors (LSD acts as a receptor agonist) and blocks other serotonin receptors (LSD acts as a receptor antagonist).[1]

A third way to affect synaptic transmission is to alter the removal of neurotransmitters from the synapse. Cocaine and amphetamines work this way (this is the second way in which amphetamines can alter neurotransmission).[1, 3] Both drugs block the dopamine transporter (reuptake pump) that removes dopamine from the synapse. The result is a fairly rapid rise of dopamine in the synapse, leading to feelings of euphoria and well-being. There are no drugs of abuse that block enzymatic destruction of neurotransmitters, although some antidepressants work by this mechanism.

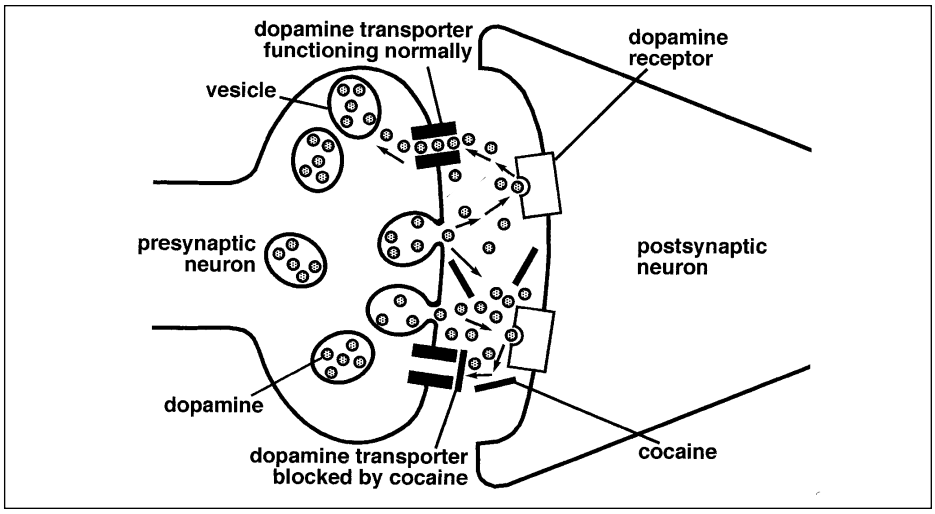


Figure 3.3: When cocaine enters the brain, it blocks the dopamine transporter from pumping dopamine back into the transmitting neuron, flooding the synapse with dopamine. This intensifies and prolongs the stimulation of receiving neurons in the brain's pleasure circuits, causing a cocaine "high."

Drugs of abuse share a common action: they act on the brain's reward system. Within that system, they all (except perhaps for LSD) share the ability to increase the levels of dopamine in the nucleus accumbens. This almost certainly accounts for the rewarding (pleasurable) effects of abused drugs.

The effects of drugs are not limited to the reward pathway in the brain. Drugs can act in various regions of the brain to exert their effects, but their ability to alter dopamine neurotransmission in the ventral tegmental area (VTA) and the nucleus accumbens is one of the most important factors that drives continued drug use.

Drugs Mimic Natural Body Chemicals

The ability of drugs to interrupt normal synaptic transmission may seem odd. After all, if receptors have such great specificity for a single type of binding partner, how can drugs disrupt the process? The answer lies in the similarity in conformation, or structure, of the drugs to natural body chemicals. For example, the receptors that bind morphine and other opiates are expressed in the brain to recognize natural opioid peptides called endorphins and enkephalins that are made by our brains and used as neurotransmitters.[4] It is an evolutionary coincidence that these receptors recognize a plant-derived chemical (drug) as well. This coincidence is a double-edged sword. Opiate compounds that come from plants are both the most potent analgesics (pain relievers) available and some of the most potent addictive drugs as well. Morphine continues to be one of the most effective drugs to relieve the pain associated with many chronic diseases. The doses of opiates used by addicts simply overwhelm the opiate receptors in the VTA and nucleus accumbens and cause profound feelings of pleasure (euphoria). Tetrahydrocannabinol (THC), the active ingredient in marijuana, binds to receptors in the brain that are specific for anandamide, an endogenous chemical that is similar in structure to THC. Because THC is similar in structure to anandamide, it binds to the same receptor. Scientists do not yet fully understand anandamide's function in the body, but it may play a role in memory functions. Marijuana disrupts short-term memory in humans. Anandamide may be involved in eliminating unneeded information from memory, but much remains to be learned before its functions are understood. Other studies indicate anandamine in an area of the brain called the dorsal striatum inhibits movements that are stimulated by dopamine.[5] This finding may enable scientists to develop medications for treating diseases such as schizophrenia, Gilles de la Tourette syndrome, or Parkinson's disease. Each of these diseases involves dopamine imbalances in the brain.

The Dose Changes the Drug's Effects

For drugs to exert their effects, a person must take them into the body and absorb them into the bloodstream. Some of these effects relate to the amount of the drug taken. For example, at low doses no effect (or response) can be observed or measured. Once a certain amount of the drug enters the bloodstream, a response can then be measured. This point is known as the **threshold**. At doses of the drug below the threshold amount, there is too little of the drug in the body to cause neurons to be activated. For example, there may not be enough heroin in the body to bind to opiate receptors in sufficient amounts to cause a change in neuronal activity. As the amount of drug taken increases, so does the response. A response cannot continue to increase infinitely, however. At some point, the response to a given amount of drug will reach a plateau, or a maximum level. To continue our example, when levels of opiates are very high in the blood, many opiate receptors have heroin bound to them and the neurons are already activated; no additional activation is possible. At higher doses, opiates are toxic and can cause a fatal response by halting respiration.

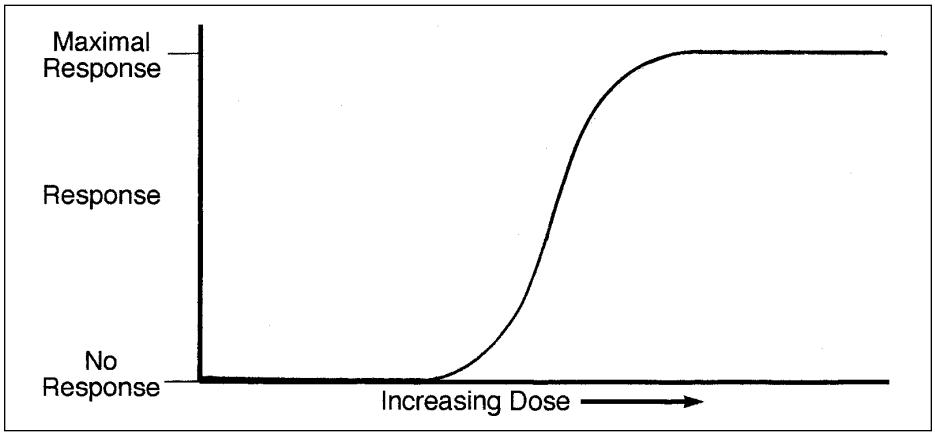


Figure 3.4: When the dose of a drug is low, no response is measurable. As the dose increases, the effect of the drug increases until it reaches a maximum. At high doses, the response to the drug remains at the maximum level.

Drugs Enter the Body in Different Ways

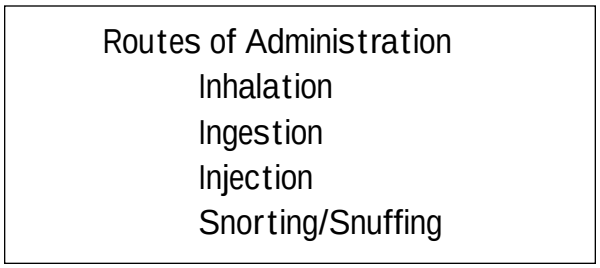


Figure 3.5: Drugs enter the bloodstream by one of four routes of administration.

The dose is not the only factor that changes the effects that a drug causes in the body. The same amount or dose of a drug can lead to milder or more severe responses depending on how the drug enters the body.[1,4] A drug that is inhaled (smoked) reaches the brain very quickly. The inhaled drugs go directly from the lungs into the left side of the heart where they enter the arterial circulation that carries them to the brain. Marijuana and nicotine are examples of drugs that are commonly taken into the body by inhalation (smoking). The intensity of the effect of inhaled drugs may be slightly less than that for injected drugs because less of the drug is taken into the body; some of the drug will be exhaled with the rest of the components of the smoke. A drug that is injected intravenously also travels quickly to the brain where it can exert its effects. The rapid passage of injected heroin, for example, brings a high risk of overdose. The heroin in the blood can reach lethal levels much faster than medical help could possibly be obtained. A third route of drug administration is by snorting or snuffing. A drug that is snorted or snuffed is taken in through the nose where it is absorbed through the mucous membranes lining the nasal passages. Television and movies often depict cocaine being snorted. The effects of drugs taken by this method will be less intense than by injection or inhalation because it takes longer for the drug to get into the bloodstream and because it does not enter the blood as efficiently. The fourth route of administration is by oral ingestion. Most people are familiar with taking a medicine, either as a solid or a liquid, by mouth. People can also take drugs of abuse this way. Drugs commonly taken orally include stimulants and depressants. Drugs taken orally enter the bloodstream more slowly than by any of the other routes. The drugs pass through the digestive tract until they reach the stomach and intestine where they are absorbed into the bloodstream. Not only do they take longer to act, but the body begins to metabolize them before they can act on the brain. Enzymes in the stomach, intestines, and liver begin breaking down the drugs so they can be cleared from the body.

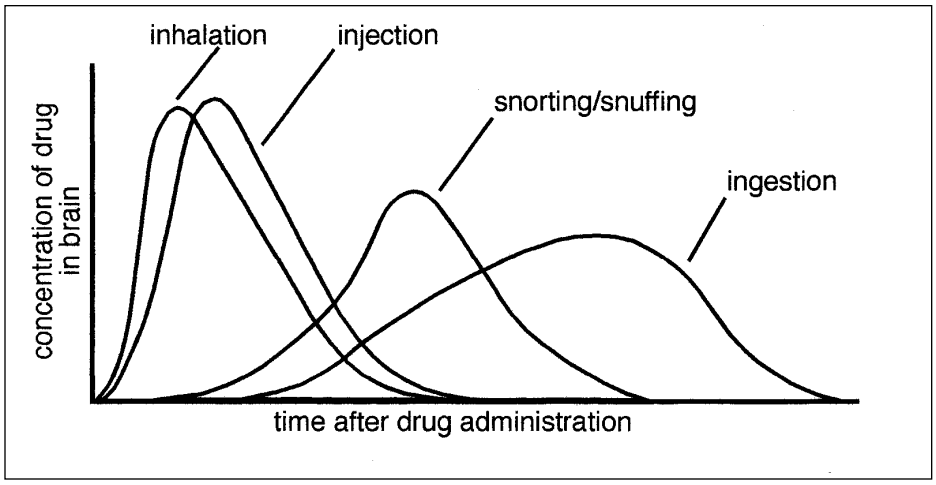


Figure 3.6: Drugs of abuse enter the body by different routes. The intensity of a drug's effect depends on how the drug is taken.

As shown on Figure 3.6, the route of administration causes dramatic differences in the onset, intensity, and duration of a drug's effect. Methamphetamine, for example, can be smoked, snorted, ingested orally, or injected. If the drug is smoked or injected, the user almost immediately experiences an intense rush or "flash" that lasts a few minutes. Snorting methamphetamine produces feelings of euphoria within three to five minutes, while oral ingestion produces effects within 15 to 20 minutes. The high resulting from snorting or ingestion is not as intense as that resulting from injection or smoking the drug.[6]

In Advance

CD-ROM Activities	
Activity Number	**CD-ROM**
Activity 1	yes
Activity 2	no
Activity 3	yes

Photocopies	
For the class	**For each student**
1 transparency of Master 3.1, *Cocaine Alters Neurotransmission* 1 transparency of Master 3.2, *Methamphetamine and Nicotine Disrupt Neurotransmission* 1 transparency of Master 3.3, *How Does Alcohol Affect Neurotransmission?* 1 transparency of Master 3.7, *What Should the Doctor Do?*	1 copy of Master 3.4, *Parent Letter* 1 copy of Master 3.5, *Caffeine: How Does Your Heart Respond?* 1 copy of Master 3.6, *How Do Drugs Get In the Body?*

Materials	
Activity 1	overhead projector computers
Activity 2	soft drinks, caffeinated and caffeine-free (see Preparation) 1 watch or classroom clock with a second hand
Activity 3	computers

Preparation

Arrange for students to have access to computers for Activities 1 and 3.

At least one week before conducting Activity 2, send a copy of Master 3.4, *Parent Letter*, home with each student to inform parents of the activity and get permission for the students to consume a caffeinated or a caffeine-free soft drink during science class. You can also use the letter to ask each student to bring in his or her own can of the designated soft drink.

Decide on a brand of soft drink that is available with and without caffeine to use in the activity. Students should drink the same brand of soft drink because each brand contains a different amount of caffeine. If students drank different brands or flavors, the results would be difficult to interpret because each student who drank a caffeinated soft drink would ingest a different dose. You will need approximately half of the students to drink a caffeinated soft drink and half the students to drink a caffeine-free soft drink. Students who do not get parental permission can participate by drinking water, thereby providing a comparison to the control group. You may obtain the necessary soft drinks through one of the following ways:

- purchase all the soft drinks yourself through your school budget,
- ask for parent or business donations to cover the cost, or
- request that each student bring in one can of soft drink, labeled with his or her name, for his or her consumption only. (If you use this approach, you will need to specify which drink each student brings to class.)

Before the day of Activity 2, have students practice taking a resting heart rate so they are used to finding their pulse, counting the beats for 15 seconds, and multiplying that number by four to get a resting heart rate for one minute (see Activity 2).

Procedure

Content Standard A: Formulate and revise scientific explanations and models using logic and evidence.
Content Standard C: Cell functions are regulated.
Content Standard C: Organisms have behavioral responses to internal changes and to external stimuli.

ACTIVITY 1: DRUGS ALTER NEUROTRANSMISSION

1. Review neurotransmission with the students. It may be helpful to have the class watch the CD-ROM animation of neurotransmission to refresh their memories. Have students refer to their summary of neurotransmission that they completed on Master 2.5.

After loading the CD-ROM on the computer, click on *Neurons, Brain Chemistry, and Neurotransmission* and then select *Neurotransmission Animation*.

2. Create a chart with the following headings on the board:

Change in neurotransmission	Effect on neurotransmitter release or availability

3. Ask students if they think there are ways that neurotransmission could be altered. As students propose ideas, fill in the chart on the board. Probe for ideas by asking questions such as:

- What would happen if certain components in the process increased or decreased in amount?
- How would that change affect the response in the responding neuron?

Students may suggest a variety of ways in which neurotransmission can be altered. For example, maybe less neurotransmitter gets released which would result in reduced (fewer) firings in the responding (postsynaptic) neuron. The postsynaptic neuron might have either more or fewer receptors; changing the number of receptors would cause an increased or decreased chance of postsynaptic neuron firing. The following chart outlines potential changes and their responses. Omit the third column on the chart at this time; you will complete that part in Step #4.

Change in neurotransmission	Effect on neurotransmitter release or availability	Drug that acts this way
increase the number of impulses	increased neurotransmitter release	nicotine alcohol* opiates*
release neurotransmitter from vesicles with or without impulses	increased neurotransmitter release	amphetamines methamphetamine
release more neurotransmitter in response to an impulse	increased neurotransmitter release	nicotine
block reuptake	more neurotransmitter present in synaptic cleft	cocaine amphetamine
produce less neurotransmitter	less neurotransmitter in synaptic cleft	probably doesn't work this way
prevent vesicles from releasing neurotransmitter	less neurotransmitter released	no drug example
block receptor with another molecule	no change in amount of neurotransmitter released, or neurotransmitter cannot bind to its receptor on postsynaptic neuron	LSD caffeine

*These drugs cause an increase in dopamine release. However, both alcohol and opiates act indirectly. See steps 10 and 11 on pages 67–68 for a more complete explanation of their actions.

4. When you have the first two columns completed on the chart, inform students that certain drugs may cause the changes in the neurons that they have suggested. Write the name of the drug next to the change as indicated in the third column on the previous chart.

Students will begin to see that drugs of abuse interfere with and disrupt the process of neurotransmission. When neurons do not communicate normally, the brain does not function normally either.

5. **Display a transparency of Master 3.1, *Cocaine Alters Neurotransmission,* showing cocaine's effect on dopamine neurotransmission. Point out that cocaine blocks the dopamine transporters. Ask the following questions:**

   • How does this blocking action of cocaine affect dopamine levels?
   • What is the effect on the responding postsynaptic neuron?

   Cocaine blocks the dopamine reuptake pumps (also called dopamine transporters). Students should recall that transporters, or reuptake pumps, carry neurotransmitter, dopamine in this case, back into the presynaptic neuron where it is repackaged into new vesicles. If the reuptake pumps cannot function, more dopamine will be present in the synaptic space where it can cause a greater stimulation of the postsynaptic neuron.

6. **After the students understand how blocking the dopamine transporters alters neurotransmission, show the CD-ROM animation on cocaine's effect on neurotransmission to the class.**

   Click *Drugs Change the Way Neurons Communicate* on the main menu and then select *How Does Cocaine Alter Neurotransmission?* to view the animation.

7. **Discuss the actions of another type of drug, methamphetamine, with the class. Display a transparency of Master 3.2, *Methamphetamine and Nicotine Disrupt Neurotransmission* (top half only). Explain that methamphetamine can act similarly to cocaine in blocking dopamine transporters (reuptake pumps). Methamphetamine also acts in another way to alter neurotransmission. Methamphetamine passes directly through the neuron cell membrane and is carried to the axon terminals. In the terminals, methamphetamine enters the vesicles that contain dopamine. This then triggers the vesicles to be released, even without an electrical signal (action potential) to cause vesicle release. Ask students how this affects the postsynaptic neuron.**

   Methamphetamine acts in two ways to change dopamine neurotransmission. Both actions lead to an increase in the amount of dopamine in the synaptic cleft. When more dopamine is present in the synaptic cleft, it is more likely to bind to the dopamine receptors on the postsynaptic neuron.

8. **Continue to assess the students' understanding of how drugs can alter neurotransmission by asking them to consider how nicotine interferes with dopamine neurotransmission in the brain. Display a transparency of Master 3.2 (bottom half). Explain that nicotine binds to receptors on the transmitting (presynaptic) neuron and causes the neuron to release more neurotransmitter each time an electrical impulse (action potential) occurs. How does this affect the activity of the postsynaptic (receiving) neuron?**

   Nicotine binds to nicotine receptors on the presynaptic neuron. The binding of nicotine to its receptor stimulates the generation of action potentials in the neuron that cause dopamine to be released from the neuron. The released dopamine can then bind to its receptor on the postsynaptic neuron. Nicotine also changes the amount of dopamine that is released. When

the presynaptic neuron fires an action potential, more dopamine is released than normal. The increased amount of dopamine in the synaptic cleft will bind to dopamine receptors on the postsynaptic neuron.

9. Display a transparency of Master 3.3, *How Does Alcohol Affect Neurotransmission?* Inform students that alcohol is an inhibitory signal and point out that alcohol acts on the dendrites of the presynaptic neuron. Ask students what other inhibitory signal they have learned.

This exercise is similar to Activity 4 in Lesson 2. Although the activity in Lesson 2 limited the signal molecules to being neurotransmitters, drugs can also be signal molecules that affect neuron activity.

Students may benefit from reviewing their work on Masters 2.7 and 2.8. Students have learned previously that GABA is an inhibitory neurotransmitter.

Now that students have expanded their understanding of neurotransmission to include how drugs of abuse can alter the process, they should be able to determine how another drug, alcohol, changes neurotransmission.

10. Ask students to use what they have learned about neurotransmission to answer the following questions:

- **How does alcohol affect the activity of the presynaptic neuron?**

Alcohol is an inhibitory signal so it reduces the activity of the presynaptic neuron.

- **If the presynaptic neuron releases GABA as its neurotransmitter, does the amount of GABA that is released increase or decrease when alcohol is present in the body?**

If the activity of the presynaptic neuron is decreased, it releases less neurotransmitter.

- **How does this affect the release of dopamine from the postsynaptic neuron?**

Because GABA is an inhibitory neurotransmitter, smaller quantities of it in the synaptic space create less inhibition of the postsynaptic neuron. Therefore, the activity of the postsynaptic neuron increases and more dopamine is released when alcohol is present.

If you complete a line for alcohol on the chart like that on Master 2.8, it would appear as follows:

Does the signal molecule excite or inhibit Neuron #1?	Does the activity of Neuron #1 increase or decrease?	Does the amount of neurotransmitter released from Neuron #1 increase or decrease?	What is the name of the neurotransmitter released from Neuron #1?	Is the neurotransmitter released from Neuron #1 excitatory or inhibitory?	Does the activity of Neuron #2 increase or decrease?	Does the amount of dopamine released from Neuron #2 increase or decrease?
inhibit	↓	↓	GABA	inhibitory	↑	↑

11. **Now that students understand how alcohol affects neurotransmission in the brain, ask them to compare how alcohol and cocaine change neurotransmission. Use the following questions to guide the discussion.**

    - **How does the way in which alcohol alters dopamine neurotransmission differ from the way in which cocaine changes dopamine neurotransmission?**

    Unlike cocaine, alcohol does not act directly on the dopamine-producing neuron. Alcohol acts on another neuron that regulates the activity of a dopamine-producing neuron. In other words, alcohol acts indirectly on dopamine neurotransmission whereas cocaine acts directly on the neuron that produces dopamine. (Opiates act by a mechanism similar to that of alcohol.)

    - **Are there any similarities in how alcohol and cocaine change neurotransmission?**

    Both alcohol and cocaine change dopamine neurotransmission and increase the amount of dopamine present in the synaptic cleft. The increased amount of dopamine increases the activity of the postsynaptic neuron.

ACTIVITY 2: HOW DOES CAFFEINE AFFECT YOU?

In Activity 1, students learned that drugs change the communication between neurons. However, hands-on classroom investigations of drugs' effects on the brain are impossible. The following activity is an exercise that students can do to learn more about how a drug, caffeine, affects their body.

Note: Before beginning this investigation, be sure to have permission forms signed by parents or guardians for the students to drink either a caffeinated or caffeine-free soft drink (use Master 3.4, *Parent Letter*). Those students who do not have permission can participate in the investigation by drinking water, thereby providing a comparison or second control for the activity.

Content Standard A: Design and conduct scientific investigations.
Content Standard A: Mathematics is essential in scientific inquiry.
Content Standard C: Organisms have behavioral responses to internal changes and to external stimuli.

1. **Several days prior to conducting Activity 2, decide which students will be in the group that drinks a caffeinated soft drink and which students will be in the group that drinks a caffeine-free soft drink. Tell students which group they will be a part of if you are asking them to bring a can of soft drink to class. Make sure students understand the need to bring only the specified type of drink.**

   Approximately half of the class should be assigned to each group. You should have permission letters specifying the type of drink for both of these groups. Any student who does not have parental permission can participate in the activity by drinking water.

2. **Because their heart rates might be elevated from their walk to class, spend several minutes allowing students to rest and talk quietly. Find out what students know about caffeine.**

   Caffeine is a mild stimulant contained in coffee and some soft drinks. People often report that mild doses of caffeine increase their alertness and

their ability to concentrate. Higher doses can cause a person to feel jittery or nervous. High doses can cause sleeplessness.

Related chemicals, theophylline (found in tea) and theobromine (found in cocoa and tea), are very mild stimulants also.

3. If you have not already done so, teach students how to find their pulse, count their heartbeats, and calculate their resting heart rate.

A student can find his or her pulse most easily by pressing two fingers against the artery in the neck or on the inside of the wrist. It is easiest to count for 15 seconds and then multiply that number by four to obtain the resting heart rate for one minute. Students should repeat the process several times until they get a consistent resting heart rate.

4. Distribute one copy of Master 3.5, *Caffeine: How Does Your Heart Respond?*, to each student. On your signal, ask students to measure their heartbeats one more time for 15 seconds, stopping when you call time. Instruct students to calculate their resting heart rate for one minute by multiplying the number they counted by four. Direct them to record it on the data table on the master.

5. Ask students to work in pairs. Distribute cans of the appropriate soft drink, one to each student. Instruct students to follow the directions on the master, and remind them to continue to sit at rest. They can talk to their partner or work on Activity 3 in this lesson, but should keep their bodies still so that they do not elevate their heart rate with activity.

6. When all the students have filled in their data tables and calculated the difference between their resting heart rate and their heart rate after drinking a soft drink, discuss their findings by asking:

- **Did your heart rate go up, down, or stay the same after you drank a caffeinated soft drink?**
- **If you drank a caffeine-free soft drink, how did your heart rate change?**
- **What happened if you drank water?**

On average, most students should have seen their heart rate go up after drinking the caffeinated soft drink. Drinking a caffeinated soft drink increased the heart rate of students in a field-test class by an average of 15 beats per minute. Drinking either a caffeine-free soft drink or water should not change the heart rate significantly.

One effect of caffeine is an increase in a person's heart rate. Scientists don't know exactly how caffeine produces its effects, but it is likely to affect the heart in two ways:

* It acts on parts of the brain that regulate the heart rate.
* It acts directly on the heart.

- **Why was it important that some students drink the same amount of a caffeine-free soft drink? Why did some students drink water?**

These questions address the need for controls in scientific investigations. Students will recognize that they are interested in determining the effect of caffeine on their heart rate. Because caffeine-free soft drinks generally contain the same ingredients as caffeinated varieties except for the caffeine, the caffeine-free soft drink serves as a control to ensure that the response is due to the caffeine in the soft drink rather than some other ingredient. Water is a second control; it ensures that the effect on the heart rate after drinking a soft drink is not caused by a different ingredient.

- **How long did the effect of caffeine last?**

Most students will find that their heart rates are either back to the resting rate or very close to it after one hour.

- **Did all the members of the class have exactly the same results when they drank a caffeinated soft drink?**

While most members of the class will see their heart rate increase, the amount of increase will vary.

- **Why do some people respond differently to caffeine than others?**

Students vary from one another in gender, size, frequency of caffeine consumption, metabolic rates, genetic makeup, and so on. This variability makes each student react differently to exposure to caffeine.

- **What could your results from the caffeine investigation tell you about how individuals respond to drugs of abuse?**

Just as individuals vary in their response to caffeine, individuals will vary in their response to drugs of abuse. The same factors: gender, body size, frequency of use (development of tolerance), genetics, and the individual's metabolic rate will influence a person's response.

7. **If you are conducting this activity in several classes, you may wish to pool the data from all classes to have a larger sample size.**

8. **Discuss the last item on the master that asks students to consider how different doses of caffeine might affect the response. Encourage students to design an experiment to investigate this.**

   Students likely will propose that drinking a small amount of soft drink will cause only a slight increase, if any, in a person's heart rate, while drinking a large volume of soft drink will cause a larger increase in heart rate. This leads students to consider the concept of dose.

   To investigate the effect of dose on the body's response to caffeine, students may propose that different groups of students drink different amounts of caffeinated soft drink. For example, students could drink 1 ounce, 2 ounces, 4 ounces, 8 ounces, or 16 ounces of soft drink. The design should include appropriate controls. Caffeine-free soft drink again could serve as the control if it were consumed in equal amounts to the caffeinated variety.

Many soft drinks popular among youth contain caffeine. The accompanying table lists some soft drinks (12-ounce size) and the amounts of caffeine they contain.

Compared with other caffeinated drinks popular with adults, the caffeine content in soft drinks is lower. Coffee can contain between 80 and 175 milligrams of caffeine (per seven ounces) depending on how it is brewed; espresso has 100 milligrams in just 1.5 to 2.0 ounces. Tea can contain 40-60 milligrams of caffeine (per seven ounces). Ice tea contains 70 milligrams of caffeine in 12 ounces.

Caffeine in Soft Drinks

Soft Drink	Milligrams in 12 ounces
Jolt Cola	71 mg
Josta	58 mg
Mountain Dew	55 mg
Surge	51 mg
Diet Coke	45 mg
Coca-Cola	45 mg
Dr Pepper	41 mg
Sunkist Orange Soda	40 mg
Pepsi Cola	37 mg
Barqs Root Beer	23 mg
7-Up	0 mg
Minute Maid Orange Soda	0 mg
Mug Root Beer	0 mg

Source: Center for Science in the Public Interest. Soft drinks and health: Caffeine content of foods and drugs. Retrieved August 17, 2000 from the World Wide Web: *www.cspinet.org/new/cafchart.htm.*

ACTIVITY 3: ROUTES OF ADMINISTRATION

1. Give students the opportunity to view the CD-ROM segment, *Paths to the Brain.*

After loading the CD-ROM on the computers, pull up the main menu. Click on *Drugs Change the Way Neurons Communicate* and then select *Pathways to the Brain*.

Content Standard A: Communicate and defend a scientific argument.

2. Give each student a copy of Master 3.6, *How Do Drugs Get In the Body?* Students may work in groups of three to analyze the graph and answer the questions.

Note to Teachers: The graph shown on Master 3.6 is a generalized representation of the speed and intensity of response to drugs. Very few, if any, drugs are commonly taken by all of the different routes.

SAMPLE ANSWERS TO QUESTIONS ON MASTER 3.6

Question 1. Four drug abusers each take a drug. One person injects 100 milligrams of a drug into a vein, one person smokes 100 milligrams of the drug, one person snorts 100 milligrams of the drug, and one person swal-

lows or ingests 100 milligrams of the drug. Who will experience the greatest effect of the drug? The individual with the greatest concentration of drug in the brain will have the greatest effect.

The graph indicates that the individuals who inhale the drug or inject the drug into a vein will experience the greatest effect from the drug. These individuals will have a higher concentration of the drug in the brain than the people who snort (absorption through the mucous membranes) or ingest the drug. The concentration of drug in the brain will be slightly lower for inhalation than injection because some of the smoked drug is exhaled in the smoke.

Question 2. Who will experience the quickest effect from the drug?

The person who inhales the drug will experience the quickest effect from the drug (assuming the person inhales the whole 100 mg). The inhaled drug goes directly into the left side of the heart and then enters the arterial circulation to the brain, while injected drugs enter the venous circulation that returns the blood to the right side of the heart. The drug that enters the venous system takes longer to exert its effect because the blood must go to the lungs and then to the left side of the heart before it is pumped to the brain and the rest of the body.

Question 3. Who will experience the least effect from the drug?

The person who ingests, or swallows, the drug will experience the least effect.

Question 4. Who will experience the slowest effect from the drug?

The person who ingests, or swallows, the drug will also have the slowest effect.

Question 5. Tobacco smokers can use nicotine patches to help them quit smoking. The nicotine patches help the smoker slowly lower the amount of nicotine that enters the body. How does the nicotine in the patch enter the body?

Nicotine would enter the body by absorption through the skin.

Question 6. Explain why the different ways of taking drugs cause different responses.

Taking drugs by inhalation causes a very rapid increase in the level of drug in the brain. Inhaled drugs are absorbed into the arterial bloodstream in the lungs and then pumped to all parts of the body including the brain. Taking drugs by intravenous (IV) injection also causes a rapid increase in the drug level in the brain. It is slightly slower than inhalation because the drug goes first to the right side of the heart, is then pumped to the lungs where the blood is oxygenated, then goes back to the left side of the heart, and finally to the brain and body. Absorption through the skin or mucous membranes would be slower yet because the drug has a longer path to

travel before being circulated throughout the body. Drug response would be the slowest after ingestion because the drug goes into the digestive tract and then must pass through the walls of the stomach and intestine to enter the blood capillaries.

3. Display a transparency of Master 3.7, *What Should the Doctor Do?* Discuss the reasons why one action may be more appropriate than others.

Based upon what you have learned about how drugs act in the body, how should morphine be given to the patient? Should the morphine be given as a pill, as a shot, or as an inhalant? Consider each alternative and explain why the different methods should or should not be chosen.

If students understand that taking drugs into the body by different routes causes different responses, they should be able to explain that the different ways of administering drugs can have advantages and disadvantages. Use this scenario to evaluate students' understanding.

The question concerning how morphine should be administered to a patient to relieve pain is designed to assess if students understand how different ways of getting drugs into the body changes their effects. The doctor's goal is to relieve the patient's pain quickly so that the fracture can be set.

Based on the graph that students analyzed on Master 3.6, the doctor should elect to give morphine as an inhalant or an injection. In each case, the drug reaches the brain quickly. Inhaled drugs may reach the brain even faster than injected drugs. Perhaps the main disadvantage of giving the morphine as an inhaled drug is the amount of drug that actually enters the bloodstream is more variable. After inhaling the drug, the person exhales; some of the drug is carried out of the body during the exhalation. If the drug is injected, all of the drug is delivered into the bloodstream. The doctor knows how much morphine enters the bloodstream. Giving a pill to the patient would be less effective than the other means for pain relief because it would take longer for the drug to act and its concentration in the bloodstream would be lower.

Lesson 4
Explain/ Elaborate

Drug Abuse and Addiction

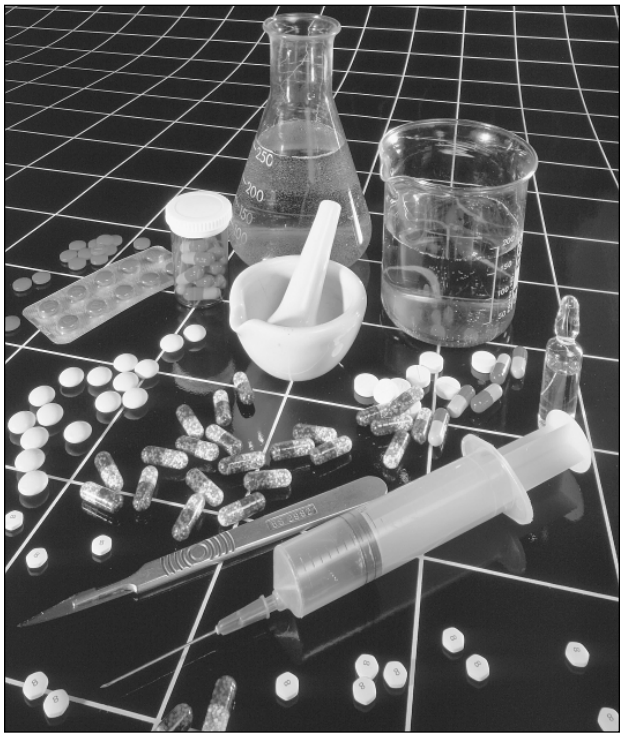


Photo: Corel

At a Glance

Overview
Students will examine data from animal experiments. Through this activity, a card game, and a case study, students learn that although the initial decision to take drugs of abuse is voluntary, continued use may lead to addiction, which is the continued compulsive abuse of drugs in spite of adverse consequences. Students then watch a CD-ROM mini-documentary to learn how drugs cause long-term changes in the brain.

Major Concept
Addiction is a brain disease.

Objectives
By the end of these activities, the students will

- understand that drug abuse initially is a voluntary behavior,
- be able to define drug addiction as the continued compulsive drug abuse in the presence of adverse health or social consequences,
- understand that drug abuse and addiction are associated with long-term physical and functional changes in the brain, and
- recognize that addiction is influenced by the social and behavioral context of drug use.

Basic Science–Health Connection
Drug addiction is a complex brain disease. Preventing drug abuse and addiction and treating the disease effectively requires understanding the biological, genetic, social, psychological, and environmental factors that predispose individuals to drug addiction.

Background Information

Individuals make choices to begin using drugs. Some people begin using drugs to relieve a medical condition and then continue to use the drugs after the medical need is over. Children who are depressed or who have a psychiatric disorder sometimes begin using illicit drugs to self-medicate. Other people begin taking drugs to feel pleasure, to escape the pressures of life, or to alter their view of reality. This voluntary initiation into the world of addictive drugs has strongly influenced society's view of drug abuse, drug addiction, and its treatment.

When does drug abuse become drug addiction? No one becomes addicted with the first use of a drug. Drug abuse and drug addiction can be thought of as points along a continuum. Any use of a mind-altering drug or the inappropriate use of medication (either prescription or over-the-counter drugs) is **drug abuse**, but the point when drug abuse becomes drug addiction is less clear. Different drug abusers may reach the point of addiction at different stages. Scientists continue to investigate the factors that cause the switch between the two points.

Figure 4.1: The continuum of drug abuse and addiction.

Currently, **drug addiction** is defined as the continued compulsive use of drugs in spite of adverse health or social consequences.[1] Drug addicts have lost control of their drug use. Individuals who are addicted to drugs often become isolated from family or friends, have difficulty at work or school, and become involved with crime and the criminal justice system. For addicts, continuing their drug habit becomes their primary focus in life.

Certain drugs, including opiates and alcohol, cause strong physical reactions in the body when drug use stops. When a heroin addict stops taking heroin, he or she can experience a variety of symptoms ranging from watery eyes and a runny nose to irritability and loss of appetite and then diarrhea, shivering, sweating, abdominal cramps, increased sensitivity to pain, and sleep problems.[2] In general, withdrawal from heroin makes the abuser feel miserable. Withdrawal from other drugs, such as cocaine and amphetamines, does not lead to strong physical reactions. For most drugs, physical withdrawal symptoms can usually be controlled effectively with medications. Even though withdrawal from some drugs does not cause the abuser to have physical reactions, stopping drug use is difficult because of the changes the drugs have caused in the brain. Once the drugs stop, the abuser will have **cravings**, or intense desire for the

drugs.[3] Craving arises from the brain's need to maintain a state of homeostasis that now includes the presence of the drug. A person may experience cravings at any stage of drug abuse or addiction, even early in the experimentation phase of drug abuse. Cravings have a physical basis in the brain. Using PET imaging, scientists have shown that just seeing images of drug paraphernalia can stimulate the amygdala (part of the brain that controls memory) in drug addicts.[4]

Drugs of addiction do not merely cause short-term changes in an individual's cognitive skill and behavior. A drug "high" lasts a short time, ranging from less than an hour to twelve hours depending on the drug and dose. The changes in the brain that result from continued drug use, however, can last a long time. Scientists believe that some of these changes disappear when drug use stops; some disappear within a short time after drug use stops, and other changes are potentially permanent. One of the first changes in the brain that occurs in response to repeated drug abuse is tolerance. **Tolerance** develops when a person needs increasing doses of a drug to achieve the same "high" or "rush" that previously resulted from a lower dose of the drug. Two primary mechanisms underlie the development of tolerance.[3] First, the body may become more efficient at metabolizing the drug thereby reducing the amount that enters the bloodstream. Second, the cells of the body and brain may become more resistant to the effect of the drug. For example, after continued cocaine use, neurons decrease the number of dopamine receptors, which results in decreasing cocaine's stimulatory effect. Opiates, on the other hand, do not cause a change in the number of receptors. Instead the opiate receptors become less efficient in activating the second messenger system thus reducing the effects of the opiates.

Drugs can cause other long-term changes in the anatomy and physiology of the brain's neurons. Alcohol, methamphetamine, and MDMA (Ecstasy) can kill neurons.[3] Unlike other types of cells in the body, neurons in many parts of the brain have little or no capability to regenerate. (Recent studies have shown that the adult human brain can generate new neurons in the hippocampus, a part of the brain important for learning and memory.[5] Other parts of the brain do not show this ability.) Alcohol kills neurons in the part of the brain that helps create new memories. If those neurons die, the capability for learning decreases. Methamphetamine kills dopamine-containing neurons in animals and possibly in humans as well.[6] MDMA kills neurons that produce another neurotransmitter called serotonin.[7] In addition to neurotoxic effects, drugs can significantly alter the activity of the brain. PET scans of cocaine addicts show that the metabolism of glucose, the primary fuel for cells, is drastically reduced in the brain, and that this decrease in metabolism can last for many months following cessation of drug abuse.[8]

In addition to the functional and anatomical changes in the brain, drug abuse puts addicts at higher risk for other health problems. For example, inhalant abuse can lead to disruption of heart rhythms and snorting cocaine can lead to ulcerations in the mucous membranes of the nose. In addition, drug addicts are at increased risk of contracting HIV or AIDS through shared needles. Similarly,

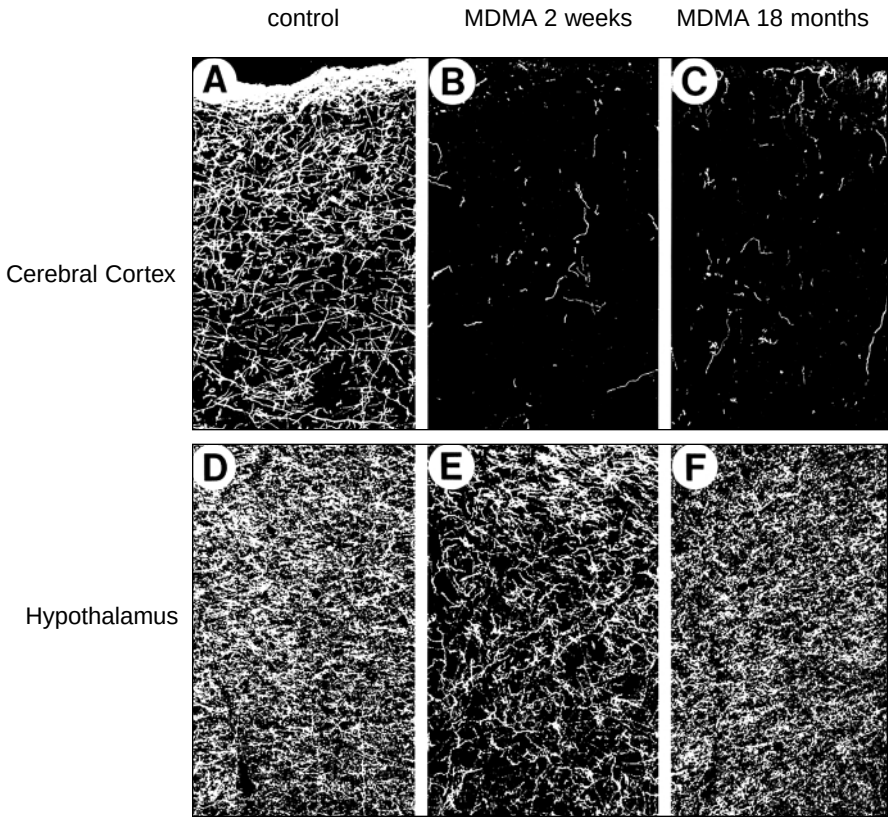


Figure 4.2. Photographs of serotonin axons in the cerebral cortex labeled with a fluorescent marker. The number of serotonin-labeled axons is dramatically reduced in the cerebral cortex at 2 weeks (B) and 18 months (C) after the last drug use. The brain of the control animal that did not receive MDMA (A) shows the dense network of labeled axons. Images E and F show changes caused by MDMA use on a different brain region, the hypothalamus. The control showing the hypothalamus in the absence of MDMA is shown in D. Photographs courtesy of G.A. Ricaurte, with the permission of the *Journal of Neuroscience.*

hepatitis B and hepatitis C are much more common among drug addicts than the general population. Tuberculosis is another concern. Drug abuse and addiction also are contributing factors in motor vehicle accidents.

Genetic, Behavioral, and Environmental Influences on Drug Addiction

Drug addiction is not simply continuous drug abuse. Many more individuals will try an addictive drug than will become addicted. Most people know of situations in which two people use the same amount of alcohol or tobacco, but have very different responses to them. Environmental, social, behavioral, and genetic factors also contribute to the development of drug addiction. Stress can increase the susceptibility to addiction.

Scientists continue to investigate the factors that place one individual at greater risk of becoming addicted than another individual with a similar pattern of drug use. Individuals who have developed strong coping skills to deal with life's pressures have less risk of becoming addicted to drugs. The younger a person is when he or she begins using drugs, the more likely he or she is to become addicted. This may be true because younger individuals have not developed the

Medical Uses of Addictive Drugs

Drugs of abuse can cause long-term impairment in brain function. But, are there times when addictive drugs can be beneficial to human health? The first drug that may come to mind is morphine. During the Civil War, doctors gave morphine to wounded soldiers to relieve the pain of brutal injuries. Doctors didn't realize how addictive injected morphine was until many soldiers became addicted to the drug.[2] Morphine addiction became known as "soldiers' disease." Today, morphine is a valuable medicine to relieve pain when administered with the appropriate medical supervision. Patients in hospitals receive morphine to ease their pain after surgery, and during cancer and burn treatment. Very few of these patients become addicted to morphine even though they may take it for extended periods of time.[9]

Another drug that has received considerable attention for its potential benefits is marijuana. Television and newspaper reports periodically present stories on the use of marijuana by terminal cancer or AIDS patients to ease their discomfort and pain. Scientists continue to investigate the potential benefits of marijuana because the studies conducted so far have been limited in focus or quality. In addition to causing changes in the brain, marijuana smoke contains many chemicals, some of which are carcinogenic to lung tissue.[10] Therefore, if it is to be an effective medicine, marijuana must be available in a safer form. The active ingredient in marijuana, tetrahydrocannabinol (THC), is currently available by prescription as an oral medication. This form of the drug is likely to be neither as addictive, nor as effective, as the smoked form because the drug breaks down in the digestive tract and takes longer to get into the bloodstream. Additional studies are needed to develop a form of THC that may be inhaled. The availability of an inhalable form of THC would stimulate research into its use as a medicine. However, other obstacles also exist. Are other medications safer and more effective than THC without causing the impairment of brain function and other health problems? If so, use of THC would be difficult to justify. In March 1999, the Institute of Medicine issued a report assessing what scientific studies have shown about marijuana's potential medicinal qualities.[10, 11] That report concluded that smoking marijuana may lead to significant health problems and that additional studies are necessary before the medical use of marijuana can be justified. The National Institutes of Health (NIH) does support quality, controlled research studies to investigate whether marijuana, and more specifically THC, may have potential beneficial effects as a medicine. Until those studies can be completed to determine if there is a scientific basis for medicinal claims, NIH believes marijuana should be viewed as an addictive drug that causes brain impairment, not as a medicine.

coping skills necessary to deal with life's ups and downs. Furthermore, the earlier drug use begins, the less likely treatment is to be effective. In addition, genetic factors probably influence who engages in higher-risk behaviors.

The context in which a person uses an addictive drug is important. For example, some cancer patients take relatively large doses of morphine for extended periods to control pain without becoming addicted. In one study of 12,000 patients who were given opioids (primarily morphine) for acute pain, only four individuals became addicted to the drugs. In another study of 38 chronic pain patients, most of whom received opioids for four to seven years, only two patients became addicted, and both had a history of drug abuse.[9] It is thought that addiction is rare in these pain patients because, unlike the stereotypical street addict, they are not taking the drugs to get "high" and to escape life, rather they take the drugs so they can get on with life. The drugs ease their pain and improve their quality of life.

In the 1970s, news media reported the use of marijuana and heroin by soldiers who were serving in Vietnam. Combat stress, the easy availability of drugs, and the relaxation of taboos against drug use at the time all contributed to the problem. While many soldiers did have drug problems while in Vietnam, 95 percent who were addicted to narcotics have had no addiction problems since they returned to the United States.[13]

Scientists continue to learn more about how genetic factors influence drug abuse and addiction. Heredity influences whether an individual has positive or negative sensations after smoking marijuana. One study demonstrated that identical male twins were more likely than non-identical male twins to report similar responses to marijuana use, indicating a genetic basis for their sensations.

Animals as Research Models

Why do scientists study the brains of non-human animals? Scientists use animals in research studies because the use of humans is either impossible or unethical. For example, when scientists investigate the effects of drugs of abuse on brain function, either the question they are asking cannot be answered in a living human or it would be inappropriate to give drugs to them.

The use of animals as subjects in scientific research has contributed to many important advances in scientific and medical knowledge. Scientists must analyze the goals of their experiments in order to select an animal species that is appropriate. Scientists often use fruit flies (*Drosophila melanogaster*) when they want to learn more about genetics. However, fruit flies are not a very good model if a scientist is investigating muscle physiology; a mouse may be a

Guidelines for the Use of Animals in Scientific Research

Scientists who use animals as research subjects must abide by federal policies that govern the use and care of vertebrate animals in research. The Public Health Service established a policy that dictates specific requirements for animal care and use in research. This policy conforms to the Health Research Extension Act of 1985 (Public Law 99-158) and applies to all research, research training, biological testing, and other activities that involve animals.[14] The principles for using and caring for vertebrate animals in research and testing are as follows:

- The transportation, care, and use of animals should be in accordance with the Animal Welfare Act and other applicable Federal laws, guidelines, and policies.
- Procedures involving animals should be designed with consideration of their relevance to human or animal health, the advancement of knowledge, or the good of society.
- The animals selected should be of an appropriate species and quality and the minimum number required to obtain valid results. Methods such as mathematical models, computer simulation, and *in vitro* biological systems should be considered.
- Procedures should minimize discomfort, distress, and pain to the animals.
- Procedures that may cause more than momentary or slight pain should be performed with appropriate sedation, analgesia, or anesthesia.
- Animals that would suffer severe or chronic pain or distress that cannot be relieved should be painlessly killed.
- The living conditions of animals should be appropriate for the species. The housing, feeding, and care of animals must be directed by a veterinarian or a trained, experienced scientist.
- Investigators who work with animals must be appropriately qualified and trained for conducting procedures on living animals.
- Exceptions to any of these principles must be reviewed and approved by an appropriate committee prior to the procedure.
- An Institutional Animal Care and Use Committee (IACUC) oversees all animal use in each institution where animal research is conducted. The IACUC must give approval for the research plan and species to be used. IACUCs include both scientists and nonscientists from outside the institution. Nonscientists are often representatives of humane organizations.

better model for those experiments. Although scientists strive to develop non-animal models for research, these models often do not duplicate the complex animal or human body. Continued progress toward a more complete understanding of human and animal health depends on the use of living animals.

In Advance

CD-ROM Activities	
Activity Number	**CD-ROM**
Activity 1	no
Activity 2	no
Activity 3	no
Activity 4	no
Activity 5	yes

Photocopies	
For the class	**For each student**
1 transparency of Master 4.4, *Playing the Game* 1 transparency of Master 4.5, *Who Is Addicted?*	1 copy of Master 4.1, *Data for Rat Self-administration Experiment* 1 copy of Master 4.2, *Worksheet for Rat Experiment Data* 1 copy of Master 4.3, *Evaluating the Experiment* 1 copy of Master 4.6, *Long-term Effects of Drugs on the Brain* (only if using the non-CD-ROM activity)

Materials	
Activity 1	none
Activity 2	colored pencils overhead projector transparency
Activity 3	playing cards (one deck for each group of 3 students; see Preparation section) overhead projector
Activity 4	overhead projector
Activity 5	computers

Preparation

Gather decks of playing cards for use in Activity 3. Each group of 3 students can share one deck of cards. Separate the face cards (jacks, queens, and kings) and place them in one pile. Place the aces and number cards in another pile.

Arrange for students to have access to computers for viewing the CD-ROM mini-documentary in Activity 5.

Procedure

Content Standard F: An individual's mood and behavior may be modified by substances.

ACTIVITY 1: HOW DOES DRUG ABUSE BEGIN?

1. **Begin the activity by holding a class discussion. Ask students "What is a drug?" Write their answers on the chalkboard or on an overhead transparency. Give students the opportunity to present differing views.**

   Students will respond with a variety of answers. Some will give examples of illegal drugs, such as marijuana or cocaine, others may give the names of prescription medications. If so, prompt students to think about a definition for the word *drug*. Some students will describe a drug either as an illegal substance that harms a person's health or as a chemical that a person takes to treat a disease or illness. At this point, based on students' knowledge, both definitions are correct.

   Several terms will be introduced in this lesson. It is **very important** to use these terms according to the definitions provided.

2. **Write the following definitions for *drug* and *medication* on the board or transparency and inform students that, for this discussion, you will use the terms according to the following definitions.**

   - **A *medication* is a drug that is used to treat an illness or disease according to established medical guidelines.**
   - **A *drug* is a chemical compound or substance that can alter the structure and function of the body. Psychoactive drugs affect the function of the brain, and some of these may be illegal to use and possess.**

3. **If the students didn't do this in the previous question, ask them to consider examples for both medications and drugs. List each response in the proper category as a medication or a drug.**

   According to these definitions, all medications are drugs, but not all drugs are medications. This unit uses the word "drug" to refer to psychoactive drugs, or drugs of abuse. Drug abuse refers to the use of illicit drugs or to the inappropriate use of a legal drug, such as alcohol or nicotine.

   Societal and political factors sometimes influence into which category a substance falls. Alcohol and nicotine (tobacco) are drugs that are illegal to use and possess if the individual is below legal age, but not for adults to possess and use responsibly. Also, inhalants (paints, glues, and sprays, for example) are not illegal to possess when they are used for their intended purposes. However, they are drugs when used improperly to alter brain function.

Some students will raise the idea that medications can also be drugs if they are used inappropriately. For example, overuse of a prescription medication, such as a sedative, is inappropriate and could be considered a drug in that case. Alternatively, students may indicate that morphine is an illegal drug when used without medical supervision, but is a valuable medicine when used appropriately in a hospital, or at home, to relieve pain associated with various diseases. Students may also propose that marijuana can be a medication to relieve the pain that accompanies various diseases. (In some states, marijuana is legal as a medication, but is illegal according to Federal law.) If students bring this up, point out to them that scientists need to continue studying marijuana to determine if it may be effective as a medicine. Marijuana contains hundreds of chemical compounds; the effects of most of these compounds in the body are unknown. Marijuana also poses many problems outside of the brain, such as cancer. Use this as an opportunity to inform students that scientific research is being done to determine if marijuana is more effective than other medicines (see the Background Information section).

4. **Ask students to respond to the question: Why do people start abusing drugs?**

   Students may provide a wide range of answers to this question including peer pressure, experimentation, boredom, or fun. Some students may also respond that people take drugs to escape from life's pressures.

ACTIVITY 2: DRUG ABUSE IS VOLUNTARY; ADDICTION IS COMPULSIVE

1. **For this activity, students will work in groups of four. Prior to having students divide into their small groups, set the stage for the activity. Tell students they will be analyzing data from experiments using rats. For the experiments, rats were placed in individual cages with two levers that the rat could press. If the rat pressed the food lever, a pellet of food was released. If the stimulus lever was pressed, the rat received an injection or an electrical stimulus.**

   Students may ask what substance was injected in response to the press of the stimulus lever. Tell students that the answer to that question will be revealed during the activity.

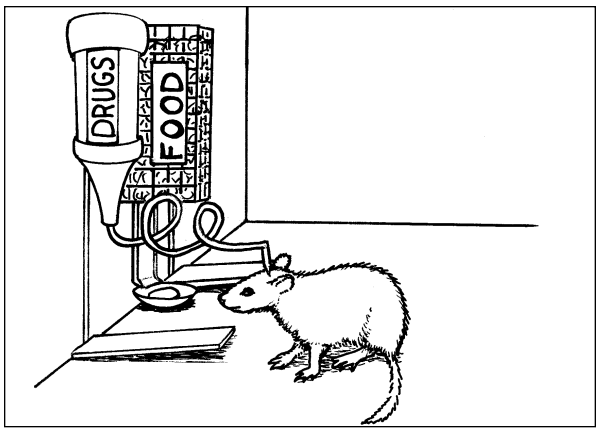


Figure 4.3 Diagram of a rat in a cage during a drug self-administration experiment.

Content Standard A: Mathematics is essential in scientific inquiry.
Content Standard A: Scientists rely on technology to enhance the gathering and manipulation of data.
Content Standard C: Organisms have behavioral responses to internal changes and to external stimuli.
Content Standard F: An individual's mood and behavior may be modified by substances.

2. **Give each student a copy of Masters 4.1, *Data for Rat Self-administration Experiments*, and 4.2, *Worksheet for Rat Experiment Data*. Each student will graph on Master 4.2 the data for only one of the rats. Instruct the teams to decide which member will graph the data for rat A, B, C, and D. The students will plot the total number of times that the rat presses the stimulus lever vs. time and the total number of times that the rat presses the food lever vs. time.**

   The graph of the data for each rat will have two lines, one for the stimulus lever and one for the food lever. Students can use a different color of pencil for plotting each set of data, or they can use a solid line and a dashed line to distinguish between the two graph lines.

3. **After students have completed their graphs, give each student a copy of Master 4.3, *Evaluating the Experiment*. Each student should share his or her graph with the other members of the group. Group members then discuss the similarities and differences among the rats' responses and answer the questions on Master 4.3.**

4. **When the groups are finished answering the questions, hold a class discussion to ensure that each group has come to the appropriate conclusions.**

SAMPLE ANSWERS TO QUESTIONS ON MASTER 4.3

Question 1. Why do the rats press a lever the first time?

The rats initially press a lever while they are exploring the cage. The rat may even press the lever by accident. Whether the rat presses the food lever or the stimulus lever first is usually random.

Question 2. Compare the lever-pressing behaviors of the four different rats. Which rat pressed the stimulus lever the most? Which one pressed the stimulus lever the least? Which rat pressed the food lever the most? Which one pressed the food lever the least?

Rats A and C pressed the stimulus lever about the same number of times and many more times than either Rat B or Rat D. Rats B and D did not press the stimulus lever very many times, but they pressed the food lever more times than Rats A and C did. Overall, Rats A and C behaved similarly and Rats B and D behaved similarly.

Question 3. Rat A was injected with cocaine each time it pressed the stimulus lever. Can you use this fact to explain why Rat A behaved the way it did?

The cocaine activated the reward system in the brain and caused the rat to continue its stimulus lever-pressing behavior. If necessary, remind students that the reward system is the part of the brain stimulated by drugs to cause feelings of pleasure.

Question 4. Based on the data you analyzed, do you think Rat B was injected with cocaine when it pressed the stimulus lever? From what you have learned so far in this unit, do you think Rat B was injected with a different addictive drug when it pressed the stimulus lever? Why?

It appears that Rat B was not injected with cocaine when it pressed the stimulus lever because its behavior was very different from Rat A. If Rat B was injected with cocaine or another addictive drug, it should display behavior similar to Rat A.

(Rat B actually received a saline injection when it pressed the stimulus lever.)

Question 5. Do you think Rat C received cocaine when it pressed the stimulus lever? Why?

It is possible that Rat C received cocaine when it pressed the stimulus lever because its behavior was very similar to that of Rat A. However, you cannot be sure if it was cocaine.

Question 6. Rat C did not receive an injection of cocaine when it pressed the stimulus lever. When Rat C pressed the stimulus lever, it received a mild electrical stimulation in the brain. Based on what you have learned, can you predict what part of the brain was stimulated?

The reward system (ventral tegmental area or nucleus accumbens) is the part of the brain stimulated. Stimulation in that area of the brain caused the rat to continue pressing the stimulus lever.

Question 7. Rat D also received a mild electrical stimulation in the brain when it pressed the stimulus lever. Do you think the same part of the brain was stimulated in Rat D as was stimulated in Rat C? Why?

Rat D did not receive an electrical stimulation in the same part of the brain that was stimulated in Rat C. If the same part of the brain, the reward system, was stimulated, Rat D should behave similarly to Rat C.

(Rat D received an electrical shock in the cerebellum, which is not part of the reward pathway.)

Question 8. Why did Rats A and C press the stimulus lever more than the food lever?

Rats A and C received a greater "reward" when they pressed the stimulus lever than they did when they pressed the food lever.

Question 9. Why did Rats B and D press the food lever more than the stimulus lever?

Rats B and D received greater "reward" when they pressed the food lever than they did when they pressed the stimulus lever.

Question 10. Why did the scientists who conducted this experiment include Rats B, C, and D in this experiment? How did the data from those rats help scientists understand more about how cocaine acts in the brain?

Rats B, C, and D were used as controls in this experiment. Rat B received a saline injection after pressing the stimulus lever. (The cocaine that Rat A received was dissolved in a saline solution.) Because Rat B's behavior

differed from Rat A's behavior, this suggests that the cocaine that Rat A received caused the frequent stimulus lever-pressing behavior. Because both rats had a canula inserted to deliver the solution, the process of inserting the canula is not sufficient to cause Rat A's behavior.

The data from Rat C reveal that electrical stimulation of the VTA elicits behavior similar to that caused by cocaine injection. Because cocaine is known to act on neurons in the VTA, these data reinforce the findings from Rat A that the cocaine acting on the VTA neurons causes the frequent stimulus lever-pressing behavior.

Rat D received electrical stimulation in the cerebellum after pressing the stimulus lever. The cerebellum is not part of the reward system. These data show that stimulation to a discrete brain area, the reward system, causes Rat C's behavior. Inserting the electrode into other areas of the brain is not sufficient to elicit the rapid stimulus lever-pressing behavior observed in Rat C.

Question 11. Do you think that Rats A and C will stop pressing the stimulus lever if they continue to receive the same stimulation each time they press it? Why?

Based on the data, it does not seem likely that Rats A and C would stop pressing the stimulus lever because the number of times it is pressed continues to increase within each five minute period. Students may notice that Rat A pressed the stimulus lever more times during the last five-minute period of the experiment than it did during the first five-minute period

Question 12. Based on what you learned from these data, what might this investigation tell you about drug use by humans? Explain your view.

The data from the rat experiment show that the use of addictive drugs is reinforcing. Rats who are given cocaine want more cocaine. Because rats are mammals just as humans are and many of their organs function in ways similar to those in humans, the data suggest that drug use in humans is likely to be reinforcing as well: humans who take drugs will probably want to continue taking drugs.

5. Have students consider the question, Why do humans continue to abuse drugs?

Drug addicts continue to take drugs in spite of negative consequences. They know that their family, social, or career interactions are disrupted by their drug abuse, but they cannot stop. Drug-taking becomes *compulsive.* Rats A and C became conditioned to the activation of the reward system by the administration of cocaine or electrictrical stimulation in the VTA in response to a lever press. Those rats continued to press the stimulus bar in their cages and ignored the food lever. The cocaine or electrical stimulation in the VTA was a bigger reward for the rats than was the food. In humans, drugs cause a compulsive need for more drugs.

6. Write the following definition of addiction on the chalkboard or overhead transparency.

- ***Addiction* is the continued compulsive use of drugs in spite of adverse health or social consequences.**

7. Ask students to consider what they learned from the data concerning the continued use of cocaine by Rat A and the continued stimulation of the reward pathway in Rat C. Did Rat A and Rat C experience any adverse effects from their treatments? What adverse consequences do human drug addicts experience?

Although it is not appropriate to refer to the rats as addicted to cocaine, those rats would have experienced adverse effects if the experiment continued for a long time. If the experiments continued and the rats continued to push only the stimulus lever, the lack of food and water would lead to adverse health consequences. If the scientists did not stop the experiment, the rats would have continued to press the stimulus lever until they died from a cocaine overdose.

Human addicts are most concerned with their next drug use. Because of this, they often eat little or poorly and consequently suffer the adverse health consequences of poor nutrition.

8. Ask students to consider the distinction between drug abuse and drug addiction in humans.

- **When does abuse become addiction?**
- **What causes abuse to become addiction?**
- **Does the change from abuse to addiction occur at the same level (amount of drug taken, duration of drug abuse) of drug abuse for different individuals?**

Students should be able to use the previously given definition of addiction and the results of the cocaine self-administration experiments with rats to differentiate between drug abuse and addiction. Abuse is voluntary; addiction is the compulsive, continued drug use in spite of adverse health or social consequences.

Scientists do not know what causes a drug abuser to become an addict. Continuing research is attempting to answer this question.

ACTIVITY 3: WHEN DOES ABUSE BECOME ADDICTION?

1. Divide the class into groups of 3 students. Give each group a deck of cards that have been divided into two piles. Tell the students that the small pile contains the face cards and the larger pile has the aces and number cards.

2. Display a transparency of Master 4.4, *Playing the Game*, showing the instructions for the game. Have students play through the game. Each student in the group will play individually, but the group members share the deck of cards.

Content Standard F: Personal choice concerning fitness and health involves multiple factors.

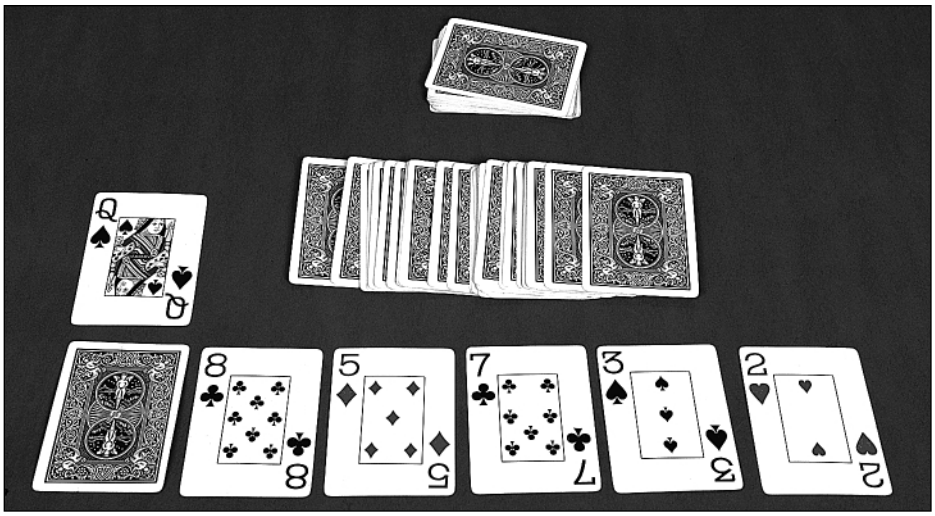


Figure 4.4: The arrangement of cards during the game.

3. **When all the groups have finished the game, discuss the game and the results of the game with them. The value of this activity lies in the discussion and questions that it may generate. The following sample questions can guide the discussion.**

   • **How many choice cards did each person pick?**

   Students will draw different numbers of cards before they decide to stop.

   • **How many people equaled or went over the value of the switch card?**

   Some students will decide to play it safe whereas other students will risk going over the switch value.

   • **How does this game relate to drug abuse and drug addiction?**

   This game relates to abuse and addiction in that each person who continues to abuse drugs will reach some point that, if surpassed, will change the person and the person's brain from a drug abuser to a drug addict. Each person has risk factors and each person can make choices about abusing drugs.

   • **What does the switch card mean in regard to drug addiction?**

   When a person abuses drugs, there is some point at which the person's brain changes and the individual becomes compulsive about using drugs despite negative consequences. Scientists do not know what factors control the "switch" between drug abuse and addiction.

   • **Is everyone's switch level the same?**

   In the card game, students choose one of three cards, each assigned an arbitrary value, as their *switch* card. In life, a person does not know when he or she will reach the point where drug abuse switches to drug addiction. For

some people, that change will occur earlier in their drug abuse while other people will abuse drugs extensively before they become addicted.

• **What does the risk card mean?**

The risk card symbolizes that there are factors that influence the outcome. An individual does not know what all the risks are or how great their influence is.

• **Is everyone's risk card the same?**

Different students will have different risk cards. In life, people who abuse drugs have different risks of becoming addicted.

• **Why is the risk card face down?**

The risk card is face down because a person does not know all of the risk factors that help determine if a person becomes addicted.

• **What factors influence a person's risk of becoming addicted to drugs?**

Many factors influence whether a person becomes addicted to drugs. Some of these include genetics, family influence, influence of friends, age at which drug abuse begins (a person who begins using drugs early in life is more likely to become addicted), context of drug use, and the development of coping skills.

• **What do the choice cards represent?**

Each choice card in this model represents an episode of drug use.

Students likely will try to assign meaning to the numbers on the choice cards. For example, they may equate a 2 with drinking a low alcohol beer and a 10 with heroin injection. These correlations are difficult to make with any accuracy. For example, a person may smoke a small amount of marijuana believing that it contains a low dose of THC. If that marijuana is of a potent strain that contains a high level of THC, the individual could receive a higher dose than if he or she smoked a larger dose of a less potent strain of marijuana.

Like most models, this one has imperfections. The discussion that this issue may generate among students can be valuable because it causes them to question drug abuse.

• **If a total score that equals or goes over the switch value indicates addiction, did anyone become addicted to drugs with the first drug use?**

The point values in the game have been assigned so that the player cannot reach the switch value after drawing one choice card. This correlates with addiction; no one becomes addicted with one episode of drug abuse.

Important note: This is true with the outcome of the game being *drug addiction* if the switch value is reached. This is not true if the designated outcome is *death* if the switch value is reached. A person can die from the first

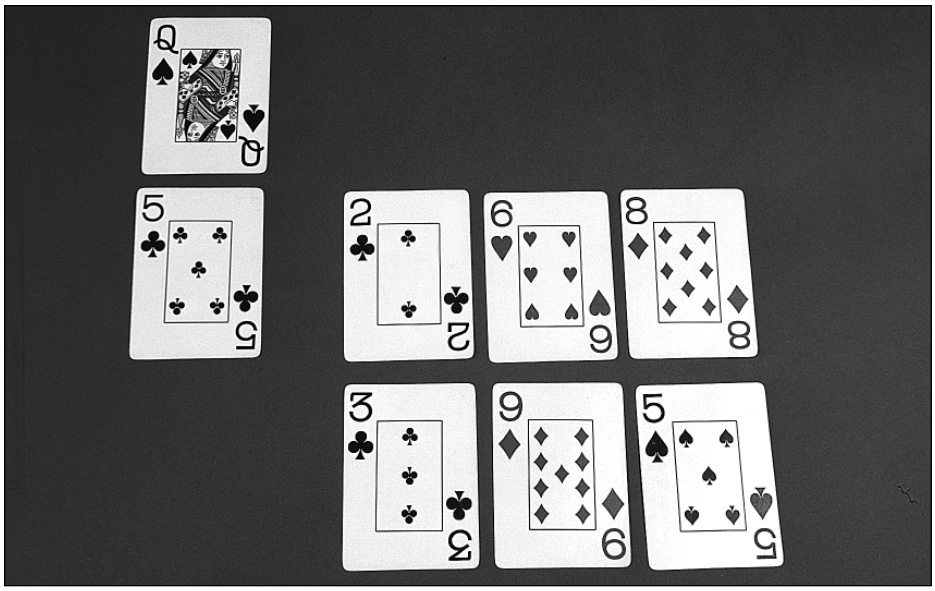


Figure 4.5: Sample card hand #1. The player had a moderate switch value (the switch card is a queen). The student elected to draw 6 choice cards totaling 33 points before finding out that the risk card had a value of 5. The 38-point total put the score over the switch value (35), signifying addiction.

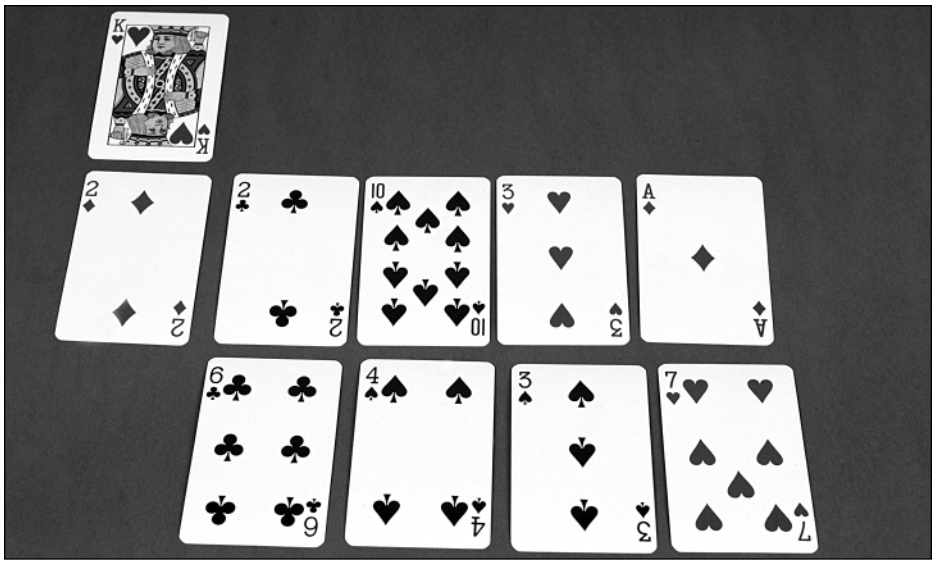


Figure 4.6: Sample card hand #2. The player had a higher switch card (king = 45 points) and elected to draw 8 choice cards totaling 36 points. Because the risk card was low (a 2), the 38-point total was still below the switch value, signifying drug abuse.

episode of drug abuse. After one use, drugs do not change the brain sufficiently to cause addiction. However, drugs can affect other body systems and cause them to fail. See Step #9 (on page 92) for a modification of the game to address this. Also, although a person does not become *addicted* to drugs after one use, one episode can cause some changes to start occurring in the brain. For example, one use of crack cocaine can cause the abuser to experience cravings for the drug.

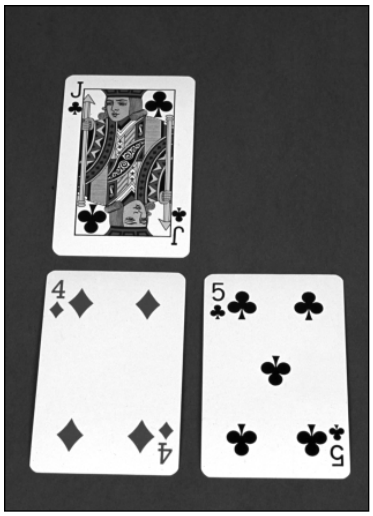


Figure 4.7: Sample card hand #3. The player elected to draw only one choice card, a 5, to ensure that the total of risk (which turned out to be a 4) and choice cards remained below the switch value of 25 points (jack = 25 points).

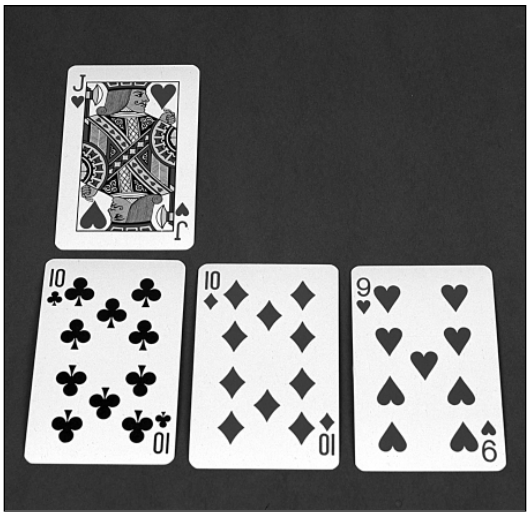


Figure 4.8: Sample card hand #4. The player drew a low switch card (a jack = 25 points) and a high risk card (a 10). Because the choice cards have high point values, the total of just two cards totaled more than the switch value, signifying drug addiction.

4. Have the students play the game again now that they can relate the game to the issues of drug abuse and drug addiction.

5. Ask students if they played the game any differently this time. Did they make different choices?

Some students will continue to risk drawing more choice cards and get closer to the switch value. Other students may elect not to draw any choice cards.

Some students might bring up questions relating to a hand containing a high switch card, a low risk card, and some low choice cards so that they can continue to draw more cards. Students may feel that this scenario would lead them to continue to experiment with drugs. You can respond by asking them what choices they would make if they drew a low switch card and a high risk card. (Perhaps the numbers on the cards are lower or higher than the assigned values. For example, what if the switch card had a value of 22 points and the risk card had a value of 12 points? Would this change the decision about drawing additional cards?) This scenario leads into the next step of the activity in which students consider that the switch point really is unknown.

6. **Discuss the idea of the switch card with students. Does anyone really know at what point in drug abuse the brain changes and the abuser becomes an addict? How could you modify the card game to account for this?**

   In life, a person does not know when he or she will reach the point at which drug abuse becomes drug addiction. To reflect this in the card game, students can play the game leaving the switch card face down.

7. **When the students play the game this time, they will not look at the switch card. Have them keep the switch card face down and continue the game as before.**

8. **Continue the discussion of the game and its relation to drug abuse and drug addiction.**

   The main points that students should learn through this activity are:

   - Drug abuse involves choice.
   - The point at which a person's brain is changed and drug abuse becomes drug addiction is different and unknown for each individual.
   - Everyone has risk factors.
   - A person does not become addicted to drugs after one episode of abuse.

9. **(optional) A person does not become addicted to drugs after one episode of abuse, but a person can die as a result of one episode of drug abuse. The drugs can act on other body systems with a lethal outcome. If you want to modify the game to add this scenario, insert the jokers into each pile of choice cards and have the students play the game a fourth time. If a student draws a joker, the game is over for that student.**

   If you decide to do this optional modification to the game, make sure that students understand that the joker does *not* indicate addiction. The joker would, perhaps, represent a batch of drugs that contain a lethal contaminant that would cause some body organ to fail and, therefore, cause the abuser to die. Another person, for example, takes a large enough dose of opiates to completely inhibit the neurons in the brain that control respiration; those neurons no longer stimulate the lungs to contract, causing death.

Content Standard C: An individual's mood and behavior may be modified by substances.
Content Standard F: Personal choice concerning fitness and health involves multiple factors.

ACTIVITY 4: ENVIRONMENTAL, BEHAVIORAL, AND SOCIAL INFLUENCES ON DRUG ABUSE AND ADDICTION

Note to teachers: This activity, as described in the following steps, is designed as a class discussion. An alternative approach is to have individual students write their answers to the questions and then discuss the questions as a class.

1. **Display a transparency of Master 4.5, *Who Is Addicted?*, showing only the top section (to the first horizontal line). Ask students to answer the question.**

Students may respond differently to the question about who is addicted to morphine. At this stage, any answer is acceptable if the student can explain the reasoning underlying his or her answer. Some students will say that Chris is addicted because of the higher dose of morphine being taken over a longer period of time. Some students will say Pat because this could be a larger dose than what Chris is taking (if Chris is at 50 mg per day). Students could also believe that both individuals are addicted because of their continued drug abuse. Conversely, students could respond that possibly neither one is addicted and more information is needed before a judgment could be made.

2. Reveal the next section on Master 4.5 (to the next horizontal line). Again have students answer the question and discuss the responses.

Students may respond in a variety of ways. Answers could involve aspects of genetics, dose, or even random chance.

3. Reveal the remaining section of Master 4.5 and have students read the case studies.

4. Discuss the cases with the class. Use the following questions to guide the discussion.

- **Why did these two individuals begin taking morphine and then continue to take morphine?**

Pat began abusing morphine basically for social reasons. Chris began taking morphine for medical reasons.

- **What are the differences in *how* Chris and Pat take morphine?**

Pat takes an injection of morphine one time each day. Chris also receives morphine through injection, but he receives a dose many times each day.

- **How may these differences have influenced whether addiction develops?**

Although Chris receives a higher total dose of morphine during a day, each single injection is a smaller dose. The smaller single dose does not lead to the same "high" that results from a larger dose. Perhaps the fact that Chris does not feel the euphoria when he receives the morphine is important in keeping him from being addicted. (It is acceptable for students to propose answers here even if they cannot be sure.)

- **Is a larger dose of a drug the only factor to consider when thinking about the causes of drug addiction? Explain your answer based on the case studies**.

No, because Chris took a larger dose and did not become addicted.

- **Is the length of time that someone has been taking drugs enough to determine if addiction will develop? Explain your answer based on the case studies**.

No, because Chris took morphine for a longer period of time and did not become addicted while Pat took morphine for a shorter period of time and did become addicted.

- **What factors other than the amount (dose) of the drug taken and the period of time for which the drug is taken may contribute to addiction?**

The expectation of feeling a "rush" may be a factor. A person getting morphine in a hospital would not be taking morphine just to get that feeling. The context of drug (medication) use influences whether a person becomes addicted. Pat's use of drugs to escape problems contributed to the development of drug addiction.

The cases should reveal to the students that just a high dose of a drug is not enough to cause addiction. The behaviors and motivations for taking drugs are important factors in the development of addiction. The street addict was using drugs with the expectation of a rush, or high, and trying to escape life. The patient was taking drugs without the expectation of a high. The patient experiencing pain uses drugs in order to function normally. Scientists do not completely understand why pain patients do not become addicted after drug use, but the statistics clearly show that these individuals are at very low risk of becoming addicted.

You may also want to discuss the case of Vietnam veterans with students. For many years, the media portrayed Vietnam veterans as hopeless drug addicts. Although drug addiction was a problem for some men while in Vietnam, the vast majority of those veterans have had no problems with drug addiction since returning to the United States. They may have started using drugs (and subsequently became addicted) to relieve the stress of combat, to rebel against society, or even to relieve boredom, but once they were back in a "normal" environment, they were able to function without drugs.

Content Standard A: Scientists rely on technology to enhance the gathering and manipulation of data.

ACTIVITY 5: LONG-TERM EFFECTS OF DRUG ABUSE AND ADDICTION

Having students view the CD-ROM mini-documentary on the long-term effects of drugs on the brain is the strongly preferred approach for this activity. If computers with a CD-ROM drive are not available, follow the procedure for the alternate version of the activity (provided on page 95).

1. **Have students view the mini-documentary, *Long-Term Effects of Drugs on the Brain,* on the CD-ROM.**

To view the mini-documentary, load the CD-ROM onto the computers. From the main menu, select *Drug Abuse and Addiction*.

2. **After viewing the CD-ROM segment, ask students to write their answers briefly to the following questions.**

   - **What was the most surprising thing you learned about the effect of drugs?**

- **What makes this fact surprising to you?**
- **Based on what you have learned through the rat experiment analysis, the card game, and the mini-documentary, would you say that drug addiction is a disease? Justify your answer.**

Students should be encouraged to relate what they learned in Activities 1 through 4 to what they learned from the mini-documentary.

Having students write their answers to the questions encourages them to organize their thoughts and reflect on what they have learned. Listening to students explain their view about drug addiction as a disease will help you evaluate their understanding.

3. After students have completed their answers to the questions, discuss the questions as a class.

Drug addiction is a disease that causes physical and functional changes in the brain. This is similar to other diseases in which a part of the body does not function properly.

4. Encourage students to learn about how drugs affect other body systems by doing library or Internet searches.

Because the focus of this unit is on the brain, the curriculum supplement does not address how drugs act on other parts of the body. However, a great deal of additional information is available online. See the section, *Additional References for Teachers*, for some informative Web sites.

ALTERNATE VERSION OF ACTIVITY 5 FOR CLASSES WITHOUT ACCESS TO COMPUTERS

1. Give each student a copy of Master 4.6. Instruct students to read the handout *Long-term Effects of Drugs on the Brain* and answer the questions.

After students finish reading and answering the questions, discuss the responses as a class.

SAMPLE ANSWERS TO QUESTIONS ON MASTER 4.6

Question 1. What are some of the ways that drugs cause long-term changes in the brain?

The continued use of drugs may cause the brain to become resistant to the effects of the drug (tolerance). Some drugs, such as alcohol and MDMA, can kill brain cells. Cocaine and amphetamine can cause the activity level of the brain to decrease for a long period of time after drug use is stopped.

Question 2. How does the brain adapt to the presence of drugs?

The brain adapts to the presence of drugs by developing tolerance for the drug and by the development of cravings if drug use is stopped.

Question 3. How may the abuse of drugs relate to the plasticity of the brain?

Plasticity means that the brain can modify connections (synapses) in response to experiences. Drugs that cause neuron death can decrease the plasticity of the brain because neurons are not present to form new connections and because existing connections are lost.

Question 4. What are some problems that scientists have when they investigate the effects of drugs on the brain?

Scientists have difficulty investigating the effects of drugs on the brain because many drug abusers abuse more than one drug. Scientists must understand how each drug affects the brain and body because drugs taken in combination may have different effects. Also, many drug abusers have other medical conditions that make it difficult for scientists to determine what effects are due to the drug and what effects are due to the other medical problem.

2. **If students want to learn more about how drugs affect other parts of the body, encourage them to do library or Internet searches for additional information.**

   Because the focus of this unit is on the brain, the curriculum supplement does not address how drugs act on other parts of the body. A great deal of information is available online. See the section, *Additional References for Teachers*, for some informative Web sites.

Lesson 5
Elaborate/ Evaluate

Drug Addiction Is a Disease—So What Do We Do about It?

Photo courtesy of Gray Wolf Ranch Wilderness Recovery Lodge.

At a Glance

Overview

Students make predictions about the success rate for treatment of addiction compared with treatment for other chronic diseases. Then students evaluate case studies of individuals with different diseases to compare and contrast how the diseases are similar to, or different from, the others.

Major Concept

Drug addiction is a recurring chronic disease that can be treated effectively similar to other chronic diseases.

Objectives

By the end of these activities, the students will

- understand that addiction is a chronic disease that is likely to recur;
- recognize that treatment is most effective when it combines pharmacological and behavioral treatments;
- be able to explain how treatment for addiction is similar to that for other chronic diseases, such as diabetes or heart disease; and
- recognize that treatment is more effective if addicts, like people with other chronic diseases, choose to participate actively in their treatment.

Basic Science–Health Connection

Addiction has many dimensions and disrupts many aspects of a person's life. Scientific research and clinical practice have yielded a variety of effective approaches to treatment for addiction to certain drugs, such as heroin. Continuing research is yielding new approaches to developing medications to treat addiction to other drugs, such as cocaine, for which no medications are currently available.

Background Information

Drug abuse and addiction lead to long-term changes in the brain's chemistry and anatomy. The changes in the brain cause drug addicts not only to lose the ability to control their drug use, but their addiction also changes all aspects of their lives. Drug addicts often become isolated from family and friends and have trouble in school or work. In addition, the compulsive need for drugs can lead to significant legal problems. While the biological foundation for drug addiction does not absolve an individual from the responsibility of his or her actions, the stigma of drug addiction needs to be lifted so individuals may receive proper medical treatment, similar to that for other chronic diseases.[1]

Addiction is a recurring chronic disease. No cure is available at this time, but addiction can be treated effectively. Drug addiction is often viewed as a lapse in moral character. This value judgment influences how society deals with the disease, both socially and medically. Unfortunately, because people, including physicians, have often viewed addiction as a self-inflicted condition, drug addicts have not always received the medical treatment common for other chronic diseases. Treating addiction requires more than a "just say no" approach.

Treatment for addiction is often very effective. Treatment is successful when the addict reduces or abstains from drug use, improves his or her personal health or social function, and becomes less of a threat to public health and safety.[2] Certain addictions, such as heroin addiction, can be treated with pharmacological agents.[3,4] Methadone, the most common pharmacological treatment, prevents craving and withdrawal symptoms in heroin addiction. Methadone is an opiate receptor agonist. That is, methadone binds to the opiate receptor just as heroin does. Methadone, however, does not produce the euphoria or "high" that results from heroin use.

Figure 5.1: Methadone can be part of an effective treatment plan for addiction to opiates. Photograph of pills by, and used with permission of, Roxane Laboratories, Inc. All Rights Reserved.

A second medication prescribed for heroin addiction is naltrexone. Unlike methadone, naltrexone is an opiate receptor antagonist. Instead of competing with heroin for the opiate receptor, naltrexone prevents heroin from binding to the receptor, thereby preventing heroin from eliciting the euphoric high.

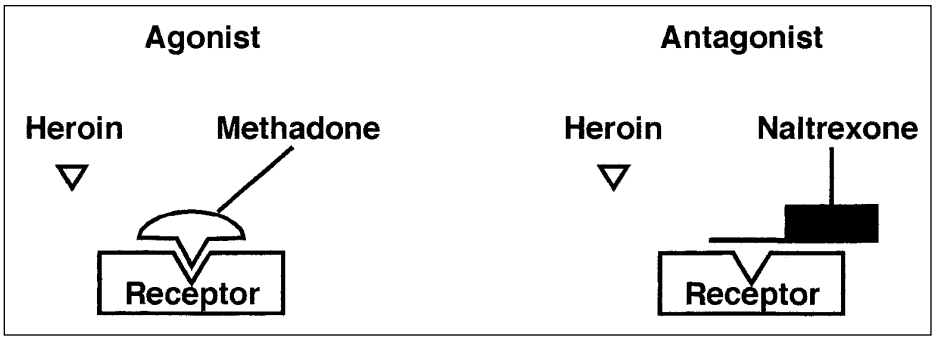


Figure 5.2: **Agonists** are chemicals that bind to a specific receptor to elicit a response, such as excitation or inhibition of action potentials. Methadone is an agonist that, like heroin, binds to opiate receptors. Unlike heroin, however, methadone does not produce the same level of euphoria. **Antagonists** are chemicals that bind to a receptor and block it, producing no response and preventing other chemicals (drugs or receptor agonists) from binding or attaching to the receptor. Naltrexone is an antagonist that binds to the opiate receptor and blocks heroin from binding.

Table 5.1 outlines the different pharmacological agents used to treat addiction. The development of medications to treat drug addiction has been difficult because the brain, the target of addictive drugs, is such a complex organ. Until scientists understand how drugs affect the chemistry of the brain, they cannot develop medicines that will alter the effects of addictive drugs.

Table 5.1: Pharmacological Treatments for Addiction[4]

Medication	Treatment for addiction to:	Mechanism
Methadone	Heroin	Opiate receptor agonist
LAAM	Heroin	Opiate receptor agonist
Naltrexone	Heroin	Opiate receptor antagonist
Naloxone	Heroin, alcohol	Opiate receptor antagonist
Buprenorphine	Heroin	Mixed opiate receptor agonist and antagonist
Nicotine gum, patches	Nicotine	Provide low doses of nicotine

Pharmacological therapies, if available, are not sufficient for effective treatment. Behavioral treatment in combination with pharmacological treatment is the most effective way to treat drug addiction.[5, 6] Recovering addicts need to address the behavioral and social consequences of their drug use and learn to cope with the social and environmental factors that contribute to their illness.[7] Behavioral treatments can occur either individually or as a group.[6]

Relapse is a common event for recovering drug addicts. In many ways, relapse should be thought of as a normal part of the recovery process. A recovering drug addict is more likely to experience a relapse if he or she also has other psychiatric conditions or lacks the support of family and friends.

Principles of Effective Drug Addiction Treatment

1. No single treatment is appropriate for all individuals. Matching treatment settings, interventions, and services to each individual's particular problems and needs is critical to his or her ultimate success in returning to productive functioning in the family, workplace, and society.

2. Treatment needs to be readily available. Because individuals who are addicted to drugs may be uncertain about entering treatment, taking advantage of opportunities when they are ready for treatment is crucial. Potential applicants can be lost if treatment is not immediately or readily available.

3. Effective treatment attends to multiple needs of the individual, not just his or her drug use. To be effective, treatment must address the individual's drug use and any associated medical, psychological, social, vocational, and legal problems.

4. An individual's treatment and services plan must be assessed continually and modified as necessary to ensure that the plan meets the person's changing needs. A patient may require varying combinations of services and treatment components during the course of treatment and recovery. In addition to counseling or psychotherapy, a patient at times may require medication, other medical services, family therapy, parenting instruction, vocational rehabilitation, and social and legal services. It is critical that the treatment approach be appropriate to the individual's age, gender, ethnicity, and culture.

5. Remaining in treatment for an adequate period of time is critical for treatment effectiveness. The appropriate duration for an individual depends on his or her problems and needs. Research indicates that for most patients, the threshold of significant improvement is reached at about three months in treatment. After this threshold is reached, additional treatment can produce further progress toward recovery. Because people often leave treatment prematurely, programs should include strategies to engage and keep patients in treatment.

6. Counseling (individual and/or group) and other behavioral therapies are critical components of effective treatment for addiction. In therapy, patients address issues of motivation, build skills to resist drug use, replace drug-using activities with constructive and rewarding nondrug-using activities, and improve problem-solving abilities. Behavioral therapy also facilitates interpersonal relationships and the individual's ability to function in the family and community.

7. Medications are an important element of treatment for many patients, especially when combined with counseling and other behavioral therapies. Methadone and levo-alpha-acetylmethadol (LAAM) are very effective in helping individuals addicted to heroin or other opiates stabilize their lives and reduce their illicit drug use. Naltrexone is also an effective medication for some opiate addicts and some patients with co-occurring alcohol dependence. For persons addicted to nicotine, a nicotine replacement product (such as patches or gum) or an oral medication (such as bupropion) can be an effective component of treatment. For patients with mental disorders, both behavioral treatments and medications can be critically important.

8. Addicted or drug-abusing individuals with coexisting mental disorders should have both disorders treated in an integrated way. Because addictive disorders and mental disorders often occur in the same individual, patients presenting for either condition should be assessed and treated for the co-occurrence of the other type of disorder.

9. Medical detoxification is only the first stage of addiction treatment and by itself does little to change long-term drug use. Medical detoxification safely manages the acute physical symptoms of withdrawal associated with stopping drug use. While detoxification alone is rarely sufficient to help addicts achieve long-term abstinence, for some individuals it is a strongly indicated precursor to effective drug addiction treatment.

10. Treatment does not need to be voluntary to be effective. Strong motivation can facilitate the treatment process. Sanctions or enticements in the family, employment setting, or criminal justice system can increase significantly both treatment entry and retention rates and the success of drug treatment interventions.

11. Possible drug use during treatment must be monitored continuously. Lapses to drug use can occur during treatment. The objective monitoring of a patient's drug and alcohol use during treatment, such as through urinalysis or other tests, can help the patient withstand urges to use drugs. Such monitoring also can provide early evidence of drug use so that the individual's treatment plan can be adjusted. Feedback to patients who test positive for illicit drug use is an important element of monitoring.

12. Treatment programs should provide assessment for HIV/AIDS, hepatitis B and C, tuberculosis and other infectious diseases, and counseling to help patients modify or change behaviors that place themselves or others at risk of infection. Counseling can help patients avoid high-risk behavior. Counseling also can help people who are already infected manage their illness.

13. Recovery from drug addiction can be a long-term process and frequently requires multiple episodes of treatment. As with other chronic illnesses, relapses to drug use can occur during or after successful treatment episodes. Addicted individuals may require prolonged treatment and multiple episodes of treatment to achieve long-term abstinence and fully restored functioning. Participation in self-help support programs during and following treatment often is helpful in maintaining abstinence.

Source: *Principles of Drug Addiction Treatment: A Research-based Guide* (1999) National Institute on Drug Abuse [online] *http://www.nida.nih.gov/PODAT/PODATIndex.html*.

Despite the preconceptions and value judgments many people place on addiction, it is, in many ways, similar to other chronic diseases such as diabetes and coronary artery disease. Genetic, environmental, and behavioral components contribute to each of these diseases. Some people may argue that drug addiction is different because it is "self-inflicted." As presented in Lesson 4, the initial choice to use drugs is voluntary but, once addiction develops, drug use is compulsive—not voluntary. Moreover, voluntary choices do contribute to the onset or severity of other chronic diseases as well. For example, a person who chooses to eat an unhealthy diet and not exercise increases his or her risk for coronary heart disease.

Successful treatment for any chronic disease necessitates patient compliance with the prescribed treatment regimen. Adhering to a treatment plan is difficult for those with any chronic disease. Less than 50 percent of diabetics follow their routine medication plan, and only 30 percent follow their dietary guidelines.[2] Problems adhering to a treatment plan lead to about 50 percent of diabetics needing to be treated again within one year of diagnosis and initial treatment. Similar statistics hold true for other chronic diseases: approximately 40 percent of patients with hypertension need emergency room treatment for episodes of extreme high blood pressure, and only about 30 percent of adult asthma sufferers take their medication as prescribed. Although treatment for drug addiction statistically is more successful than treatment for other chronic diseases, drug addicts commonly have relapses during treatment and recovery and begin using drugs again. The difficulties in following a treatment plan and coping with the stresses of a chronic disease illustrate how difficult changing human behavior is. Activities 2 and 3 of this lesson provide more insight into this topic.

Scientific research is likely to change how drug addiction is treated. Research to understand how the brain works and how drugs cause changes in the chemistry and function of the brain may lead to new medications to treat disease. Scientists continue to work on developing medications that relieve the cravings, experienced when drugs are withdrawn. Also, scientific advances may reveal ways to reverse the long-term damage to the brain that drugs inflict.

In Advance

CD-ROM Activities	
Activity Number	**CD-ROM**
Activity 1	no
Activity 2	yes
Activity 3	no
Activity 4	no

Photocopies		
For the class	**For each group of 3 students**	**For each student**
1 transparency of Master 5.1, *Ranking Disease Treatment Outcomes*	1 copy of Master 5.2, *Ruth's Story* [a] 1 copy of Master 5.3, *Mike's Story* [a] 1 copy of Master 5.4, *Carol's Story* [a] 1 copy of Master 5.5, *Disease Reference Information* [a]	1 copy of Master 5.6, *Evaluating the Cases*

[a] The CD-ROM version of Activity 2 is the preferred approach. Copies of Masters 5.2, 5.3, 5.4, and 5.5, are needed only if the CD-ROM is unavailable for classroom use.

Materials	
Activity 1	overhead projector
Activity 2	computers (optional)
Activity 3	overhead projector
Activity 4	none

Preparation

Arrange for students to have access to computers for viewing the case studies in Activity 2.

Procedure

This activity is intended to be a quick method to assess students' prior conceptions about treating drug addiction as a disease.

ACTIVITY 1: HOW EFFECTIVE IS TREATMENT?

1. **Begin the activity by holding a classroom discussion about illness and disease. Ask students to name some diseases. Write their responses on the board. What is a disease? What do you do when you have a disease? Why?**

   Students are likely to say a disease is some problem with the body that makes a person feel bad. They may also respond that a disease is something for which you see a doctor or for which you take medicine.

2. **Do all diseases or illnesses affect people in the same way? Are different diseases treated the same way?**

No, some are longer lasting and require more intervention from a doctor. Some require medicines and some require psychological treatment. The students may give a cold as an example of a short-term illness that doesn't require a great deal of treatment. Some students may bring up diabetes or heart disease as a longer-lasting illness that does require a great deal of treatment. Through these questions, students realize that there are similarities as well as differences in disease treatment.

3. **Introduce the terms *chronic* and *acute* and give examples of chronic and acute conditions. Categorize the diseases that were listed in Step 1 as either chronic or acute.**

   Chronic diseases are those that persist over a long period of time whereas *acute* diseases are of short duration but may have marked intensity and a rapid onset. Diabetes, heart disease, asthma, and cancer are examples of chronic diseases. Colds, flu, or a broken bone are acute conditions.

4. **Ask students to consider whether addiction is chronic or acute. Have them explain their answer based upon what they have learned in the unit so far.**

   Addiction is a chronic disease. The explanations should include something about the changes that occur in the brain as a result of drug use (Lessons 2, 3, and 4) and something about the compulsive, non-voluntary nature of addiction.

5. **Display a transparency of Master 5.1, *Ranking Disease Treatment Outcomes* (or write a similar chart on the board). Ask several students to rank the diseases according to success of treatment. The most successfully treated disease is assigned the #1 and the least successfully treated disease is assigned the #3. Write the responses given by many students. At this time, students can give reasons for their guesses. Summarize the rankings acknowledging the different opinions. Tell them you will return to this activity later.**

   Students will have misconceptions about how successful the treatment for addiction is. Students are likely to guess that treatment for addiction is less successful than treatment for other diseases. They may base their explanations on societal perceptions of addiction and not on knowledge of the biology of addiction. Some students may say that they do not have any information on which to base a ranking because each individual is different. Acknowledge that this is true, but point out that you are asking them to make a judgment about a group of people who are affected with each disease, not on how a specific individual will do in treatment. At this point, accept the students' rankings of treatment success.

ACTIVITY 2: EVALUATING THE CASE STUDIES

The following procedures describe how to conduct the CD-ROM version of this activity, which is the preferred method of instruction. Instructions for conducting the alternative print version follow.

Content Standard F: An individual's mood and behavior may be modified by substances.
Content Standard F: Personal choice concerning fitness and health involves multiple factors.
Content Standard F: Families serve basic health needs, especially for young children.

1. **Divide the class into groups of three students. Give each student a copy of Master 5.6, *Evaluating the Cases*. Have the students complete the CD-ROM activity, *Dealing with a Chronic Disease*. Each member of the group should answer questions 1-6 for a different case study. After they watch the three cases, the group should answer questions 7-11.**

   From the main menu on the CD-ROM, select *Drug Addiction Is a Disease—So What Do We Do About It*? Then click to watch the video interviews.

2. **As a class, discuss the case studies and the answers to Master 5.6.**

SAMPLE ANSWERS TO QUESTIONS ON MASTER 5.6

Case Study: Ruth

Question 1. What disease does the individual have? Is it chronic or acute?

Ruth is a heroin addict. Addiction is a chronic disease.

Question 2. How did the disease change the individual's life?

Ruth, like other addicts, was spending most of her energy focusing on how and where she was going to get her next drugs. She became isolated from her friends, lost her job, and got into trouble with the law.

Question 3. What is the recommended treatment?

The prescribed treatment for Ruth is a combination of medication (methadone) and behavioral treatments.

Question 4. What did the individual do to improve his or her recovery?

Ruth followed her doctor's advice and got both medicine to treat the physical side of addiction and psychological treatment to help her deal with the nonphysical problems of drug addiction. She also worked to change her life by enrolling in college, making new friends, and getting involved in running. After a recurrence of her drug problem, she again started her medical and psychological treatment.

Question 5. What did the individual do that impaired his or her recovery?

Ruth thought she had conquered her disease and didn't need to continue her treatment. She went back to the friends who started her on drugs in the first place.

Question 6. Are there other things the individual could do to help with the disease?

As long as Ruth continues her treatment plan, she should be able to manage her disease. If she ignores her treatment, her chance of having a recurrence increases.

Case Study: Mike

Question 1. What disease does the individual have? Is it chronic or acute?

Mike has diabetes, a chronic disease.

Question 2. How did the disease change the individual's life?

After being diagnosed with diabetes, Mike had to check his blood glucose levels regularly, give himself insulin injections, and watch his diet.

Question 3. What is the recommended treatment?

Mike's doctors placed him on insulin therapy. The doctors also prescribed behavioral treatments.

Question 4. What did the individual do to improve his or her recovery?

To help learn about diabetes, Mike attended a camp where he received information about coping with the disease. After some problems, Mike learned to control his blood sugar levels.

Question 5. What did the individual do that impaired his or her recovery?

Mike had trouble in social situations because he couldn't do the same things his friends did. When he ignored his treatment, Mike had trouble in school and ended up in the hospital.

Question 6. Are there other things the individual could do to help with the disease?

Mike needs to continue to follow his treatment plan and monitor his blood glucose level.

Case Study: Carol

Question 1. What disease does the individual have? Is it chronic or acute?

Carol has hypertension. Hypertension is a chronic disease.

Question 2. How did the disease change the individual's life?

Because of the disease, Carol had problems at work as well as with her family interactions. Her health problems became more severe and she had a mild stroke.

Question 3. What is the recommended treatment?

Initially, the doctor prescribed medication as well as a change in Carol's diet to reduce her salt intake. The doctor also told Carol that exercise would be beneficial.

After Carol had problems following the plan, the doctor recommended that Carol get additional help from other health professionals.

Question 4. What did the individual do to improve his or her recovery?

Carol followed the treatment plan for a while.

Question 5. What did the individual do that impaired his or her recovery?

Carol didn't follow her doctor's advice after the initial period and then ignored her doctor's suggestion that she get additional help from other specialists.

Question 6. Are there other things the individual could do to help with the disease?

Carol needs to fit her treatment into her life.

Comparing the Cases

Question 7. Which individuals were successful in their treatment? Which individuals were not?

Ruth and Mike were both successful in their treatment. Although they had problems, both of them decided to again comply with their treatment. Carol was not successful; she did not follow the recommended treatment.

Question 8. Who was cured of their disease? What is the difference between treatment and cure?

None of the individuals was cured of his or her disease. Treatment eliminates or reduces the effects of the disease, but does not eliminate the disease. If a disease is cured, the problem is fixed and requires no additional treatment.

Question 9. How are the treatments for the different diseases similar?

In each case, the prescribed treatment included both medication and behavioral treatments. In each case, treatment is a long-term process.

Question 10. How are the treatments different?

Different medications are used to treat different diseases.

Question 11. Can you identify similarities and differences in the actions or strategies that individuals took to help them deal with their disease?

All three individuals initially complied with the prescribed treatment. All three individuals experienced a time when they ignored the treatment plan and had reoccurring problems with the disease. Ruth and Mike chose to get additional treatment and learned to cope with their disease. Carol, on the other hand, made the choice to continue to ignore the treatment plan and her doctor's advice.

ALTERNATE VERSION OF ACTIVITY 2 FOR CLASSES WITHOUT ACCESS TO COMPUTERS

The following procedure provides instruction for completing Activity 2 without the use of a computer. Use this version if your students do not have access to computers equipped with a CD-ROM drive.

1. **Break the class into groups of three students. Give one copy of each of the following masters to each group: Master 5.2, *Ruth's Story*, Master 5.3, *Mike's Story*, Master 5.4, *Carol's Story*, and Master 5.5, *Disease Reference Information*. Each student in the group should read a different case. Give each student a copy of Master 5.6, *Evaluating the Cases*. Each**

student should answer questions 1-6 about the case study that he or she read. The students should answer questions 7-11 as a group. Give students time to discuss and write answers to the questions. They may refer to the case studies for help.

2. **After all the groups have finished the questions, discuss the cases with the class.**

   Sample answers for the questions on Master 5.6 are given in the procedures for the CD-ROM based version of this activity.

ACTIVITY 3: SUCCESS RATES FOR TREATING CHRONIC ILLNESS

Content Standard A: Formulate and revise scientific explanations and models using logic and evidence.

1. **Display the chart (Master 5.1) used in Activity 1 of this lesson showing the students' rankings. Ask them if they want to change their answers after reading the case studies. Change the rankings according to the students' responses.**

2. **Next, fill in the correct data for the chart (see below). Ask students what the data tell them about the different diseases. Also, ask students why treatment is not 100 percent successful for any of the diseases.**

Disease	Predicted success	Medical compliance*[2,4]
Heroin addiction		60%
Hypertension		<30%
Diabetes		<50%

*Medical compliance is the adherence to a physician's treatment plan. This is one of the best indicators of treatment success.

Now that students have evaluated the case studies, they should understand that addiction is a disease that is treated as effectively as, or more effectively than, other chronic diseases.

Treatment for addiction is often more successful than treatment for other diseases. The data show that addiction can be treated effectively. Students should also realize that treatment is not always completely successful and that relapse is common. Use this opportunity to make connections back to the case studies. Some students will suggest that treatment is not always successful because patients do not always comply with their treatment. This is correct. Treatment is more effective if the patient participates actively in the process. This is an important point for students to understand. After all, therapies will not be effective if the patient does not take the medicine or attend the counseling session. The students should also realize after reading the case studies that drug addiction and other chronic diseases affect more than the physical body. A person's social, economic, and emotional well-being also need to be addressed. Reinforce to students that behavioral therapy and counseling help individuals cope with the problems in life that can trigger a relapse. Some students may cite an example about counseling from the case studies.

3. **To get students to consider the problems of following a treatment plan, ask them if they have ever made New Year's resolutions. How long did they keep the resolution and why did they break it?**

One of the hardest things humans attempt is to change their behaviors. This is true for adhering to a treatment plan for disease just as it is with other types of behavior changes.

ACTIVITY 4: ADDICTION IS A BRAIN DISEASE

1. **Read the following scenario to the class:**

   Robert has been arrested several times for drug possession. After the first arrest, he was given probation. After the second and third arrests, he was sentenced to jail for one year each time. The police arrested him a fourth time, but instead of having Robert serve more time in jail, the judge ordered him to enter a drug treatment program.

2. **Ask students to write a paper that provides scientific information that would support the judge's decision to have Robert undergo drug treatment instead of going to jail. Instruct the students that they must incorporate information they have learned from Lessons 1–5 to support their position.**

   Students may benefit from reviewing their work from all of the lessons. The crux of the paper should be that drug addiction is a brain disease and drugs cause long-term changes in the function of the brain.

This activity asks students to integrate the information they have learned in all of the lessons. Review their papers to evaluate their understanding.

Additional Resources for Teachers

The following resources may provide additional background information for you or your students about neurobiology or drugs of abuse.

RESOURCES ON THE WORLD WIDE WEB

National Institute on Drug Abuse (NIDA)
http://www.nida.nih.gov
NIDA is the world's leading supporter of research on the health aspects of drug abuse and addiction. This site provides current and authoritative information about the latest research on drugs and addiction.

National Clearinghouse for Alcohol and Drug Information (NCADI)
http://www.health.org
NCADI is part of the U.S. Department of Health and Human Services and functions as the information service for the Center for Substance Abuse Prevention. NCADI is the world's largest resource for current information and materials concerning substance abuse. At this site, you may obtain information about alcohol and other drugs.

Office of National Drug Control Policy
http://www.whitehousedrugpolicy.gov
The purpose of the Office of National Drug Control Policy (ONDCP) is to establish policies, priorities, and objectives for the Nation's drug control program. The National Drug Control Policy is available on this Web site. This site also provides information about specific drugs (including statistics on their use), treatment, research, and enforcement.

Society for Neuroscience
http://www.sfn.org
The Society for Neuroscience is the world's largest organization of scientists and physicians dedicated to understanding the brain, spinal cord, and peripheral nervous system. This site provides a wide variety of information on topics related to the function of the brain and nervous system. The site also provides an opportunity to submit a specific question that may be answered online.

Partnership for a Drug-free America
http://www.drugfreeamerica.org
Information posted at this address includes information about specific drugs and their effects.

The Dana Foundation
http://www.dana.org
The Charles A. Dana Foundation is a private philanthropic foundation with principal interests in health and education. Their Web site provides information for the general public on the latest research findings about the brain and brain disorders. The Web site also provides access to their publications.

The Reconstructors
http://reconstructors.rice.edu
This Web game enables students to learn more about the history of opioids, their use in pain management, and the neuroscience underlying their actions. The activities incorporate aspects of chemistry, neuroscience, medicine, public policy, and history.

Office of Science Education
http://science-education.nih.gov
This address takes you directly to the home page of the National Institutes of Health's Office of Science Education. This site provides access to a variety of resources for teachers and students, including NIH publications on drug abuse and brain function.

United States National Library of Medicine
http://www.nlm.nih.gov
The U.S. National Library of Medicine is the world's largest medical library. This site provides extensive online information about health issues.

This includes access to Medline and MedlinePlus to search for the information about specific health topics.

BOOKS AND VIDEOTAPE

Friedman, D.P. and Rusche, S. 1999. *False Messengers: How Addictive Drugs Change the Brain*. Amsterdam: Harwood Academic Publishers.

Kuhn, C., Swarzwelder, S., and Wilson, W. 1998. *Buzzed: The Straight Facts About the Most Used and Abused Drugs From Alcohol to Ecstasy*. New York: W.H. Norton & Company.

Gross de Núñez, G. and Schwartz-Bloom, R.D. 1998. *Animated Neuroscience and the Action of Nicotine, Cocaine, and Marijuana in the Brain.* Princeton, NJ: Films For the Humanities & Sciences.

Glossary

Definitions for the following terms were adapted from a variety of sources. Specific sources are listed in the reference section.

absorption: The process by which elements move from outside of the body into the blood and other tissues. Food is absorbed through the stomach and intestines. When tobacco is smoked, nicotine is absorbed through the lungs.

acetylcholine: A neurotransmitter that may function in the brain to regulate memory and that controls the actions of skeletal and smooth muscle in the peripheral nervous system.

action potential: The electrical part of a neuron's two-part, electrical-chemical message. An action potential consists of a brief pulse of electrical current that travels along the axon. When the action potential reaches the axon terminal, it triggers neurotransmitter release.

acute: Refers to a disease or condition that has a relatively rapid onset, marked intensity and a short duration.

addiction: A chronic brain disorder characterized by the loss of control of drug-taking behavior, despite adverse health, social, or legal consequences to continued drug use. Addiction is characterized by relapses during recovery.

adenosine: A neurotransmitter that binds to the adenosine receptor. Adenosine is a by-product of ATP metabolism and is an important regulator of sleep. Caffeine is an adenosine antagonist.

agonist: A chemical that produces a response, such as excitation or inhibition of action potentials when it binds to a specific receptor. Opiates, cannabis, nicotine, and some hallucinogens are agonists.

alcohol: A psychoactively complex drug in beverages such as beer, wine, and whiskey. Alcohol is a depressant drug with potential for abuse and addiction.

all-or-none phenomenon: The principle that a nerve fiber will respond maximally or not at all to a stimulus. The strength of the impulse is not dependent on stimulus strength.

amphetamine: Stimulant drugs whose effects are very similar to cocaine.

amygdala: A part of the brain that is an important component of the limbic system.

anandamide: The neurotransmitter produced in the body that binds to the cannabinoid receptor; this receptor also binds THC, the psychoactive component in marijuana.

antagonist: A chemical that, when it binds to a receptor, blocks the receptor and prevents it from responding. Antagonists prevent agonists from binding, or attaching, to the receptor. Antagonists include caffeine and naloxone.

axon: The fiber-like extension of a neuron by which the cell carries information to target cells.

axon terminal: The structure at the end of an axon that produces and releases chemicals (neurotransmitters) to transmit the neuron's message across the synapse.

astrocyte: A type of glial cell that provides nutrients, support, and insulation for neurons of the central nervous system.

barbiturates: Depressant drugs that produce relaxation and sleep. Sleeping pills such as pentobarbital and secobarbital are barbiturates.

bind: The attaching of a neurotransmitter or other chemical to a receptor. The neurotransmitter is said to "bind" to the receptor.

blood-brain barrier: A network of tightly packed cells in the walls of capillaries in the brain that prevents many molecules, including poisons, from entering the brain.

brainstem: The major route by which the forebrain sends information to, and receives information from, the spinal cord and peripheral nerves.

buprenorphine: A long-lasting opiate analgesic that has both opiate agonist and antagonist properties. Buprenorphine may be useful for treating heroin addiction.

caffeine: A mild stimulant found in coffee and kola nuts. Caffeine is the most widely used drug in the world.

cannabinoid receptor: The receptor in the brain that recognizes anandamide and THC, the active ingredient in marijuana.

cannabis: The botanical name for the plant from which marijuana comes.

cannula: A tube that is inserted into a cavity or duct.

cell body (or soma): The central structure of a neuron, which contains the cell nucleus. The cell body contains the molecular machinery that regulates the activity of the neuron.

central nervous system: The brain and spinal cord.

cerebellum: A portion of the brain that helps regulate posture, balance, and coordination.

cerebral cortex: The outer layer of the cerebral hemispheres that controls conscious experience, including perception, emotion, thought, and planning.

cerebral hemispheres: The two specialized halves of the brain. The left hemisphere is specialized for speech, writing, language, and calculation; the right hemisphere is specialized for spatial abilities, face recognition in vision, and some aspects of music perception and production.

cerebrum: The upper part of the brain consisting of the left and right hemispheres.

chronic: Refers to a disease or condition that persists over a long period of time.

cocaine: A highly addictive stimulant drug derived from the coca plant that produces profound feelings of pleasure.

craving: Hunger for drugs. It is caused by drug-induced changes that arise from a need of the brain to maintain a state of homeostasis that includes the presence of the drug.

dendrite: The specialized branches that extend from a neuron's cell body and function to receive messages from other neurons.

depressants: Drugs that relieve anxiety and produce sleep. Depressants include barbiturates, benzodiazepines, and alcohol.

dopamine: The neurotransmitter that produces feelings of pleasure when released by the brain reward system.

dopamine transporter: A protein structure on the cell membranes of axon terminals of dopamine-releasing neurons that carries dopamine back into the presynaptic neuron thereby rapidly removing dopamine from the synapse.

drug: A chemical compound or substance that can alter the structure and function of the body. Psychoactive drugs affect the function of the brain, and some of these may be illegal to use and possess.

drug abuse: The use of illegal drugs or the inappropriate use of legal drugs. The repeated use of drugs to produce pleasure, to alleviate stress, or to alter or avoid reality (or all three).

drug addiction: The continued compulsive use of drugs in spite of adverse health or social consequences.

ecstasy (MDMA): A chemically modified amphetamine that has hallucinogenic as well as stimulant properties.

electroencephalogram (EEG): A graphic record of the electrical activity of the brain made by attaching electrodes to the scalp.

endogenous: Something produced by the brain or body.

endorphins: Peptides with opiate-like effects that bind to opiate receptors. Endorphins are made by neurons and used as neurotransmitters.

enkephalins: One of the endogenous opioids that binds to opiate receptors and is used as a neurotransmitter.

enzyme: A large molecule that living organisms use to catalyze chemical reactions. Enzymes are used to build, modify, or break down different molecules without themselves being permanently altered or destroyed.

excitatory neurotransmitter: A neurotransmitter that acts to elicit an action potential or make it more likely that one will be elicited.

exocytosis: A process by which secretory products are released from a cell via transport within vesicles to the cell surface and subsequent fusion with the plasma membrane, resulting in the extrusion of the vesicle contents from the cell.

forebrain: The largest division of the brain, which includes the cerebral cortex and basal ganglia. It is credited with the highest intellectual functions.

frontal lobe: One of the four divisions of each cerebral hemisphere. The frontal lobe is important for controlling movement and associating the functions of other cortical areas.

GABA (gamma-amino-butyric acid): The major inhibitory neurotransmitter in the brain.

glial cells (glia): Brain cells that support neurons by performing a variety of "housekeeping" functions in the brain.

glutamate: The most common excitatory neurotransmitter in the brain.

hallucinogens: A diverse group of drugs that alter perceptions, thoughts, and feelings. Hallucinogenic drugs include LSD, mescaline, MDMA (ecstasy), PCP, and psilocybin (magic mushrooms).

heroin: The potent, widely abused opiate that produces addiction. It consists of two morphine molecules linked together chemically.

hippocampus: A brain structure that is involved in emotions, motivation, learning, and memory.

homeostasis: The process of keeping the internal environment of the body stable by making adjustments to changes in the external environment.

hypothalamus: The part of the brain that controls many bodily functions, including feeding, drinking, and the release of many hormones.

ingestion: The act of taking in food or other material into the body through the mouth.

inhalant: Any drug administered by breathing in its vapors. Inhalants commonly are organic solvents, such as glue and paint thinner, or anesthetic gases, such as ether and nitrous oxide.

inhalation: The act of administering a drug or combination of drugs by nasal or oral respiration. Also, the act of drawing air or other substances into the lungs. Nicotine in tobacco smoke enters the body by inhalation.

inhibitory neurotransmitter: A neurotransmitter that acts to prevent a neuron from firing an action potential.

injection: A method of administering a substance such as a drug into the skin, subcutaneous tissue, muscle, blood vessels, or body cavities, usually by means of a needle.

limbic system: A set of brain structures that generates our feelings, emotions, and motivations. It is also important in learning and memory.

localization of function: A principle of brain organization that states that specific places (circuits) in the brain carry out specific functions.

LSD (lysergic acid diethylamide): An hallucinogenic drug that acts on the serotonin receptor.

magnetic resonance imaging (MRI): An imaging technique that uses magnetic fields to take pictures of the structure of the brain.

marijuana: A drug, usually smoked but can be eaten, that is made from the leaves of the cannabis plant. The main psychoactive ingredient is THC.

medication: A drug that is used to treat an illness or disease according to established medical guidelines.

metabolism: The processes by which the body breaks things down or alters them so they can be eliminated.

methadone: A synthetic opiate used to treat cancer pain and heroin addiction.

methamphetamine: A commonly abused, potent stimulant drug that is part of a larger family of amphetamines.

morphine: The most potent natural opiate compound produced by the opium poppy. Morphine is a very effective medicine for treating pain.

myelin: Fatty material that surrounds and insulates axons of some neurons.

naloxone: A short-acting opiate antagonist that binds to opiate receptors and blocks them, preventing opiates from binding to these receptors.

naltrexone: An opiate antagonist used to treat heroin addiction, and more recently for the treatment of alcohol addiction.

neuron (nerve cell): A unique type of cell found in the brain and body that is specialized to process and transmit information.

neurotransmitter: A chemical produced by neurons to carry messages to other neurons.

neurotransmission: The process that occurs when a neuron releases neurotransmitters to communicate with another neuron across the synapse.

nicotine: The addictive drug in tobacco. Nicotine activates a specific type of acetylcholine receptor.

norepinephrine: A neurotransmitter and a hormone. It is released by the sympathetic nervous system onto the heart, blood vessels, and other organs, and by the adrenal gland into the bloodstream as part of the fight-or-flight response. Norepinephrine in the brain is used as a neurotransmitter in normal brain processes.

nucleus: A cluster or group of nerve cells that is dedicated to performing its own special function(s). Nuclei are found in all parts of the brain but are called cortical fields in the cerebral cortex.

nucleus accumbens: A part of the brain reward system, located in the limbic system, that processes information related to motivation and reward. Virtually all drugs of abuse act on the nucleus accumbens to reinforce drug taking.

occipital lobe: The lobe of the cerebral cortex at the back of the head that includes the visual cortex.

opiate receptors: Receptors that recognize both opiates and endogenous opioids. When activated, they slow down or inhibit the activity of neurons on which they reside.

opiates: Any of the psychoactive drugs that originate from the opium poppy or that have a chemical structure like the drugs derived from opium. Some opiates (such as opium, codeine, and morphine) are derived from the plant, while others were first synthesized by chemists.

opioid: Any chemical that has opiate-like effects; commonly used to refer to endogenous neurochemicals that activate opiate receptors.

parallel processing: The division of an information-processing job into smaller parts that are each handled simultaneously by various cortical fields and brain nuclei.

parietal lobe: One of the four subdivisions of the cerebral cortex; it is involved in sensory processes, attention, and language.

phencyclidine (PCP): Originally developed as an anesthetic, PCP may act as an hallucinogen, stimulant, or sedative.

pituitary gland: An endocrine organ closely linked with the hypothalamus. The pituitary secretes a number of hormones that regulate the activity of other endocrine organs in the human body.

plasticity: The capacity of the brain to change its structure and function within certain limits.

Plasticity underlies brain functions such as learning and allows the brain to generate normal, healthy responses to long-lasting environmental changes.

positron: A positively charged particle having the same mass and spin as, but opposite charge of, an electron.

positron emission tomography (PET): An imaging technique for measuring brain function in living subjects by detecting the location and concentration of small amounts of radioactive chemicals.

postsynaptic neuron: A neuron that receives messages from other neurons.

presynaptic neuron: A neuron that releases neurotransmitters into synapses to send messages to other neurons.

psychedelic drug: A drug that distorts perception, thought, and feeling. This term is typically used to refer to drugs with actions like those of LSD.

psychoactive drug: A drug that changes the way the brain works.

psychosocial therapy: Therapy that uses a combination of individual psychotherapy and group (social) therapy approaches to rehabilitate or provide the interpersonal and intrapersonal skills an addict needs to live without drugs.

receptor: A large molecule that recognizes specific chemicals (normally neurotransmitters, hormones, and similar endogenous substances) and transmits the message carried by the chemical into the cell on which the receptor resides.

relapse: In drug abuse, relapse is the resumption of drug use after trying to stop taking drugs. Relapse is a common occurrence in many chronic disorders, including addiction, that require behavioral adjustments to treat effectively.

resting membrane potential: The difference in electrical charge between the inside and the outside of a nerve cell when the cell is not firing. The inside of a resting neuron has a greater negative charge than the outside of the neuron.

reuptake: The process by which neurotransmitters are removed from the synapse by being "pumped" through transporters back into the axon terminals that first released them.

reuptake pump (transporter): The large molecule that actually transports neurotransmitter molecules back into the axon terminals that released them.

reward: The process that reinforces behavior. It is mediated at least in part by the release of dopamine into the nucleus accumbens. Human subjects report that reward is associated with feelings of pleasure.

reward system (or brain reward system): A brain circuit that, when activated, reinforces behaviors. The circuit includes the dopamine-containing neurons of the ventral tegmental area, the nucleus accumbens, and part of the prefrontal cortex. The activation of this circuit causes feelings of pleasure.

route of administration: The way a drug is put into the body. Drugs can enter the body by eating, drinking, inhaling, injecting, snorting, smoking, or absorbing a drug through mucous membranes.

rush: Intense feelings of euphoria a drug produces when it is first consumed.

second messenger: A molecule produced inside neurons as a step in the process of communication between cells. The second messenger lets other parts of the cell know that a specific receptor has been activated, thereby completing the message carried by the neurotransmitter that bound to the receptor. Some receptors (dopamine and opiate receptors, for example) use second messengers. Others (nicotine and GABA receptors, for example) do not.

sensitization: An increased response to a drug caused by repeated administration. Sensitization is most commonly seen in some responses to stimulants.

serotonin: A neurotransmitter that regulates many functions, including mood, appetite, and sensory perception.

single photon emission computed tomography (SPECT): An imaging process that measures the emission of single photons of a given energy from radioactive tracers in the human body.

stimulants: A class of drugs that elevates mood, increases feelings of well-being, and increases energy and alertness. These drugs produce euphoria and are powerfully rewarding. Stimulants include cocaine, methamphetamine, and methylphenidate (Ritalin).

synapse: The site where presynaptic and postsynaptic neurons communicate with each other.

synaptic space (or synaptic cleft): The intercellular space between the presynaptic and postsynaptic neurons.

temporal lobe: The lobe of the cerebral cortex at the side of the head that hears and interprets music and language.

thalamus: Located deep within the brain, the thalamus is the key relay station for sensory information flowing into the brain, filtering out important messages from the mass of signals entering the brain.

tetrahydrocannabinol (THC): The active ingredient in marijuana that is primarily responsible for producing the drug's psychoactive effects.

temporal lobe: One of the four major subdivisions of each hemisphere of the cerebral cortex. It functions in auditory perception, speech, and visual perceptions.

tolerance: A physiological change resulting from repeated drug use that requires the user to take larger amounts of the drug to get the same effect initially felt from a smaller dose.

transporter: A large protein on the cell membrane of the axon terminals. It removes neurotransmitter molecules from the synapse by carrying them back into the axon terminal that released them.

ventral tegmental area (VTA): The group of dopamine-containing neurons that make up a key part of the brain reward system. These neurons extend axons to the nucleus accumbens and the prefrontal cortex.

vesicle: A membranous sac within an axon terminal that stores and releases neurotransmitter.

withdrawal: Physical symptoms in the body and brain that occur when a person who is physically dependent stops using the drug.

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Masters-

Refer to the *In Advance* section in each lesson for more information about the number of copies required for each master. Masters marked with an asterisk (*) are not needed if you use the CD-ROM version of the activity.

Lesson 1, The Brain: What's Going On In There?

Lesson 2, Neurons, Brain Chemistry, and Neurotransmission

Lesson 3, Drugs Change the Way Neurons Communicate

Activity 1: Drugs Alter Neurotransmission
- Master 3.1, *Cocaine Alters Neurotransmission* . . . . . Transparency
- Master 3.2, *Methamphetamine and Nicotine Disrupt Neurotransmission* . . . . . Transparency
- Master 3.3, *How Does Alcohol Affect Neurotransmission?* . . . . . Transparency

Activity 2: How Does Caffeine Affect You?
- Master 3.4, *Parent Letter* . . . . . Student Copies
- Master 3.5, *Caffeine: How Does Your Heart Respond?* . . . . . Student Copies

Activity 3: Routes of Administration
- Master 3.6, *How Do Drugs Get In the Body?* . . . . . Student Copies
- Master 3.7, *What Should the Doctor Do?* . . . . . Transparency

Lesson 4, Drug Abuse and Addiction

Activity 1: How Does Drug Abuse Begin? . . . . . None

Activity 2: Drug Abuse is Voluntary; Addiction Is Compulsive
- Master 4.1, *Data for Rat Self-administration Experiment* . . . . . Student Copies
- Master 4.2, *Worksheet for Rat Experiment Data* . . . . . Student Copies
- Master 4.3, *Evaluating the Experiment* . . . . . Student Copies

Activity 3: When Does Abuse Become Addiction?
- Master 4.4, *Playing the Game* . . . . . Transparency

Activity 4: Environmental, Behavioral, and Social Influences on Drug Abuse and Addiction
- Master 4.5, *Who Is Addicted?* . . . . . Transparency

Activity 5: Long-term Effects of Drug Abuse and Addiction
- Master 4.6, *Long-term Effects of Drugs on the Brain** . . . . . Student Copies

Lesson 5, Drug Addiction Is a Disease—So What Do We Do about It?

Activity 1: How Effective Is Treatment?
- Master 5.1, *Ranking Disease Treatment Outcomes* . . . . . Transparency

Activity 2: Evaluating the Case Studies
- Master 5.2, *Ruth's Story** . . . . . Team Copies
- Master 5.3, *Mike's Story** . . . . . Team Copies
- Master 5.4, *Carol's Story** . . . . . Team Copies
- Master 5.5, *Disease Reference Information** . . . . . Team Copies
- Master 5.6, *Evaluating the Cases* . . . . . Student Copies

Activity 3: Success Rates for Treating Chronic Illness . . . . . None

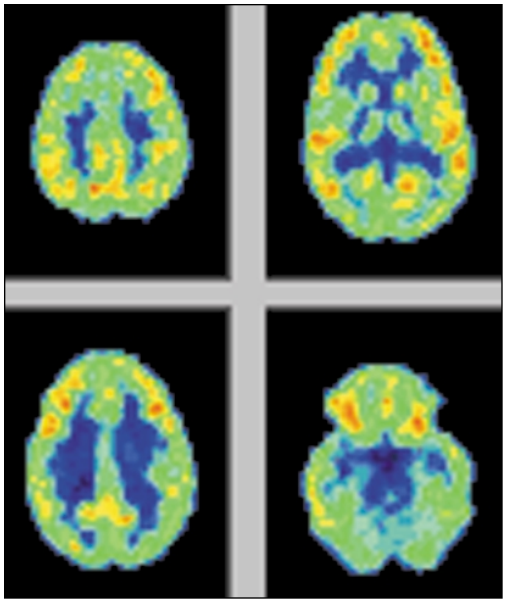
Activity 4: Addiction Is a Brain Disease . . . . . None

Positron Emission Tomography (PET) Images

Each set of PET images below contains four images of a human brain. The four images show cross-sections taken at different levels of the brain.

Set 1

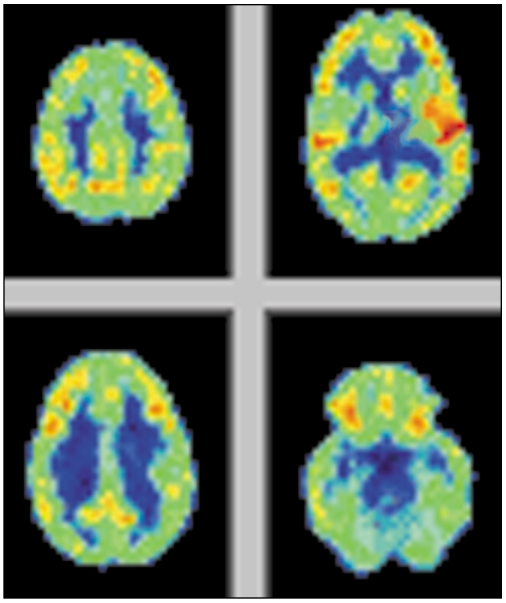
a b



c d

Set 2

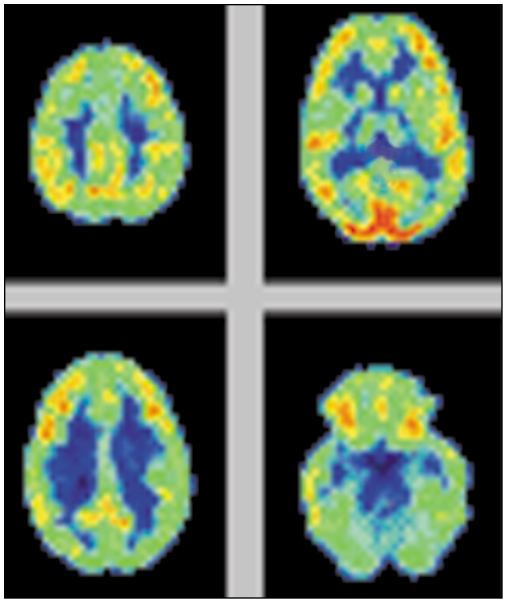
a b



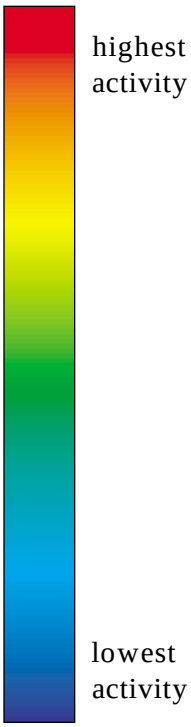
c d

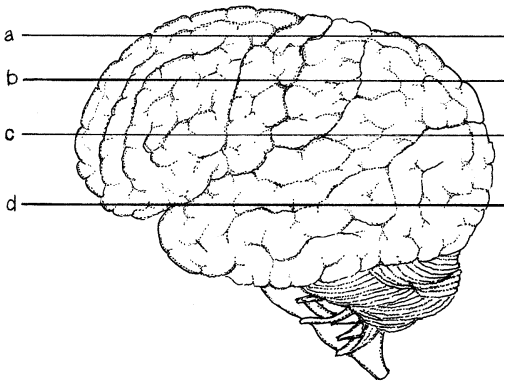
Set 3

a b



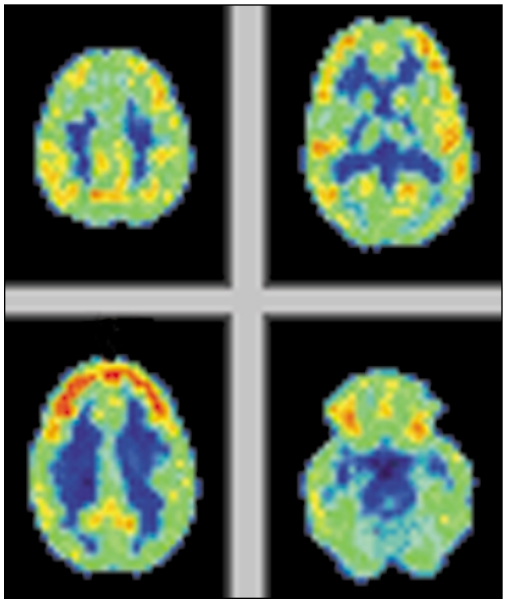
c d





Set 4

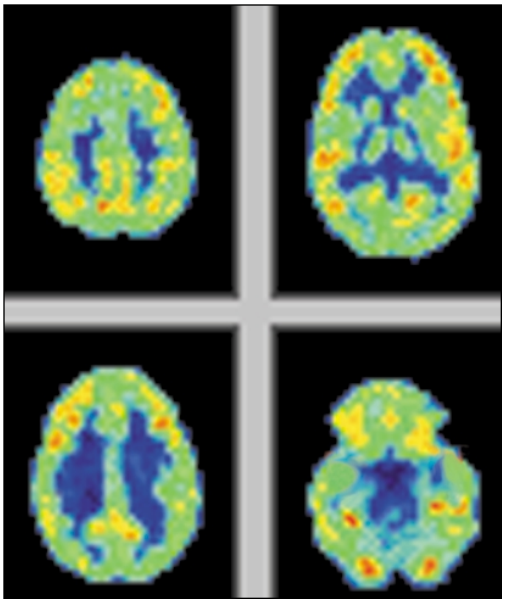
a b



c d

Set 5

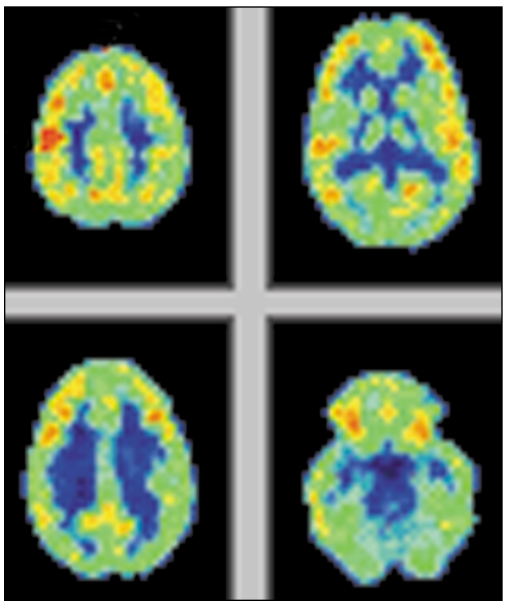
a b



c d

Set 6

a b



c d

PET images provided by:

Sanjiv S. Gambhir, M.D., Ph.D.
Let's Play PET
UCLA School of Medicine
Crump Institute for Biological Imaging

Let's Play PET website:
http://www.crump.ucla.edu/lpp/clinpetneuro/function.html.

Interpreting PET Images

1. When you look at the images that make up Set #1, how do the four images differ from each other?

2. Why are four images shown in each set of PET images? Why would scientists need to examine more than one PET image taken of a subject's brain?

3. When comparing the images in Set #1 to the images in Sets #2, 3, 4, 5, and 6, how is the activity of the brain in each of these sets different from Set #1?

Set Number	Identify the image that shows the greatest change (a, b, c, or d)	Describe the change in brain activity
2		
3		
4		
5		
6		

4. The PET images shown in Set #1 show brain activity in a resting brain. The images in Sets #2-6 show activity in the brains of humans who are doing different tasks. When you look at the PET scans and the chart in question #3, what generalizations can you make about the activity of the brain when different tasks are performed?

5. Compare the tasks that the subject performed during each of the PET scans (as shown on the overhead transparency) to the individual's brain activity. Use the information from the overhead and from the PET images to complete the following chart.

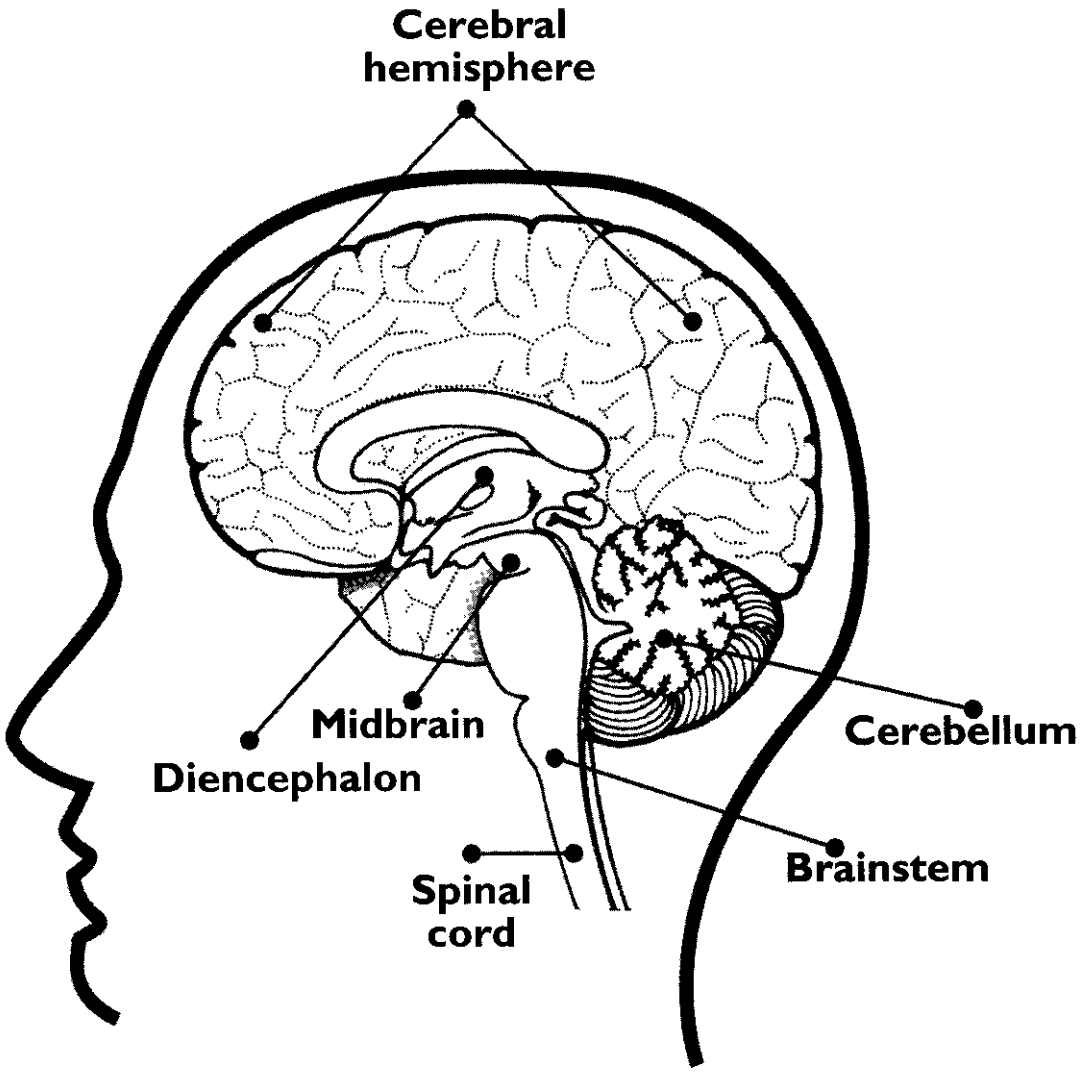
Set Number	Name of the brain region that is more active in the PET image	This part of the brain is involved in processing information related to
2	auditory cortex	
3	primary visual cortex	
4	frontal cortex	
5	hippocampus	
6	motor cortex	

PET Image Tasks

The tasks that the subject performed during each of the PET scans are as follows:

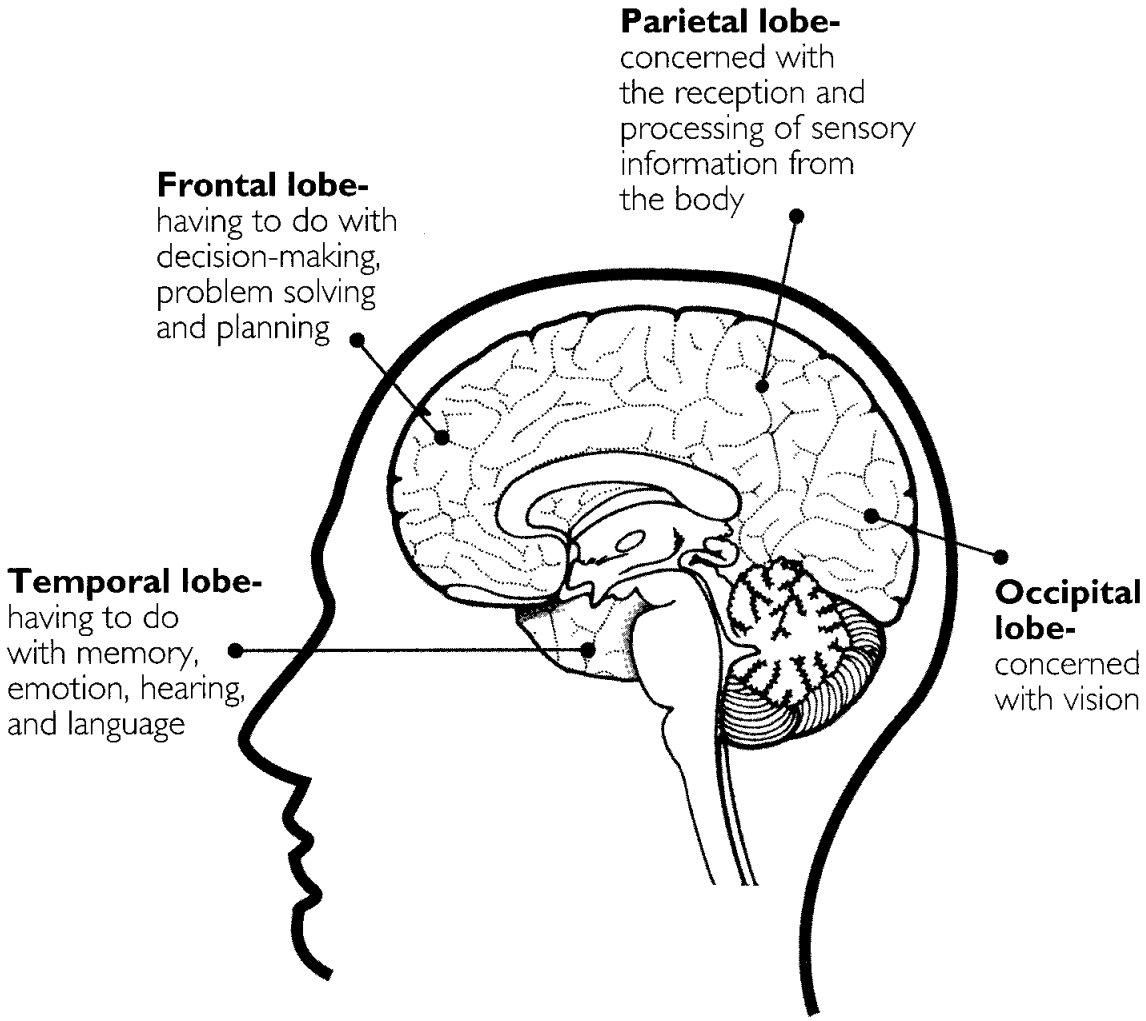
- Set #1 Subject is resting.
- Set #2 Subject is listening to music.
- Set #3 Subject is looking at a picture showing both pattern and color.
- Set #4 Subject is performing a thinking task.
- Set #5 Subject must remember an image for later recall.
- Set #6 Subject is hopping up and down on the right foot.

Major Regions of the Brain



Source: National Institute on Drug Abuse (1997) Mind Over Matter: The Brain's Response to Drugs, Teacher's Guide.

Areas of the Cerebral Cortex and Their Functions



Source: National Institute on Drug Abuse (1997) Mind Over Matter: The Brain's Response to Drugs, Teacher's Guide.

What Happened to Phineas Gage?

Due to an accident while he was working, Phineas Gage made a contribution to the understanding of how the brain works. In 1848, 25-year old Phineas Gage worked for the Rutland and Burlington Railroad Company laying railroad tracks across Vermont. Before railroad track could be laid, however, the uneven ground needed to be leveled. Gage and coworkers had to drill holes in the stone, put explosive in the holes, cover the explosive with sand, and then use a fuse and tamping iron to trigger an explosion. One day, an accident occurred that changed Gage's life forever. The explosive went off early sending the tamping iron, which was 1.25 inches in diameter and 43 inches long, shooting into Gage's face, through his skull and brain, and out the top of his head. The tamping iron landed about 25 yards away. Gage regained consciousness within a few minutes. Amazingly, he not only survived the blast, but he was able to talk and to walk! His coworkers took him to the doctor who cleaned and bandaged the wounds, the standard medical treatment at the time.

Although Gage survived the physical injuries from the blast, he was a changed man. He appeared to be just as intelligent as before the accident, and he did not have any impairment in movement, speech, or memory. But, something was different. Prior to the accident, he was a responsible, intelligent and likeable person. After the accident, he was irresponsible, used profanity extensively, and demonstrated no respect for social customs. His friends commented that "Gage was no longer Gage." He could not hold the responsible jobs that he had prior to the accident and apparently wandered for the next several years. Phineas Gage ended up in San Francisco in the custody of his family where he died approximately 12 years after the accident.

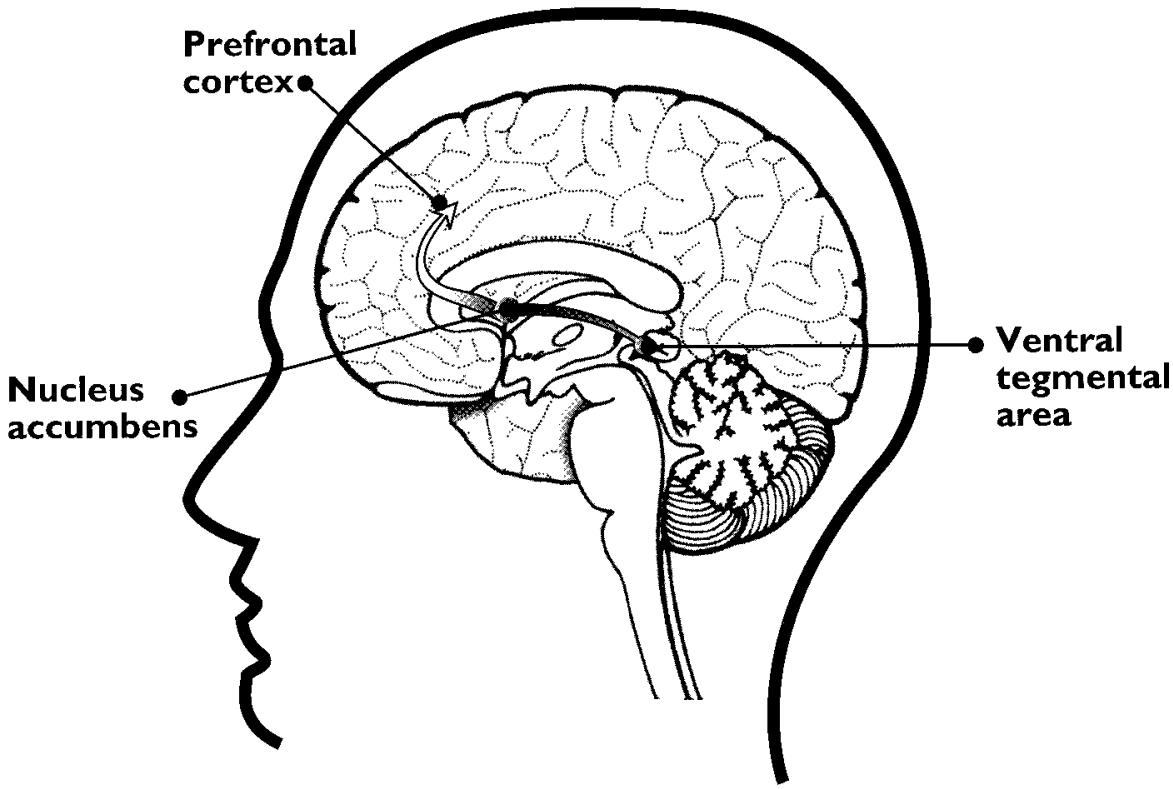
Twenty years after the accident, the physician who treated Gage correlated the behavioral changes with damage to the frontal region of the brain. At the time, the brain was thought to control language and movement, but the suggestion that the brain functioned to process emotions and social behavior was new. In addition, scientists at the time believed the brain lacked localized functions. Unknowingly, Phineas Gage contributed to our understanding of how the brain processes information.

In the 1990s, scientists used their improved understanding of brain function, computer modeling techniques, and new data from Gage's skull. Based on this information, they found that the accident damaged both hemispheres of the frontal lobe, which is the part of the brain that influences social behavior. Today, physicians see patients with damage to the frontal lobe that has occurred through motor vehicle accidents, gun accidents, or major falls. These individuals, like Phineas Gage, often have dramatic changes in their emotional and decision-making abilities.

1. How did Phineas Gage change after the accident?

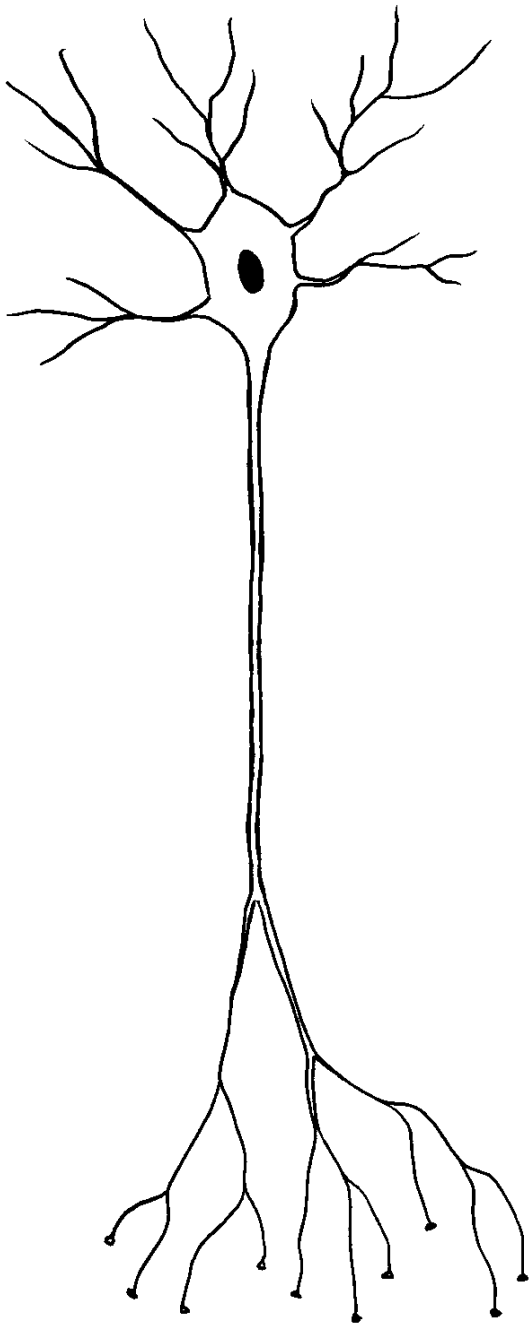
2. How did Phineas Gage's accident change scientists' understanding of the brain?

The Reward System

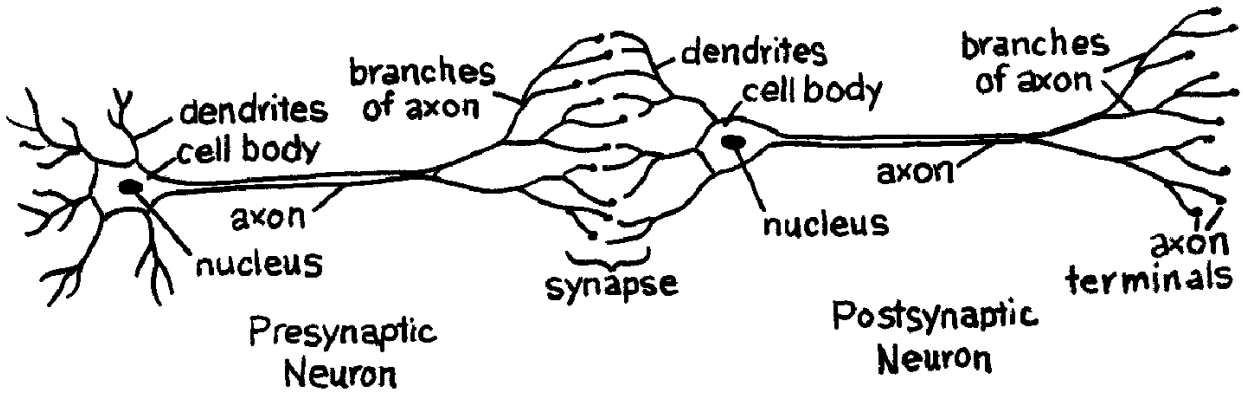


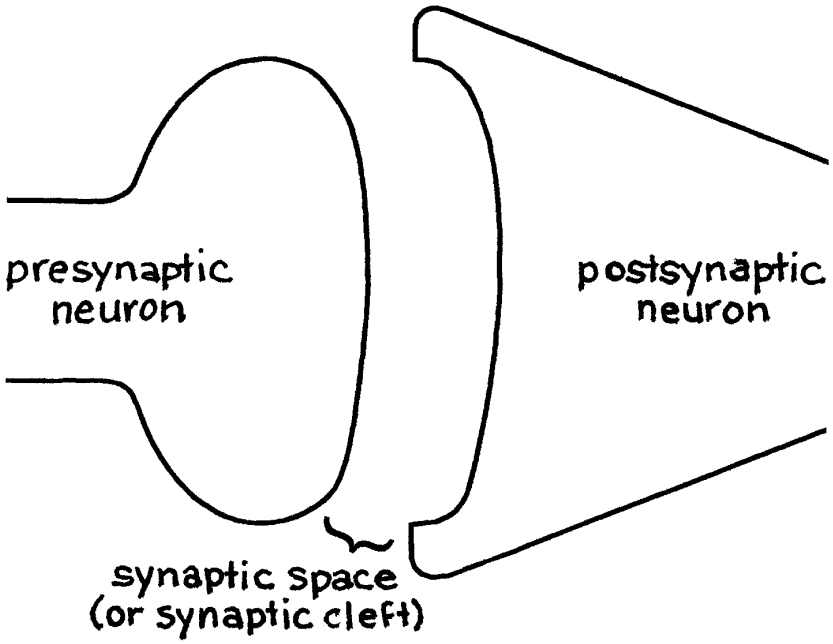
Source: National Institute on Drug Abuse (1997) Mind Over Matter: The Brain's Response to Drugs, Teacher's Guide.

Anatomy of a Neuron

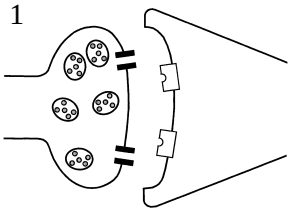
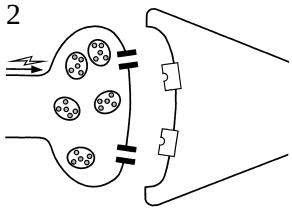
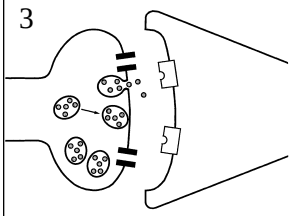
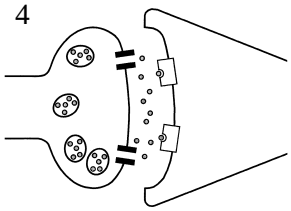
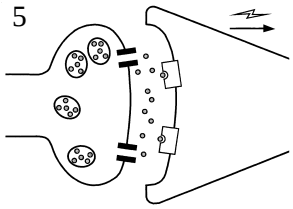
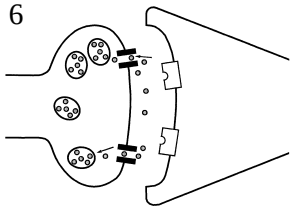


Neurons Interact With Other Neurons Through Synapses





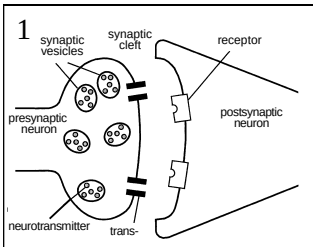
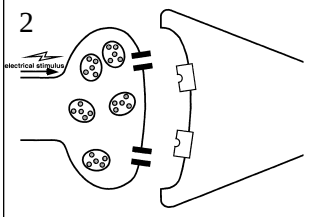
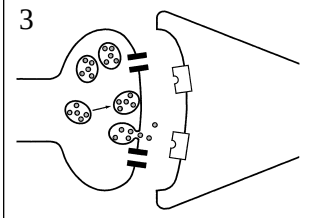
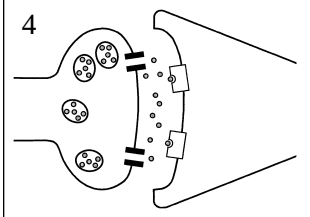
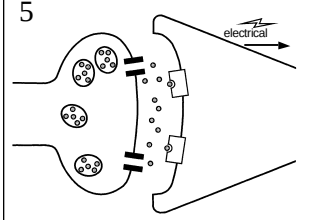
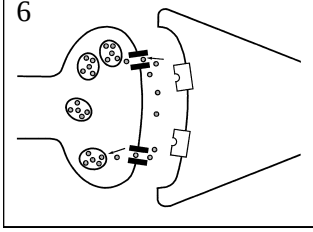
How Do Neurons Communicate?

1 	
2 	
3 	
4 	
5 	
6 	

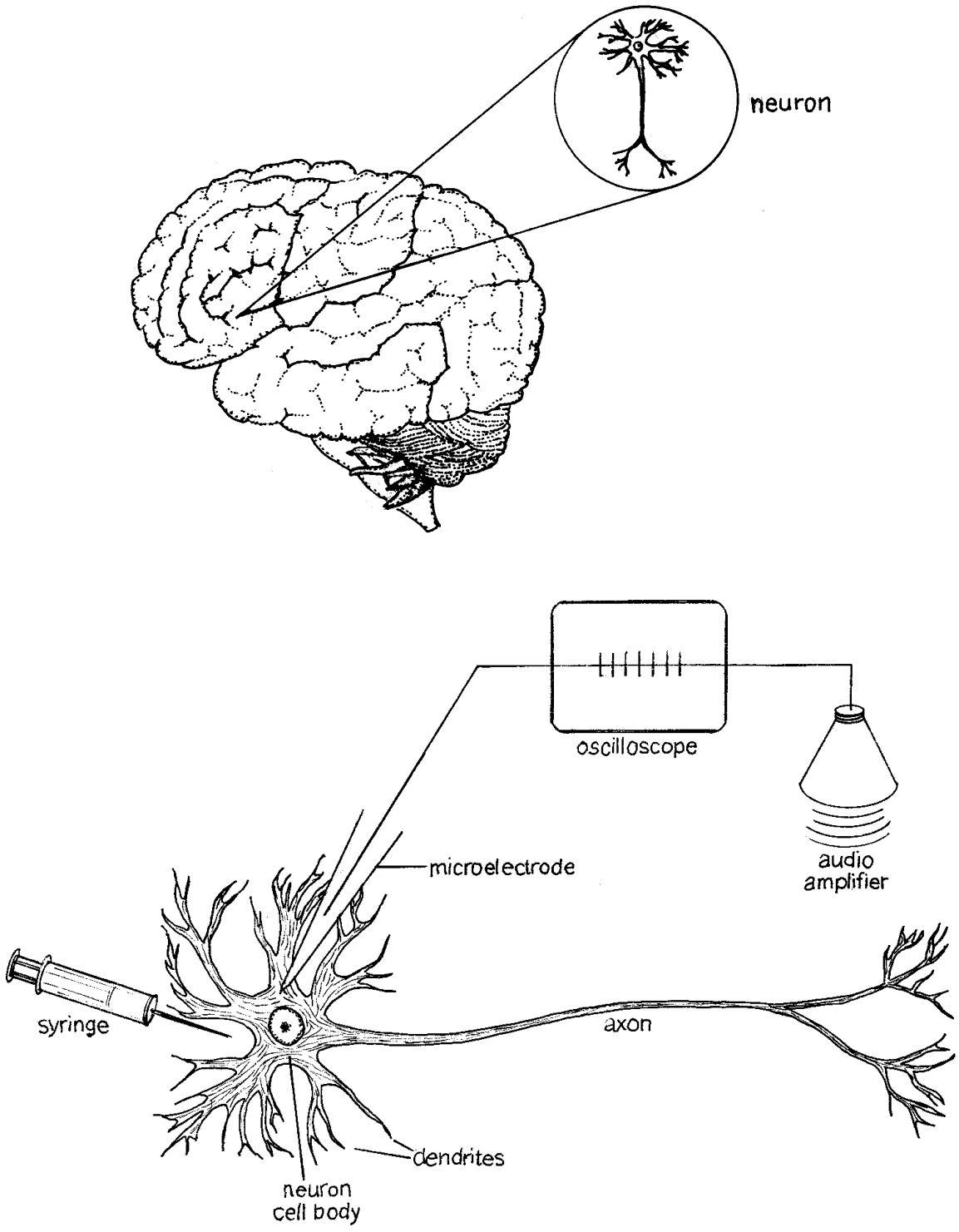
Neurons Communicate by Neurotransmission

Neurons communicate using both electrical signals and chemical messages. Information in the form of an electrical impulse is carried away from the neuron's cell body along the axon of a presynaptic neuron toward the axon terminals. When the electrical signal reaches the terminal, it cannot cross the synaptic space, or synaptic cleft, to reach the postsynaptic neuron. Instead, that electrical signal triggers chemical changes that *can* cross the synapse to affect the postsynaptic cell. When the electrical impulse reaches the presynaptic axon terminal, it causes membranous sacs, called vesicles, to move toward the membrane of the axon terminal. When the vesicles reach the membrane, they fuse with the membrane and release their contents into the synaptic space. The molecules contained in the vesicles are chemical compounds called neurotransmitters. Each vesicle contains many molecules of a neurotransmitter. The released neurotransmitter molecules drift across the synaptic cleft and then bind to special proteins, called receptors, on the postsynaptic neuron. A neurotransmitter molecule will bind only to a specific kind of receptor. The binding of neurotransmitter to its receptor causes a change in the postsynaptic neuron that in turn causes that neuron to generate an electrical impulse. The electrical impulse then moves away from the neuron ending toward the cell body. After the neurotransmitter binds to the receptor to transmit the signal to the postsynaptic neuron, it comes off of, or releases from, the receptor into the synaptic space. Specific proteins called transporters or reuptake pumps carry the neurotransmitter back into the presynaptic neuron. When the neurotransmitter molecules are back in the presynaptic axon terminal, they can be repackaged into vesicles for release the next time an electrical impulse reaches the axon terminal. Enzymes present in the synaptic space degrade neurotransmitter molecules that are not taken back up into the presynaptic neuron.

Neurotransmission

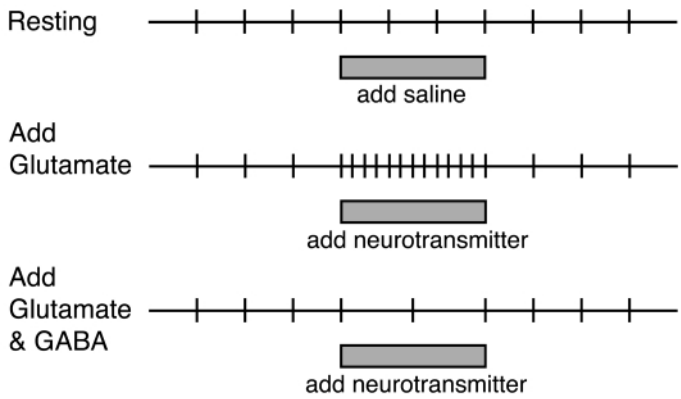
1 	
2 	
3 	
4 	
5 	
6 	

Recording the Activity of a Neuron



Neurotransmitter Actions

The following diagrams represent recordings of the electrical activity of a neuron over a period of time. Each vertical line on the diagram represents an electrical impulse, or action potential, occurring in the neuron. The first diagram represents a neuron at rest. For the other recordings, a solution containing neurotransmitter was applied to the neuron.



1. Why is saline applied to the resting neuron?

2. When the neurotransmitter glutamate is applied to the neuron, how does its activity change?

3. How does the application of the two neurotransmitters, glutamate and GABA, change the activity of the neuron?

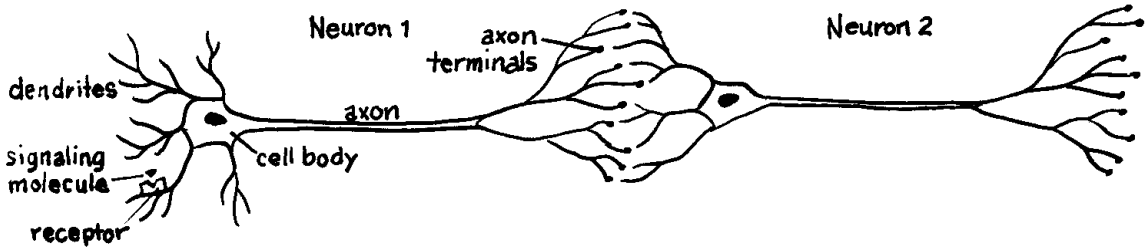
4. Predict how the activity of the neuron would change if only GABA was applied to the neuron.

5. Do all neurotransmitters affect a neuron in the same way?

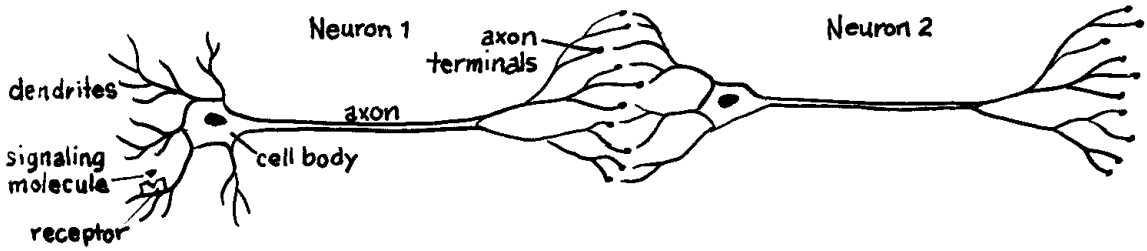
6. How would the application of glutamate to a neuron change the amount of neurotransmitter released from that neuron? How would the application of GABA to a neuron change the amount of neurotransmitter released from that neuron?

Neurons in Series

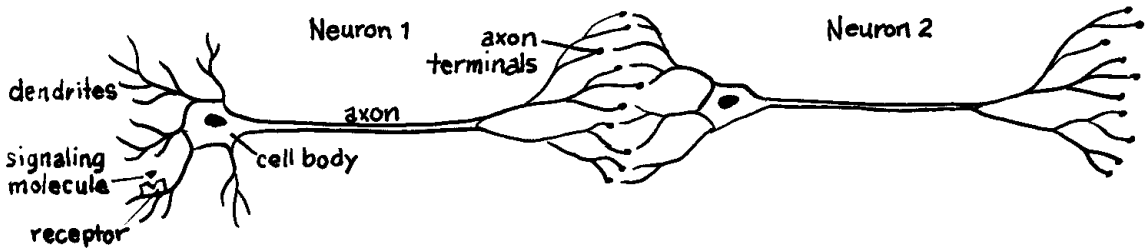
Using what you have learned about the effects of the neurotransmitters glutamate and GABA, determine how the different signals that affect Neuron #1 can change the release of the neurotransmitter dopamine from Neuron #2. Use the chart to help you work through the cases. You can use ↓ to indicate a decrease or ↑ to indicate an increase.



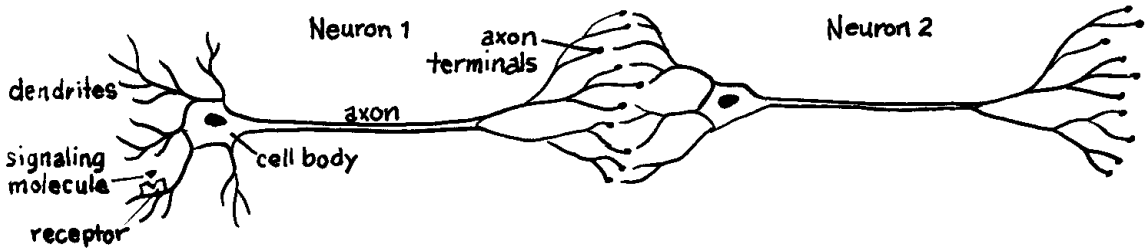
A. The signaling molecule is inhibitory. Neuron #1 releases glutamate as its neurotransmitter. Neuron #2 releases dopamine as its neurotransmitter.



B. The signaling molecule is excitatory. Neuron #1 releases glutamate as its neurotransmitter. Neuron #2 releases dopamine as its neurotransmitter.



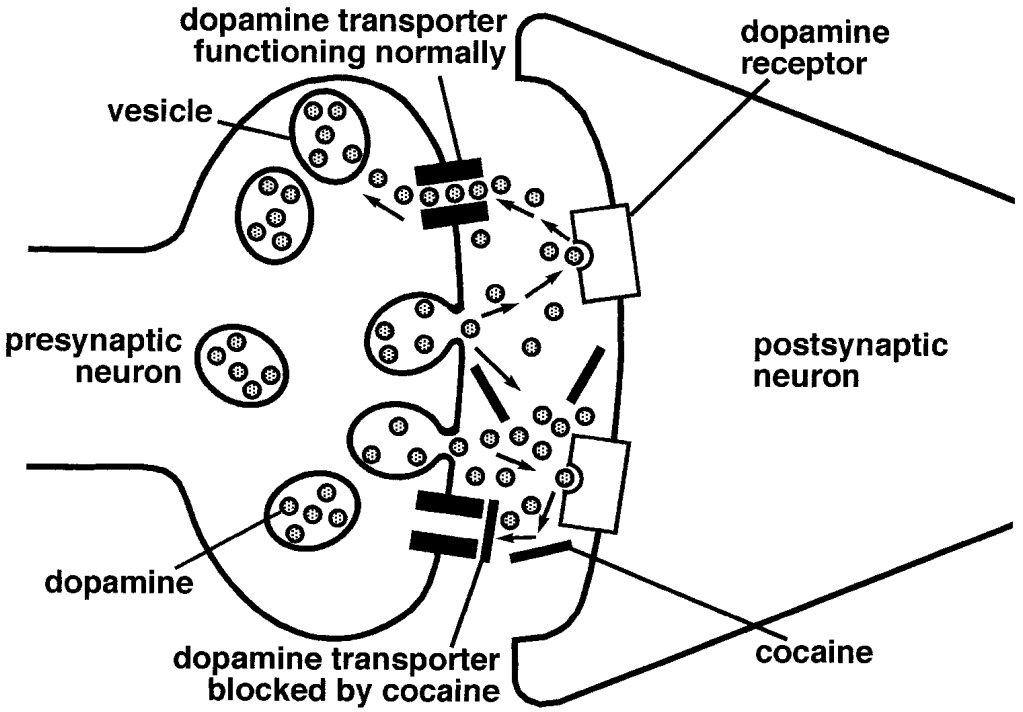
C. The signaling molecule is inhibitory. Neuron #1 releases GABA as its neurotransmitter. Neuron #2 releases dopamine as its neurotransmitter.



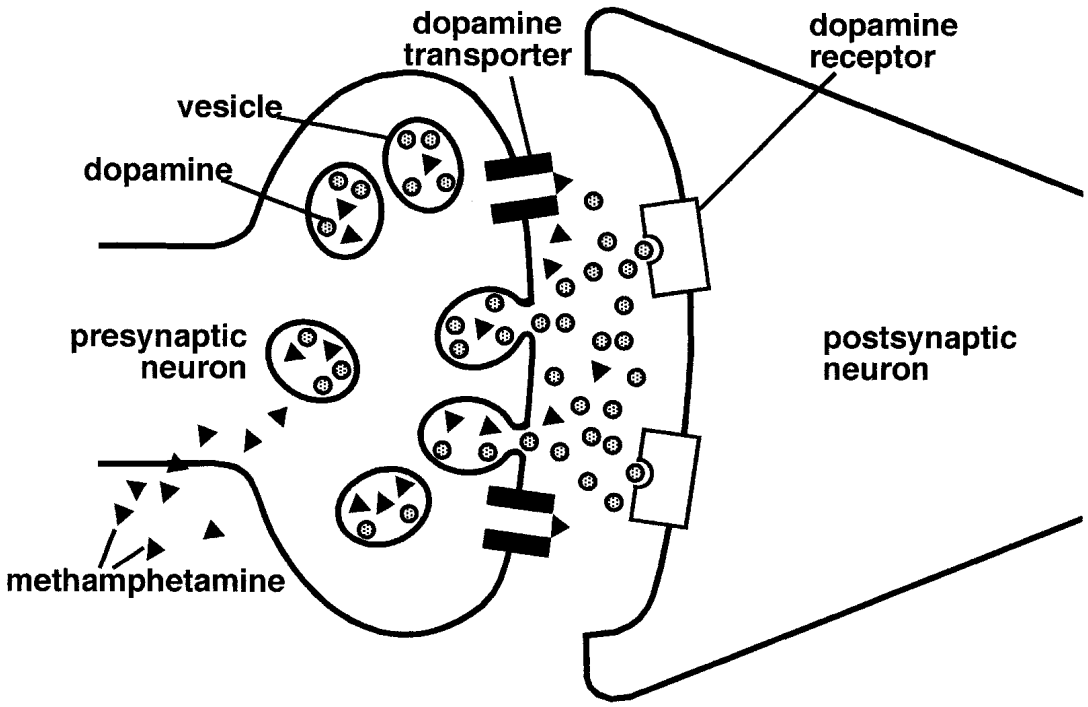
D. The signaling molecule is excitatory. Neuron #1 releases GABA as its neurotransmitter. Neuron #2 releases dopamine as its neurotransmitter.

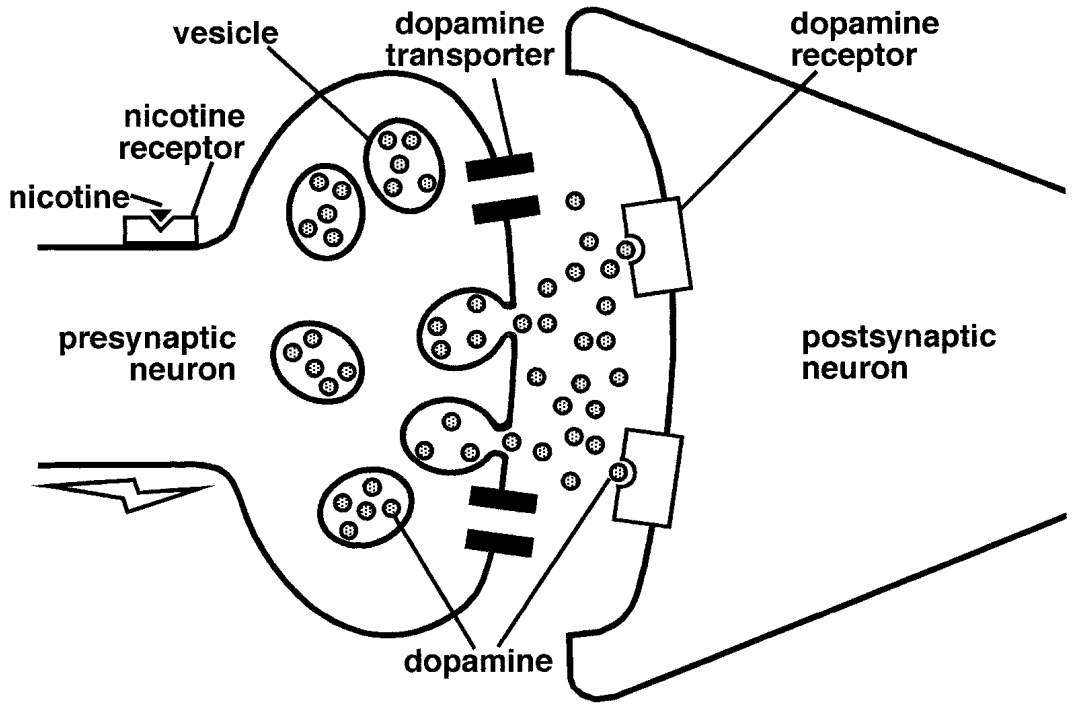
Case	Does the signal molecule excite or inhibit Neuron #1?	Does the activity of Neuron #1 increase or decrease?	Does the amount of neurotrans-mitter released from Neuron #1 increase or decrease?	What is the name of the neuro-transmitter released from Neuron #1?	Is the neuro-transmitter released from Neuron #1 excitatory or inhibitory?	Does the activity of Neuron #2 increase or decrease?	Does the amount of dopamine released from Neuron #2 increase or decrease?
A							
B							
C							
D							

Cocaine Alters Neurotransmission

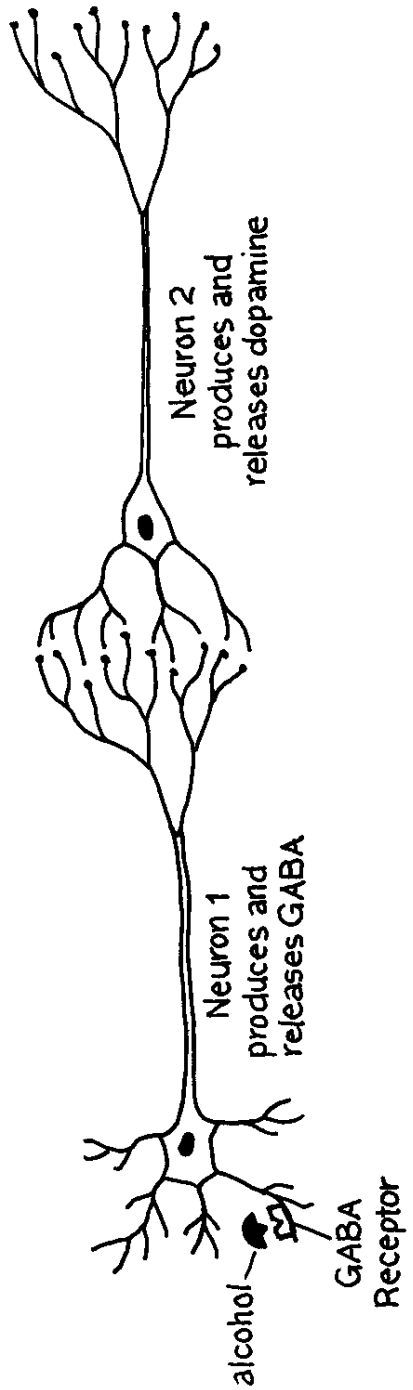


Methamphetamine and Nicotine Disrupt Neurotransmission





How Does Alcohol Affect Neurotransmission?



Parent Letter

Dear Parents,

Next week in biology class, we will investigate the effect of caffeine on the body. Each student will need to bring in a 12-ounce can of _____. Please provide one can labeled with your child's name and class period.

During the activity, students will consume 12 ounces of the above specified soft drink and measure what effect it has, if any, on their heart rates.

Students are not to bring in any soft drink other than the one specified. Because the different brands and flavors vary in their caffeine content, it is important that all students consume the same brand.

Students who choose not to bring in a soft drink, or those without signed permission forms, can participate in the activity by drinking 12 ounces of water. They will be an important part of the activity by serving as a "control."

Thank you for your continued support.

Teacher's Signature

My child, _____, has permission to participate in the caffeine activity in class and will bring in a 12-ounce can of _____ to consume as part of the activity.

My child, _____, has permission to participate in the activity in class and will bring in a 12-ounce can of **caffeine-free** _____ to consume as part of the activity.

My child, _____, will not drink a 12-ounce soft drink during the activity, but will participate by drinking 12 ounces of water.

Parent's or Guardian's Signature: _____

Date: _____

Caffeine: How Does Your Heart Respond?

MATERIALS FOR EACH TEAM

2 cans of soft drink (caffeinated or caffeine-free)
1 watch or classroom clock with a second hand

PROCEDURE

Do Steps 1-3 with your teacher.

1. When your teacher directs you to do so, find your pulse. You can find it most easily by pressing two fingers against the artery in your neck or on the inside of your wrist. Practice counting the beats.

2. When your teacher directs you to start, count the number of beats you feel in 15 seconds. Your teacher will tell you when to stop. Record the number in the data table on the next page.

3. Multiply the number of beats you counted in 15 seconds by four to calculate your resting heart rate in beats per minute.

Complete the rest of the activity with your partner.

4. Predict what you think might happen to your heart rate after you drink a caffeinated soft drink? What might happen after drinking a caffeine-free soft drink? Write your predictions here:

5. At the same time as your partner, drink your can of soft drink. Write down the time when you started drinking your soft drink. For best results, try to drink them quickly, taking less than 10 minutes to finish the can. Write the type of soft drink at the top of the data table on the next page.

6. Watch the time. Sit quietly for 5 minutes. You can talk softly with your partner or read, but keep your body still so that you will not change your heart rate due to activity.

7. After 5 minutes, have one partner measure his or her pulse rate for 15 seconds. Record the number of beats in the data table. The other partner should be the timer, saying "Start" and then "Stop" when the 15 second period is over. Now the partners should switch roles.

8. Continue to take pulse rates every 2 minutes until you have measured your heart rate at least 10 times. Record each measurement in the data table.

9. Use the data that you collected to calculate your heart rate in beats per minute.

Data Table

Name of Drink: _____ **Type: Caffeinated or Caffeine-Free**

Time (Minutes after drinking soft drink)	Heartbeats counted in 15 seconds	Multiply by 4	Heart rate (beats per minute)
0 (resting heart rate)		x 4	
5		x 4	
7		x 4	
9		x 4	
11		x 4	
13		x 4	
15		x 4	
17		x 4	
19		x 4	
21		x 4	
23		x 4	
25		x 4	
27		x 4	
29		x 4	
31		x 4	
33		x 4	
35		x 4	

Difference between resting heart rate and the highest heart rate after drinking the soft drink: _____

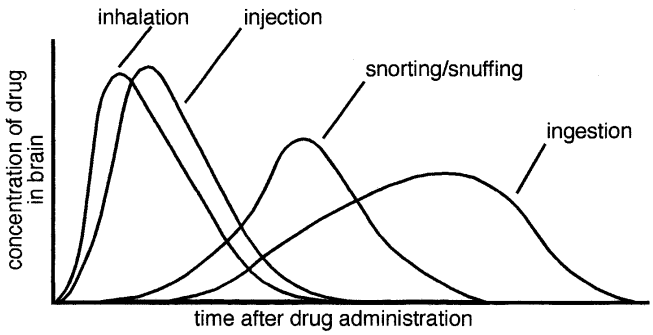
Number of minutes after finishing the drink when the heart rate reached its peak: _____

Number of minutes after finishing the drink when the heart rate returned to resting rate: _____

Could you drink some amount of caffeinated soft drink without any effect on your heart rate? What would happen if you drank a large amount of caffeinated soft drink? Design an investigation to determine how the amount, or dose, of caffeine affects your heart rate.

How Do Drugs Get In the Body?

Use the information in the graph below to help you answer the questions.



1. Four drug abusers each take a drug. One person injects 100 milligrams of a drug into a vein, one person smokes 100 milligrams of the drug, one person snorts 100 milligrams of the drug, and one person swallows or ingests 100 milligrams of the drug. Who will experience the greatest effect of the drug? The individual with the greatest concentration of drug in the brain will have the greatest effect.

2. Who will experience the quickest effect from the drug?

3. Who will experience the least effect from the drug?

4. Who will experience the slowest effect from the drug?

5. Tobacco smokers can use nicotine patches to help them quit smoking. The nicotine patches help the smoker slowly lower the amount of nicotine that enters the body. How does the nicotine in the patch enter the body?

6. Explain why the different ways of taking drugs cause different responses.

What Should the Doctor Do?

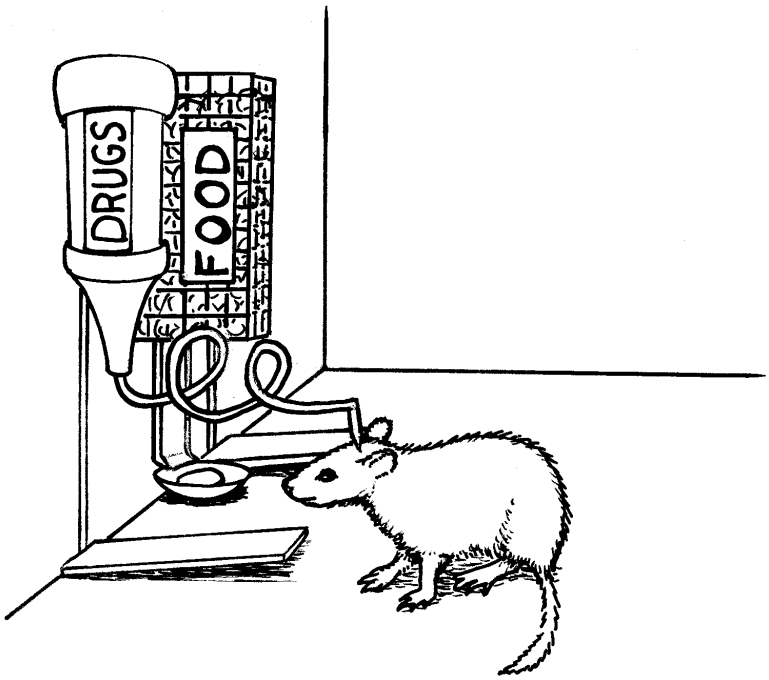
A teenage boy is brought into the hospital emergency room after a skateboarding accident. He complains of pain in his left leg. The doctor orders an x-ray of his leg, which reveals a fracture in the tibia. Before the doctor can set the fracture and put a cast on the boy's leg, he needs to relieve the patient's pain. The doctor prescribes morphine.

Based upon what you have learned about how drugs act in the body, how should the morphine be given to the patient? Should the morphine be given as a(n):

- pill
- shot
- inhalant

Consider each alternative and explain why the doctor should choose one method over another.

Data for Rat Self-administration Experiment

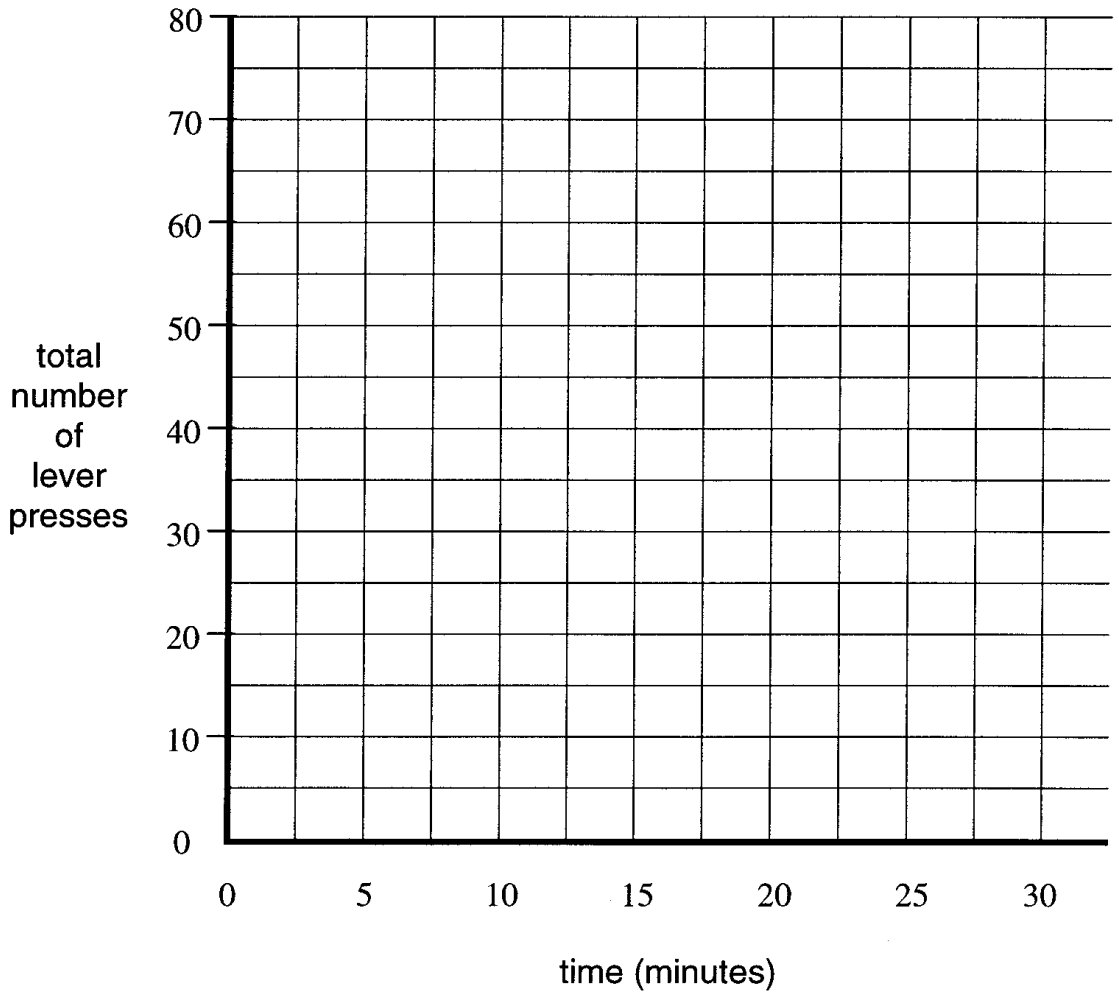


		Total number of lever presses					
Rat	Lever	**5 minutes**	**10 minutes**	**15 minutes**	**20 minutes**	**25 minutes**	**30 minutes**
A	**Stimulus**	2	7	12	29	52	73
	Food	1	3	4	6	6	6
B	**Stimulus**	1	3	3	4	6	7
	Food	2	4	5	8	9	12
C	**Stimulus**	1	6	13	26	49	70
	Food	1	1	2	4	4	4
D	**Stimulus**	1	2	2	4	4	4
	Food	2	3	5	6	8	11

Worksheet for Rat Experiment Data

Plot the data for one of the rats in the experiment in the graph below. Plot the data for the stimulus lever using a colored pencil and the data for the food lever with another color.

Rat: _____



Evaluating the Experiment

1. Why do the rats press a lever the first time?

2. Compare the lever-pressing behaviors of the four different rats. Which rat pressed the stimulus lever the most? Which one pressed the stimulus lever the least? Which rat pressed the food lever the most? Which one pressed the food lever the least?

3. Rat A was injected with cocaine each time it pressed the stimulus lever. Can you use this fact to explain why Rat A behaved the way it did?

4. Based on the data you analyzed, do you think Rat B was injected with cocaine when it pressed the stimulus lever? From what you have learned so far in this unit, do you think Rat B was injected with a different addictive drug when it pressed the stimulus lever? Why?

5. Do you think Rat C received cocaine when it pressed the stimulus lever? Why?

6. Rat C did not receive an injection of cocaine when it pressed the stimulus lever. When Rat C pressed the stimulus lever, it received a mild electrical stimulation in the brain. Based on what you have learned, can you predict what part of the brain was stimulated?

7. Rat D also received a mild electrical stimulation in the brain when it pressed the stimulus lever. Do you think the same part of the brain was stimulated in Rat D as was stimulated in Rat C? Why?

8. Why did Rats A and C press the stimulus lever more than the food lever?

9. Why did Rats B and D press the food lever more than the stimulus lever?

10. Why did the scientists who conducted this experiment include Rats B, C, and D in this experiment? How did the data from those rats help scientists understand more about how cocaine acts in the brain?

11. Do you think that Rats A and C will stop pressing the stimulus lever if they continue to receive the same stimulation each time they press it? Why?

12. Based on what you learned from these data, what might this investigation tell you about drug use by humans? Explain your view.

Playing the Game

1. Each person draws one card from the small pile of cards. Place it face up in front of you. This is your switch card. Set the rest of the cards in the short deck aside. You won't need them again.

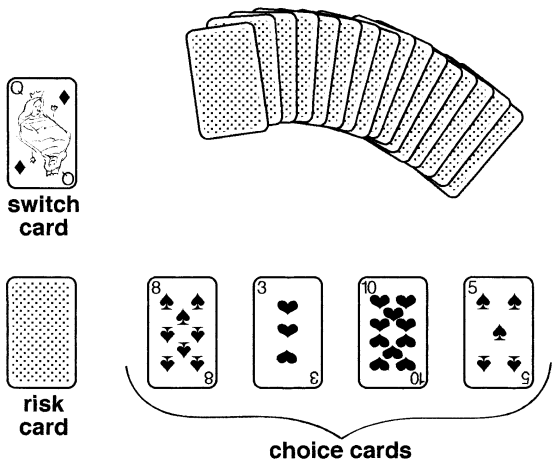
    - If you drew a jack, your switch value is 25.
    - If you drew a queen, your switch value is 35.
    - If you drew a king, your switch value is 45.

2. Draw a card face down from the larger pile that contains aces and the number cards. **Don't look at this card**. Place it face down below your switch card. This is your risk card.

3. Draw cards from the large pile and place them face up next to the risk card. These are your choice cards. Draw as many choice cards as you wish, but keep in mind that you do not want the total of these cards plus the risk card to equal or go over your switch value.

    - An ace = 1 point
    - Other cards = the number on the card

4. When you have finished drawing cards, turn over the risk card. Did you match or go over your switch value?



Who Is Addicted?

Two people have been using morphine. Chris has been taking between 50 milligrams (mg) and 500 mg each day for a year. Pat has been taking 100 mg each day for six months. Only one of these individuals is addicted to morphine.

- Who do you think is addicted to morphine? Explain your answer.

Pat is addicted to morphine.

- Can you think of any reasons to explain why Pat is addicted even though Chris has been taking a much higher dose for a longer period of time?

Pat has been living on the streets for a year after losing a job. When the savings ran out, Pat couldn't afford the rent for an apartment any longer and couldn't afford to keep a car. Pat became really depressed. When another homeless person offered some morphine, Pat thought the drug might help make the problems of life go away. For the past six months, Pat and friends have been shooting up with morphine once each day.

Twelve months ago, Chris was in an accident and received third degree burns over 30 percent of the body. While in the hospital undergoing treatment, the pain was very intense. The doctors prescribed morphine that Chris could self-administer to control the pain. After all, morphine is one of the most effective pain-relief medicines available. At first, 50 mg of morphine each day would ease the pain. Later, however, Chris needed as much as 500 mg a day to ease the pain. Chris may need a dose of morphine 12 times each day.

Long-term Effects of Drugs on the Brain

So, why are drugs so bad? After all, the "high" or "rush" only lasts a little while, right? What else could be happening in the drug abuser's brain? Consider that the brain is continuously changing. After all, learning occurs because neurons are forming new synapses. Scientists say that the brain has plasticity. That doesn't mean the brain is made of a chemical plastic like a credit card, but it refers to the brain's ability to modify connections in response to experience. When a person learns something or has new experiences, some new synapses may form or existing synapses may get stronger. Other synapses may disappear.

When a person takes drugs repeatedly, the brain changes in response to this experience. If a person takes drugs and then stops, he or she will "crave" the drug. In other words, the individual will have a strong desire to take more of the drug. Scientists can actually see evidence of cravings in the brain. If a cocaine addict sees pictures of drug paraphernalia, PET scans show that a part of the brain that is important for memory (called the amygdala) is activated. If the addict sees a video with mountains, trees, and animals, the amygdala is not stimulated. Thus, just seeing pictures of drugs or things associated with drugs can trigger an uncontrollable urge for drugs.

After taking drugs for a period of time, a person may need to take a higher dose of the drug to have the same rush that he or she did when first taking the drug. This is called tolerance. The brain has adapted to having a certain amount of drug present and does not respond the same way it did initially. That is why drug abusers and addicts take increasingly higher amounts of an abused drug. Tolerance may develop because the body may become more efficient at eliminating the chemical from the body, or because the cells of the body and brain become less responsive to the effect of the drug.

Scientific studies have shown clearly that certain drugs can cause dramatic changes in the brain, but not all questions have been answered. Drugs can change the structure of the brain. Perhaps one of the most dramatic long-term effects of a drug is to kill neurons. Many people have heard that drinking alcohol will kill brain cells. It's true. If alcohol is abused over a period of time, neurons in the brain can die. Some neurons in the brain are more sensitive to alcohol than others. Neurons that make up the mammillary bodies, areas in the brain that are important for memory, are more vulnerable to the effects of alcohol than are some other neurons in the brain. The neurons in the cerebral cortex, the part of the brain that controls most of our mental functions and endows us with consciousness, may also die if a person frequently abuses alcohol in high doses.

Another drug that is toxic to neurons is an amphetamine derivative called MDMA, or ecstasy. In rats and non-human primates, MDMA appears to kill neurons that produce serotonin, a neurotransmitter that is involved in regulating appetite, sleep, emotions, and so on. In some parts of the brain, the axons of some of these neurons may regenerate (or re-grow) after drug use is stopped, but the new growth of the neurons is not normal. Some areas are not reinnervated (nerve fibers do not grow back into the area) as they were before the drug abuse and

some areas have abnormally high regrowth of the neurons. Either way, the neurons are not normal. Studies have not yet been able to determine if MDMA has this same effect on humans, but some preliminary evidence indicates that MDMA may kill serotonin neurons in humans.

Cocaine also changes the brain in ways that may last for a long period of time. PET scans of human brains have shown that glucose metabolism is reduced even three months after the last use of cocaine. Remember that glucose metabolism is an indicator of how active the brain cells are. If the neurons are using less glucose, they are not as active. The changes that cocaine causes in the brain last much longer than the pleasurable feelings it produces. Other drugs cause similar decreases in brain activity. Even two years after the last use of amphetamines, PET images show that the drug abuser's brain is less active than the person's who never used drugs.

Scientists, for many reasons, don't know all of the effects that a drug may have. First, the brain is such a complicated organ that, despite great scientific advances, understanding all that it does will take many more years. Second, individuals may respond differently to drugs due to genetic differences among people. Third, many drug abusers abuse more than one drug. Many individuals who take cocaine, for example, also drink alcohol. The combination of the drugs makes it difficult to determine what the effect of one drug alone may be. Another complication is that drug addicts may have other health problems in addition to their drug problem. Heroin addicts, for example, spend most of their energy and activity trying to get their next "fix." Consequently, they do not eat well and may have impaired immune systems. Also, drug addicts often suffer from mental illnesses, such as depression. The changes that occur in the brain because of mental illness make it difficult to determine what changes the drugs have caused.

The brain is an incredibly complex organ. This complexity will keep scientists working for many years to understand how the brain works. Someday, scientists will answer questions about what happens in the brain to cause addiction, which will then help scientists understand how to prevent addiction.

1. What are some of the ways that drugs cause long-term changes in the brain?

2. How does the brain adapt to the presence of drugs?

3. How may the abuse of drugs relate to the plasticity of the brain?

4. What are some problems that scientists have when they investigate the effects of drugs on the brain?

Ranking Disease Treatment Outcomes

Disease	Predicted success	Medical compliance
Addiction		
Hypertension		
Diabetes		

Ruth's Story

Ruth is 24 years old and has a good job and a boyfriend. Everything seems to be going well in her life. But it hasn't always been that way. When she was 14 years old, her friends began smoking cigarettes and drinking alcohol. Because she wanted to be part of the group, she also began smoking and drinking when she went to parties with her friends. One night when Ruth was 16, her friends had some marijuana and they all tried smoking it. After using marijuana for about a year, she began experimenting with other drugs and, by the time she was 18, Ruth was using heroin every day. Her drug habit was costing her $75 a day. After awhile, her boyfriend left her and the rest of her friends were tired of her asking for money to buy drugs. She was fired from her part-time job because she had missed work so many times. She was arrested several times for shoplifting items from local department and discount stores. She tried to quit using heroin several times, but she had strong cravings for the drug. Each time she began having symptoms of withdrawal, Ruth went back to abusing drugs. When Ruth was 20, her brother convinced her to go to a drug rehabilitation center. The doctors at the center began treating her with methadone and she participated in group behavioral treatments. She followed her treatment exactly as the doctors prescribed and, after six months, Ruth thought she had beaten her addiction. She enrolled in college and made new friends. Her friends got her involved in sports, and Ruth found that she enjoyed running. She even competed in a 10K run. She continued her methadone treatment and saw her therapist every two months. When she was 22, Ruth ran into her old high school friends at a party and did some heroin with them. She thought she could handle it. Over the next couple of months, however, she quit her methadone treatment and began doing heroin more frequently, every couple of days. She was beginning to isolate herself from her friends and was having trouble at work. Ruth was scared. She called her doctors and they started her treatments again. With her doctors' help, Ruth realized that she needed to continue her medication and her counseling.

Mike's Story

Mike grew up an active boy who loved participating in sports. When he was 14, he was diagnosed with Type I diabetes. Mike learned how to measure his blood glucose levels before meals and give himself insulin injections based on his blood glucose level. He also learned how he should change his diet. Mike learned what types and amounts of foods he could eat and how he should schedule the time interval between meals. But, actually making these changes was very difficult for him. After discussions with the family doctor, Mike and his family decided he would spend six weeks at a summer camp for teenagers who have diabetes. While at camp, Mike ate the correct diet and learned how other kids cope with their diabetes. He even made several friends there. After he got home, Mike often e-mailed his friends from camp and they would talk about school, sports, and how diabetes changed their lives. Mike's life was pretty normal for a teenager—school, sports, friends. He found that as long as he regulated his blood glucose levels, he could do most of what he wanted. When he was 16, he got his driver's license. On weekends, he would sometimes forget his diet and eat hamburgers, french fries, and sodas with his friends. Because he only had a minor problem the first time he did this, he continued to ignore his diet when he was with his friends. One Saturday night, his parents had to take him to the emergency room because his blood sugar level was over 600. Although this scared him, he recovered. After a few weeks, though, he went back to eating whatever he wanted instead of the proper diet, especially if he was with his friends. Mike only checked his blood glucose level if he thought he might have a problem. He ended up back in the hospital several more times that year. His grades fell from As to Cs because he could not keep up with the work. He had trouble concentrating and was tired a lot. He and his parents argued all the time about Mike's failure to eat a healthy diet. The last time Mike went into the hospital, the doctor warned him that he was at risk for permanent health problems if he didn't control his blood glucose level: he could have kidney failure or could go blind. Mike's doctor recommended a specialist who could help Mike learn to cope with diabetes and still maintain an active social life. Mike's family also talked to the specialist to learn how they could help him. For the past four years, Mike has been able to control his blood sugar levels and has only had two minor episodes.

Carol's Story

Carol is the mother of two high school students. Although she is only 42 years old, her doctor has told her that she has high blood pressure, or essential hypertension. On one visit to her doctor, her blood pressure was 160/105. When her doctor checked her blood pressure again on another day, her blood pressure was 150/95. Her doctor prescribed medicine to lower her blood pressure. The doctor also told her to watch her diet and to begin exercising. The doctor told Carol that she needed to be very careful in controlling the amount of salt that she ate in her diet. Carol followed the doctor's plan for about six months. Gradually she started skipping her exercise sessions and gave up making healthy eating choices. Carol had a difficult time skipping the potato chips and peanuts that she liked to eat for an afternoon snack. Often she forgot to take her medication. At her next appointment, Carol and her doctor discussed the problems she was having, and the doctor informed her that her blood pressure had actually gone up. The doctor talked to her about getting advice from a nutritionist, working with a personal trainer to help her establish an exercise plan, and seeing a psychologist who could help her make the needed changes. Carol decided that she didn't need help from those people and tried again to diet and exercise on her own. But, with her long hours at work and her family to take care of, she found it difficult. Because she was missing work more often, Carol's boss gave a promotion to someone else instead of her. Carol's kids complained that she didn't come to their football games and band concerts anymore. One night, Carol complained that she was having another headache and her vision was blurry. Her kids commented that she was slurring her words when she spoke. Her husband immediately called an ambulance to take her to the emergency room. Carol received medical help in time, but the doctors told her that she had a mild stroke.

Disease Reference Information

HEROIN ADDICTION
The following information is drawn from the *NIDA Research Report Series, Heroin: Abuse and Addiction* (*www.nida.nih.gov*).

What is heroin?
Heroin is a member of the opiate family of drugs. Heroin is derived from morphine; in the brain, heroin is changed back into morphine. Because heroin enters the blood and reaches the brain more quickly than morphine, drug abusers and addicts often abuse heroin instead of morphine. Heroin is a white powder that is most often dissolved in saline and injected into the bloodstream, but it can also be snorted (sniffed) or smoked.

What does heroin do in the body?
After taking heroin, the abuser experiences a "rush," the intensity of which depends on the amount of drug taken and how the abuser takes it. The rush is accompanied by a warm flushing of the skin, dry mouth, and a heavy feeling in the extremities, which can be accompanied by nausea, vomiting, and severe itching. Heroin blocks pain messages transmitted from the body. After the initial effects, abusers will be drowsy for several hours. Mental function is clouded by heroin's effect on the nervous system. Cardiac functions slow; breathing is also severely slowed, sometimes to the point of death. Overdose is a particular risk because the amount and purity of the drug cannot be accurately known.

Treatment for heroin abuse and addiction
The first step in treatment is detoxification to rid the body of the drug. During detoxification, patients adjust to a drug-free state. This stage is short-term and needs to lead to a long-term treatment plan.

Methadone is a synthetic opiate that blocks the effects of heroin and eliminates withdrawal symptoms. Methadone binds to the same opiate receptor that morphine does (remember that heroin breaks down into morphine in the brain). Methadone, however, binds to the receptor more tightly than heroin. People usually take methadone orally one time each day to suppress cravings and withdrawal symptoms for 24–36 hours (four to six times longer than heroin). Methadone is not intoxicating or sedating, and does not produce the feelings of euphoria that heroin does, unless taken in very high doses. Individuals taking methadone do feel pain and have emotional reactions. People can take methadone continuously for many years without problems.

Other drugs used to treat heroin addiction include LAAM and naltrexone, but these are not used as extensively as methadone.

The most effective treatment combines pharmacological approaches (medications) with behavioral therapies. Behavioral therapies may be either on a residential or outpatient basis, but they need to match the needs of the patient.

Long-term consequences of uncontrolled or poorly controlled heroin abuse:
If heroin abuse is untreated, it can lead to the following health problems:

- addiction
- scarred and/or collapsed veins
- bacterial infections of the blood vessels and heart valves
- abscesses and other soft-tissue infections
- liver disease
- kidney disease
- lung diseases such as pneumonia and tuberculosis

In addition, the additives in street heroin often include substances that clog blood vessels that lead to the lungs, liver, kidneys, or brain. Contaminated injection equipment can lead to blood-borne viral infections including hepatitis B, hepatitis C, and HIV, which can then be passed on to other individuals through shared needles or sexual activity.

DIABETES TYPE I
The following information is drawn from the American Diabetes Association Web site (*www.diabetes.org*).

What is diabetes?
Type I diabetes is a disease that affects the way the body uses food. In a person with Type I diabetes, the body destroys the cells in the pancreas that produce insulin. Insulin is a hormone that regulates the level of sugar in the blood. Type I diabetes is also called immune-mediated diabetes, and was formerly known as insulin-dependent diabetes.

In Type II diabetes, once known as non-insulin-dependent diabetes, the pancreas does not make enough insulin or the body cannot use it properly. We will not discuss Type II diabetes any further.

Cause:
Scientists do not know what causes Type I diabetes, but there appears to be a genetic component to the cause. Other factors also are likely to increase the risk for getting diabetes. Diabetes is not contagious.

Symptoms and diagnosis:
Signs and symptoms of diabetes are:

- high levels of sugar in the blood
- high levels of sugar in the urine
- frequent urination (and/or bed-wetting in children)
- extreme hunger

- extreme thirst
- extreme weight loss
- weakness and tiredness
- feeling edgy and having mood changes
- feeling sick to the stomach and vomiting

Treatment:
Treatment for Type I diabetes involves keeping the level of sugar in the blood as close to normal (80-120 mg / dl) as possible. Treatment usually includes:

- Insulin injections to lower blood sugar. The number of injections required depends on the individual and the type of insulin treatment used.
- A meal plan to control changes in blood sugar levels. Food raises blood sugar levels. A dietician can help develop a plan that lets the diabetic eat the food he or she enjoys.
- Exercise to lower the blood sugar.
- Blood and urine testing to determine if the blood-sugar level is low, normal, or high. The results enable the diabetic to modify his or her food intake, exercise, or insulin injections.

Long-term consequences of uncontrolled or poorly controlled diabetes:

- blindness
- kidney disease
- nerve damage leading to abnormal sensations, including pain in the hands, feet, and legs
- vascular (blood vessel) disease leading to heart disease and strokes

Long-term outlook for diabetes if treated and controlled:
People with Type I diabetes can live happy, healthy lives if they follow their treatment plan.

HYPERTENSION
The following is drawn from materials from the American Heart Association (*www.americanheart.org*) and the National Heart, Lung, and Blood Institute (*www.nhlbi.nih.gov/health/public/heart/index.htm*).

What is hypertension?
Hypertension, or high blood pressure, is defined in an adult as a blood pressure greater than, or equal to, 140 mm Hg systolic pressure or greater than or equal to 90 mm Hg diastolic pressure. Hypertension does not refer to being tense, nervous, or hyperactive. Optimal blood pressure for an adult is 120 mm Hg systolic and 80 mm Hg diastolic. Blood pressures are normally written as systolic / diastolic, such as 120 / 80.

Cause:
In most cases, the cause of high blood pressure is unknown. This type of high blood pressure is called *essential hypertension*.

In the remaining cases (5%-10% of cases), high blood pressure, called secondary hypertension, is a result of another health problem such as a kidney abnormality, tumor of the adrenal gland, or congenital defect of the aorta. Blood pressure usually returns to normal when the underlying cause is corrected.

Symptoms and diagnosis:
Diagnosis of high blood pressure is based on the average of two or more readings taken at each of two or more visits after an initial screening.

Hypertension usually has no symptoms. Many people have high blood pressure and don't know it. If hypertension is severe, symptoms may include:

- tiredness
- confusion
- headaches
- anxiety
- excessive perspiration
- pale skin
- muscle tremors
- chest pain

Treatment:
The prescribed treatment depends on the severity of hypertension, but may involve the following components:

- taking medication
- modifying diet to reduce sodium intake
- increasing exercise
- maintaining proper weight
- limiting alcohol intake

Long-term consequences of uncontrolled hypertension:
High blood pressure directly increases the risk of coronary heart disease (which leads to heart attack) and stroke, especially along with other risk factors. Uncontrolled hypertension can also lead to renal failure.

Long-term outlook for hypertension if treated and controlled:
Hypertension is controllable with treatment, which may require periodic adjustment.

Evaluating the Cases

As a team, decide which member of the group will watch or read each case study. When you finish with your case, answer questions 1–6. Then, discuss and answer questions 7–11 with your group members. If you wish, watch or read the case studies again to help with your answers.

Case Study: _____

1. What disease does the individual have? Is it chronic or acute?

2. How did the disease change the individual's life?

3. What is the recommended treatment?

4. What did the individual do to improve his or her recovery?

5. What did the individual do that impaired his or her recovery?

6. Are there other things the individual could do to help with the disease?

Comparing the Cases

7. Which individuals were successful in their treatment? Which individuals were not?

8. Who was cured of their disease? What is the difference between treatment and cure?

9. How are the treatments for the different diseases similar?

10. How are the treatments different?

11. Can you identify similarities and differences in the actions or strategies that individuals took to help them deal with their disease?