CHAPTER 3

HOW DRUGS WORK IN THE BODY AND ON THE MIND

DISCUSSION QUESTIONS AND ASSIGNMENTS

1. Science-oriented news stories often are featured on a certain day each week in daily blogs, websites, and on a number of medical websites. During the semester, assign students to watch for articles that specifically bear upon one of the neurotransmitters described in the chapter. You might consider having a regularly scheduled “Neurotransmitter of the Week” discussion in class, where information about new findings regarding that neurotransmitter can be shared either as part of a lecture or as a class discussion/presentation.

2. Have students make a list of circumstances under which they feel they would be strongly influenced by the psychological effects of a placebo. Responses can be collected, transcribed (on an anonymous basis to protect their privacy), and photocopied for the entire class to receive as a handout. A class discussion could ensue regarding the reasons why a particular student might think that he or she would have a similar reaction. Likewise, if there is disagreement among students, an interesting discussion could follow regarding individual differences.

3. Bring a square cloth dinner napkin (approximately 18 inches by 18 inches) to class. Wrinkle it up into an oval-shaped ball by folding it into itself like a fan. Try to make it appear as an approximation of the convoluted cerebral cortex. Show it to the class then smooth the napkin out on a flat surface. This is an approximation of the surface area of the cerebral cortex if it were possible to be “un-convoluted.” The class could come up with at least two reasons why it would not have been good for humans to have a larger brain that included a cerebral cortex without convolutions. One reason is that the skull encasing the brain would have been too heavy for us to support at the neck and walk upright at the same time. Another reason is that the larger head would have not been able to fit through the birth canal during labor and delivery. Cortical convolutions have provided a greatly expanded cortical organization for higher-order information processing without requiring a greatly enlarged brain volume.

NOTE: A useful source for information about prescription and over-the-counter drugs available in the United States can be accessed through the following web site:

The National Library of Medicine/National Institutes of Health
http://www.nlm.nih.gov/

LECTURE OUTLINE FOR CHAPTER THREE

A. How Drugs Enter the Body

1. **Oral administration involves ingesting a drug by mouth, digesting it, and absorbing it into the bloodstream through the gastrointestinal tract**. Orally administered drugs have a relatively long absorption time and require specific pharmacological features and circumstances for successful passage into the bloodstream. Enzymes in the liver break down (metabolize) the structure of certain drugs, reducing the amount that eventually enters the bloodstream. This function of the liver is referred to as first-pass metabolism.

2. **Administration by injection allows a drug to be delivered directly into the bloodstream, bypassing the digestive process.** Examples of an injection administration include

intravenous (into a vein), intramuscular (into a muscle), and subcutaneous (underneath the skin) procedures. Of these possibilities, an intravenous injection is the fastest form of drug administration. Heroin injected into the forearm, for example, arrives at the brain in less than fifteen seconds.

3. **Inhalation refers to the ingestion of a drug in a gaseous or vaporous state into the lungs.** It is an extremely rapid form of drug administration. One inhalation method, smoking—burning a substance and breathing the smoke-borne particles in the air—has the disadvantage of carrying toxic particles produced by the burning process into the throat and lungs.

4. **Absorption of drugs can be accomplished by dissolving the drug and allowing it to pass through the skin or thin membranes.** Intranasal and rectal administration involves thin mucous membranes of the nose or rectum, respectively. Transdermal patches permit drugs to be absorbed slowly through the skin. Alternative methods under development include small silicon chips containing a grid of microscopic needles that painlessly pierce the skin and allow the passage of large molecules into the bloodstream.

B. How Drugs Exit the Body

1. The body eliminates drugs through a series of biotransformation processes in which the drug is chemically changed into forms called metabolites. A number of factors determine the rate of biotransformation during the elimination process. These factors include the quantity of the drug (alcohol is an exception, its elimination rate being independent of the quantity ingested), the age of the individual, and the drug's fat solubility. A fat-soluble drug will be eliminated more slowly than a water-soluble drug, all other factors being equal.

2. **The elimination half-life is the amount of time required for the drug to be reduced in the bloodstream by 50 percent. Each additional interval of time reduces the quantity of the drug by half until there is a negligible amount remaining.**

C. Factors Determining the Behavioral Impact of Drugs

1. One factor that impacts on a drug's behavioral effect is the time interval between two successive administrations of the drug. Time-release forms of medicines allow for a continual absorption over a longer period of time than would a single dose.

2. A second factor is the interacting effect of two different drugs administered at the same time. Drug combinations can be additive, hyperadditive, or antagonistic. **An additive effect produces an end result that is the mathematical sum of the effects of the two drugs separately. A hyperadditive effect produced by a combination of two or more drugs is referred to as synergism. If two drugs are perfectly antagonistic, each one cancels out the effect of the other.**

3. Some drugs can interact with each other during chronic usage. **Cross-tolerance between two drugs is a phenomenon in which the tolerance that results from the chronic use of one drug induces a tolerance effect with regard to a second drug that has not been used before.** Alcohol, barbiturates, and some antianxiety medications, for example, show cross-tolerance. **Cross-dependence is a phenomenon in which one drug can be used to reduce the withdrawal symptoms following the discontinuance of another drug.** Cross-dependence provides the means for continuing an abused drug in the guise of a new one.

4. Features of the individual who is taking the drug can influence the effect of the drug. Such features include weight, gender, ethnic background, and race.

D. Introducing the Nervous System

1. **The nervous system is divided into the central nervous system (brain and spinal cord) and the peripheral nervous system.** The peripheral nervous system either brings information in from the environment (sensory pathways) or out to the muscles (motor pathways). Motor control is exerted either through somatic nerves leading to skeletal muscle or autonomic nerves leading to cardiac or smooth muscle.

2. Autonomic nerves are divided into sympathetic and parasympathetic divisions. **Increased activity in sympathetic autonomic nerves produces body changes that are oriented toward dealing with some kind of emergency or stress. Increased activity in parasympathetic autonomic nerves produces body changes that are oriented toward calm, rest, nurturance, and internal maintenance.**

E. Understanding the Brain

1. **The brain is divided into the hindbrain, midbrain, and forebrain.** The hindbrain is concerned with basic life-support functions and primitive functions (medulla, pons, reticular formation, and cerebellum). The midbrain is a center for the control of important sensory and motor reflexes, body movements, and the processing of pain information (substantia nigra). The forebrain is concerned with motivational and emotional activity (hypothalamus and limbic system) and complex information-processing (cerebral cortex).

2. Of all the areas within the cerebral cortex, the most recently evolved is a region closest to the front of the brain called prefrontal cortex. Our higher-order, intellectual abilities (often referred to as executive functioning) as well as our personality characteristics emerge from activity in this region. It has been speculated that a dysfunction in the prefrontal cortex may be associated with a loss of personal control with respect to the abuse of alcohol and other drugs.

F. Understanding the Neurochemistry of Psychoactive Drugs

1. Psychoactive drugs work by virtue of their effects on the functioning of specialized cells called neurons. **Neurons are cells that receive and transmit information**. The principal components of a neuron are the cell body, the dendrites, and the axon. There are an estimated 100 billion neurons in the brain alone.

2. Communication between neurons is accomplished at the synapse. Synaptic communication can be either excitatory (causing an increase in the activity of the receiving neuron) or inhibitory (causing a decrease in the activity of the receiving neuron).

3. Synaptic communication comprises a sequence of three basic processes. Neurotransmitters stored in the synaptic vesicles are stimulated by a nerve impulse causing (1) neurotransmitter release from the synaptic knob, (2) binding to receptor sites on the surface of another neuron, and (3) reuptake of neurotransmitter into the synaptic knob whence it came.

G. The Major Neurotransmitters in Brief: The Big Seven

1. **Synaptic communication is achieved through the action of special molecules called neurotransmitters.** Seven major neurotransmitters in the brain are acetylcholine, norepinephrine, dopamine, 5-hydroxytryptamine (serotonin), gamma aminobutyric acid (GABA), glutamate, and a group of neurotransmitters referred to as endorphins. Whether a neurotransmitter has an excitatory or inhibitory effect depends upon the nature of the receptor at the synapse. Thus, excitation requires the activation of excitatory receptors and inhibition requires the activation of inhibitory receptors.

2. **Psychoactive drugs change the functioning of these and other neurotransmitters at the synapse or alter the functioning of receptors that are sensitive to these molecules.** As

examples, antianxiety drugs stimulate GABA receptors in the brain, cocaine and amphetamines increase dopamine and norepinephrine activity, LSD stimulates serotonin receptors, phencyclidine (PCP) and ketamine block one subgroup of glutamate receptors, and opiates (morphine, heroin, and codeine) stimulate endorphin activity.

H. Physiological Aspects of Drug-Taking Behavior

1. **The blood-brain barrier limits the passage of drugs and other molecules from the bloodstream to the brain**. Drugs that are fat-soluble and have relatively small molecular size have a relatively easier passage across the blood-brain barrier.

2. Tolerance effects—the decreased effectiveness of a drug taken in successive administrations—are achieved in two basic ways. **Metabolic tolerance occurs when the biotransformation processes in the liver are lessened over time. Cellular tolerance occurs when neuronal receptors become less sensitive to the drug over time.**

3. The craving response of individuals to certain psychoactive drugs constitutes a major aspect of the process of drug dependence. Two key elements are the neurotransmitter dopamine and a region of the brain called the nucleus accumbens where dopamine is active. Additionally, the insula of the brain has been found to be involved in the craving of drugs due to its involvement in emotion. In a study, twelve out of nineteen smokers with damage to the insula were able to quit smoking easily and were twenty-two times more likely to stop cigarette smoking than those without such damage.

I. Psychological Factors in Drug-Taking Behavior

1. **A drug effect can be considered as a three-way interaction between the drug's pharmacological properties, the individual taking the drug (set), and the environment within which drug-taking behavior occurs (setting).** The lower the drug dose, the greater the contribution made by set and/or setting.

2. The specific response to a drug can be influenced by the set of expectations a person may have about what the drug will do. This phenomenon accounts for the effectiveness of inert substances called placebos. Genuine physiological changes can occur due solely to the expectations of the drug user.

3. Due to expectation effects, the study of psychoactive drugs must have certain methodological safeguards. Drugs are tested against a placebo substance that looks and tastes like the drug but lacks the active ingredients of the drug. **In the double-blind research procedure, neither the researcher administering the drug or placebo nor the individual receiving the drug or placebo knows which substance is which.** A double-blind procedure ensures that drug effects are not influenced by either the researcher's expectations or the subject's expectations.

VIDEO SUGGESTIONS

"Addiction and the human brain" (2006), 25 min. Insight Media, 2162 Broadway, New York NY 10024-0621. Available on DVD.

Presenting studies indicating how drugs affect the developing brain more so than the adult brain and how changes in the brain result from prolonged use of such drugs as cocaine, heroin, nicotine, alcohol, and methamphetamine: there is an exploration of the changes in brain activity that underlie the development of drug dependence.

“Drugs and the brain” (2005), 5-part series, each 51 min. Films for the Humanities and Sciences, 132 West 31st Street 17th Floor New York, NY 10001. Available on DVD.

> Excellent examination of the neurochemistry of drug-taking behavior, illustrated through scientific histories and case studies.

“Constant craving: The science of addiction” (2001), 50 min. Films for the Humanities and Sciences, 132 West 31st Street 17th Floor New York, NY 10001. Available on DVD.

> A look at substance abuse from a biological perspective, including features on new medicinal treatments for addiction and brain research.

“The hijacked brain” (1998), 57 min. Part 2 of the 5-part PBS series, “Close to home: Moyers on addiction,” Films for the Humanities and Sciences, 132 West 31st Street 17th Floor New York, NY 10001. Available on DVD.

> This highly acclaimed PBS series spotlights the intimate experience of addiction as shared by the addicts themselves, their parents, children, and those helping them toward recovery. Part 2 examines the powerful new diagnostic tools (including functional MRI) that enable scientists to make discoveries about how addiction affects the brain, including the location of what is termed “the image of desire in the brain.”

“Animated neuroscience and the action of nicotine, cocaine, and marijuana in the brain with video clip” (1997), 25 min. Films for the Humanities and Sciences, 132 West 31st Street 17th Floor New York, NY 10001. Available on DVD.

> Using sophisticated 3-D animation, this program takes viewers on a journey deep into the brain to study the effects of the nicotine, cocaine, and marijuana. Viewers learn about the cellular targets of these drugs, as well as how each drug interacts with them and subsequently affects the body. Images of actual neurons used in the animations create a realistic effect that helps viewers understand the concepts presented.