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ABSTRACT

This guide provides a detailed look at the biological basis of drug addiction, examining how the brain and its reward system work and how drug abuse can cause fundamental changes in the way the brain works. It is a resource for clinicians and practitioners. The first section of the guide provides an outline of the following basic concepts presented in the videotape: (1) the electrochemical transmission system of the brain; (2) the effects of drugs on neurotransmission and on the brain's reward system; (3) two types of pharmacotherapy; and (4) approaches to treatment. The second section is a synopsis of the 26-minute videotape. The third section provides a glossary of technical terms. Section 4 provides discussion questions, and section 5 provides an annotated bibliography of resources on drug abuse and the brain. (JBJ)

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A Viewer's Guide

Drug Abuse and the Brain

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NATIONAL INSTITUTE ON DRUG ABUSE

A VIEWER'S GUIDE
DRUG ABUSE AND THE BRAIN

Office of Science Policy, Education, and Legislation
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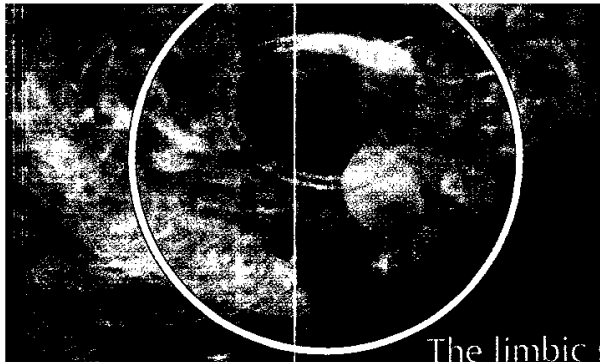


The limbic system is the region of the brain where drugs act to produce their pleasurable effect.

A depiction of multiple cells firing through the brain system.

The neurotransmission process occurs repeatedly throughout one hundred billion nerve cells in the human brain.

Axon of one cell releasing neurotransmitters across the synaptic gap to the dendrite of the receiving cell.

Close-up of a single ce
releasing neurotransmitt

INTRODUCTION

The Drug Abuse and the Brain Videotape Viewer's Guide is designed to reinforce issues discussed in the videotape and serve as a resource for clinicians and practitioners. The guide is divided into the following sections:

I. An outline of basic concepts presented in the videotape;
II. A detailed synopsis of the video;
III. A glossary of technical terms used in the video;
IV. Discussion questions for viewers to consider either individually or in groups; and
V. An annotated bibliography of resources on drug abuse and the brain.

Basic Concepts

After watching the video and reviewing the information in the viewer's guide, viewers will:

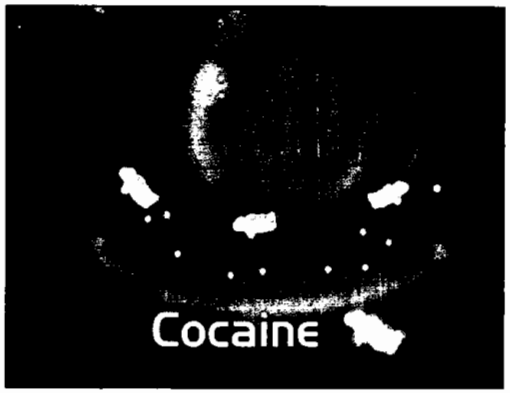
- Understand the electrochemical transmission system of the brain;
- Recognize the effects of drugs on neurotransmission and on the brain's reward system;
- Understand the way the two types of pharmacotherapy work; and
- Realize how understanding the effects of drug abuse on the brain can affect their approaches to treatment.

Synopsis

Drug Abuse and the Brain provides a detailed look at the biological basis of drug addiction. Through animation and interviews with experts in the field, clinicians will come to understand how the brain and its reward system work and how drug abuse can cause fundamental changes in the way the brain works.

Although the brain is usually considered one entity, it is in fact made up of several different structures, each of which has particular functions. The parts of the brain that are most affected by drug use are those areas that control both our feelings and our memory. Located near the top of the brain stem, the brain reward system is a major part of the brain's limbic system. Taking drugs affects this reward system, makes users feel good, and makes them want to use drugs again and again.

The brain contains a network of 100 billion nerve cells, or neurons. Neurons communicate with one another by means of electrochemical transmissions. Small amounts of



Cocaine molecules blocking reuptake of dopamine.

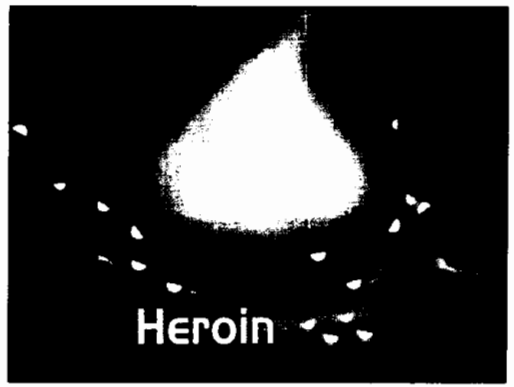
chemicals known as neurotransmitters are released from one cell and stimulate adjacent cells in a process that occurs millions of times every second.

Scientists now understand how some drugs of abuse affect the process of neurotransmission. Cocaine, for example, affects the naturally occurring chemical dopamine. In normal neurotransmission, dopamine is released from one neuron, travels across the synaptic gap between cells, and binds to receptors of adjacent cells. The action of dopamine is normally terminated primarily by reuptake by the nerve cell that released it. Dopamine is conserved in this way. The other mechanisms that terminate dopamine's actions—diffusion and metabolism—normally operate much more slowly than reuptake. Cocaine molecules interfere with the dopamine reuptake "pump" or transporter. As a result, dopamine accumulates in the synaptic gap, continuing to stimulate the receiving cell, thus creating the "high" commonly associated with cocaine use.

Heroin, morphine, and other opioids affect several brain regions, including the brain reward system. When these opioids enter the system, they bind to and activate receptors that are normally activated by naturally occurring neurotransmitters such as the endorphins. Heroin mimics the endorphins but can have a much more intense action.

Heroin or cocaine, smoked or injected intravenously, reaches the brain receptors so quickly and in such high concentrations that addicts call the intense feeling of well-being (euphoria) they produce a "rush."

Understanding how drugs affect the brain has enabled scientists to develop medications that help treat addiction. There are two types of pharmacotherapy: (1) agonist and (2) antagonist. Agonist therapy, such as methadone, mimics the effects of the drug it is working against. Methadone latches on to the same receptors as heroin, creating a similar biological response—but to a lesser degree and without the addictive side-effects. Antagonist therapy blocks the effects of the drug it is working against. For example, naltrexone binds to the same receptors that heroin does but is not capable of activating the receptors.



Heroin molecules binding to receptors.

Methadone: Agonist Therapy
Methadone molecules stimulating receptor cells.

As understanding of the biological aspects of drug abuse increases, scientists will undoubtedly develop other medications that will work against specific drugs. There will never be a magic cure-all. But when dealing with their clients, clinicians must consider not only the need for counseling but also the need to return the brain itself to a normalized state.

Key Terms

Agonist therapy.—This therapy uses drugs that mimic the responses of an addictive drug by stimulating the same receptors. An example is methadone, which can help reduce the craving associated with heroin withdrawal. Another example is the nicotine patch.

Antagonist therapy.—This therapy uses drugs that prevent the feelings produced by an addictive drug by occupying and blocking the same receptors. An example is naltrexone. Antagonists also block other effects of the abused drug, and short-acting antagonists, such as naloxone, are used to treat overdose toxicity.

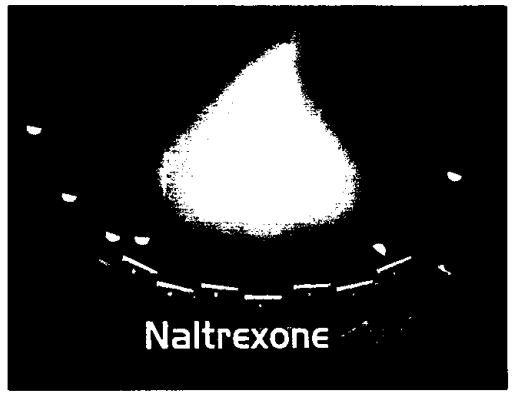
Axon.—This is an extension of the nerve cell along which electrical impulses are sent. At the end of the axon is the nerve terminal, where the neurotransmitters are stored and released.

Brain stem.—This is the brain's lowest structure which controls basic functions, including heart rate, breathing, eating, and sleeping.

Cerebral cortex.—This is the largest part of the brain. The cortex can be divided into several major areas, each of which has specific functions. Among the life functions governed by the cortex are our senses, our ability to generate movements, and our abilities to speak and understand as well as to think, plan, and remember.

Dendrite.—This is one of many branches in the nerve cell that receive messages from other nerve cells.

Dopamine.—This chemical occurs naturally in the brain, particular-



Naltrexone: Antagonist Therapy
Nalterxone molecules occupying and blocking receptors.

ly in parts of the reward system. The action of dopamine in the reward system is believed to underlie the sensation of pleasure.

Endorphin.—This is another of the brain's neurotransmitting chemicals. Endorphins are the body's internal opiate system, affecting our ability to control and deal with pain.

Limbic system.—This is a group of structures in the brain located between the brain stem and the cerebral cortex. The limbic system plays an important role in learning and memory. The brain's pleasure, or reward, circuit is part of the limbic system.

Neuron.—This is a nerve cell that has three main parts: the main cell body, axons, and dendrites.

Neurotransmitter.—This chemical enables nerve cells to communicate with each other.

Pharmacotherapy.—This treatment approach involves using medication.

Receptors.—These are molecules on the surface of dendrites that are specialized to receive messages from particular neurotransmitters.

Synapse.—This is a gap between nerve cells. Chemical neurotransmitters are transported across this gap from the axons of a sending neuron to the dendrites of a receiving neuron.

Synaptic vessicles.—These pouches, located near the ends of axons, are the places where neurotransmitters are stored.

Questions for Discussion

After viewing the video, clinicians could consider the following questions as they relate to client treatment. Such questions also could be the focus of discussion among treatment professionals.

Why does the client have such an uncontrollable desire to get and use drugs?

The cortex is unable to override the desire of the pleasure (or reward) circuit. A logical choice, which would be to avoid taking drugs, ordinarily would be made by the cortex. It is the prime information processing system in the brain. But because the drugs act directly on the more primitive midbrain, normal channels of decisionmaking are bypassed. The desire to seek the pleasure induced by drugs controls the entire thought process. Counseling can help strengthen the ability to make effective choices.

What are the biological causes of some common cocaine withdrawal symptoms?

It is possible that the brain attempts to adjust to the overabundance of dopamine in the synaptic gaps by reducing the number of dopamine receptors. Even after dopamine levels return to normal, there are fewer receptors available and therefore the nerve cell might not be fully stimulated. Depression and craving could be the result. Since prolonged use of cocaine may affect the receptors for weeks, or even months, after the last use, withdrawal symptoms also could persist for a long time.

Why would it be important for clients to understand what's going on in their brain?

Knowledge that their brain is out of control can help clients get a handle on what is happening to them. They can realize that there is more involved than just a lack of willpower on their part.

Why do drug abusers so frequently experience relapse?

In addition to the social pressures and other factors that come into play with drug abusers, the effects that drugs have on the brain do not disappear once drugs are removed from their systems. It appears that the physical changes that take place in the brain do not repair themselves overnight. Nerve cells may attempt to adjust in the presence of drugs and also have to readjust to a drug-free situation. Memory also plays a role: Addicts remember the pleasure involved in the drug-taking experience and, like any enjoyable experience, addicts want to have the experience again.

Why does the "pleasure circuit" play such an important role in understanding drug abuse?

The pleasure circuit involves structures in all parts of the brain. It involves the survival functions of the brain stem, the emotional balance of the limbic system, and the information processing of the cerebral cortex. Life's sustaining activities (e.g., eating good food and engaging in sex) activate the pleasure circuit, and we want to do them again and again. Drugs also activate the pleasure circuit and, unfortunately, seem to offer the strongest and quickest way to euphoria. To addicts, drugs can become as important to survival as food or sex.

ANNOTATED BIBLIOGRAPHY

PRINT MATERIALS

"Alcohol and the Brain." *Alcohol Health & Research World*, 14(2), 1990, pp. 81-168. (NCADI)

The brain controls our ability to think, reason, learn, and remember. The brain allows us to act and react intellectually, physically, and emotionally both to external events and to our own internal responses to those events. The brain, in all its unfolding complexity, is what makes us distinctly human. Examining the brain's complexity, and exploring both what we know and what we hope to learn about the myriad effects of alcohol on the brain, is the topic of this special focus issue. Specific topics include alcohol and the brain, the nervous system and the predisposition to alcoholism, alcohol reinforcement, complex determinants of drinking, the processes of alcohol tolerance and dependence, and liver-brain relations in alcoholics.

Blum, K., and Payne, J.E. *Alcohol and the Addictive Brain: New Hope for Alcoholics From Biogenetic Research.* New York, NY: Free Press, 1991.

This book illuminates the nature of alcoholism and explores its human costs. The book reports scientific advances that have provided new insight into the causes of alcoholism and discusses research pathways that offer promise of eventual prevention or cure. The first section deals with the problem of alcoholism, early attempts to define alcoholism and two of the treatment approaches used, and self-help and biopsychic approaches. The second section discusses the neuron, the biochemistry of alcoholism, the opiate connection, the malfunction of the reward messengers, the concept of alcoholism as a disease, the craving model, the reward cascade theory, and the alcogenes. Alcoholism is viewed in this book as a biogenetic disease characterized by genetic anomalies leading to biochemical deficiencies or imbalances and receptor malfunctions. Three alternative hypotheses that disregard the disease concept of alcoholism are described in the concluding chapter.

Cohen, S. *The Chemical Brain: The Neurochemistry of Addictive Disorders.* Minneapolis, MN: CompCare Publishers, 1988.

This book attempts to fuse recent information and hypotheses about the biochemical processes involved in mental functioning and emphasizes the neurochemistry of addictive disorders. Chapter titles include: The Chemical Neuron; Neurotransmitters, Neuropeptides,

and Neurohormones; the Chemistry of Addiction; the Pharmacotherapy of the Addictions; the Genetics of Substance Abuse; Imaging the Brain; and Future Prospects. This volume was written for health professionals and contains basic information. A certain amount of technical language is included, but explanations of such technical terms appear in the text's glossary.

Drugs and the Brain. Bethesda, MD: National Institutes of Health, U.S. Department of Health and Human Services, June 1991.

This booklet gives a general description of how drugs influence behavior by working on one important brain center. To promote an understanding of how drugs produce their effects, the booklet then discusses how nerve cells and the molecules that make up these cells interact with the molecules that make up drugs. The biological basis of addiction is discussed for opiates, cocaine, marijuana and hallucinogens, PCP (phencyclidine), depressants, and designer drugs. Drugs and the fetus, the steps to addiction, treatment, and genetics and biology also are examined. This resource is written in an understandable manner and is informative.

Drugs of Abuse: A Special Issue. *Trends in Pharmacological Sciences.* New York, NY: Elsevier Science Publishing Co., Inc., 13(5), May 1992.

This special issues considers all the scientific approaches that have been taken to understand how drugs of abuse work. While the articles in this issue are written in a technical style, the information is important to understanding how these drugs function in the human brain. Articles on the following subjects are presented:

- Drugs of Abuse: Behavioral Principles, Methods, and Terms;
- Drugs of Abuse: Anatomy, Pharmacology, and Function of Reward Pathways;
- Neurobiology of Opiate Abuse;
- Neurobiology of Cocaine Abuse;
- Neurobiology of Marijuana Abuse;
- Neurobiology of Alcohol Abuse; and
- Genetic Approaches to Drug Dependence.

Hanna, N. *Drugs—The Altered Brain.* Center City, MN: Hazelden Educational Materials, 1990.

This pamphlet describes in simple language how drugs—from alcohol and cocaine to caffeine and nicotine—interfere with the brain's chemical balance. The pamphlet explains that withdrawal is the brain's way of returning to its original chemical balance and delineates what happens when relapse occurs. Tables and figures add to an understanding of the brain's functions during these processes.

Holloway, M. "RX for Addiction." *Scientific American,* 264(3), March 1991, pp. 95-104.

This article examines various aspects of drug addiction and the brain and capsulizes the new generation of

pharmaceuticals that have been developed to combat drug addiction. PET probes, the reward pathway, unmotivated addicts, second messengers, and viral shuttle are discussed. This article is excellent for individuals who want to learn what currently is happening in the field.

Inaba, D.S. *Uppers, Downers, All Arounders.* San Francisco, CA: The Haight-Ashbury Free Clinics Press, 1989. (Cinemed, Inc.)

This book was written and designed to serve as a factual, nonjudgmental reference source and textbook about psychoactive drugs, including alcohol, crack-cocaine, marijuana, crank, tobacco, and Valium. The book provides information on the mental and physical effects of those substances and about associated issues, e.g., drug testing, treatment, drug abuse prevention, drugs in the workplace, drug use during pregnancy, drugs in school, AIDS (acquired immunodeficiency syndrome), and codependency. It is written clearly and concisely in simple language and uses more than 200 illustrations, photographs, and graphs. The book can be used by teachers and students, parents and teenagers, employers and employees, counselors and clients, medical personnel, law enforcement groups, and those who want to know more about psychoactive drugs. Reviews, questions, and suggested exercises are included.

Kirsch, M.M. *Designer Drugs.* Minneapolis, MN: CompCare Publications, 1986.

This book is a series of firsthand reports and personal interviews by researchers, narcotics detectives, physicians, underground chemists, black market dealers, and drug users. Drugs discussed include crack, China White Ecstasy, MPTP, crystal, and dust. The chapter on crack presents information on the brain and illustrates how dopamine neurotransmitters respond to normal pleasurable events as opposed to those induced by cocaine. The text is directed toward individuals who want to know more about the hazards of designer drugs.

Miller, N.S. *The Pharmacology of Alcohol and Drugs of Abuse and Addiction.* New York, NY: Springer-Verlag New York, Inc., 1991.

The content of this book is organized to flow from general concepts of abuse and addiction to specific details of the pharmacology of alcohol and drugs. Chapters on special topics, such as the pharmacology of drug-drug interactions, abstinence, and prevention, are included. This book is written especially for the clinician interested in the pharmacology of alcohol and drugs of abuse and addiction. The pharmacology is integrated into a conceptual approach to diagnosis and treatment of alcohol and drug abuse addiction. The form and style of the book are didactic, critical, and straightforward in presentation. Literature references from recent clinical research and basic research provide the foundation for

the chapters. The information is readily adaptable to clinical problems and research ideas.

Mind and Brain. *Scientific American,* 267(3), Sept. 1992.

This special issue of *Scientific American* explores the following topic areas: mind and brain, the developing brain, the visual image in the mind and brain, the biological basis of learning and individuality, brain and language, working memory and the mind, sex differences in the brain, major disorders of the mind and brain, the aging brain, the aging mind, how neural networks learn from experience, and the problem of consciousness.

Radcliffe, A., Rush, P., Sites, C.F., et al. *The Pharmer's Almanac.* Denver, CO: M.A.C. Books, 1988.

This book is designed to help nonmedically trained professionals understand the drugs that cause people to become addicted. The four major sections covered in easy-to-read language with illustrations are (1) absorption (how drugs get into the circulation system and how alcohol is absorbed into the gastrointestinal system), (2) distribution (how drugs travel throughout the body, including the brain), (3) metabolism (how drugs are transformed in the body), and (4) excretion (how drugs and metabolites are eliminated from the body).

Rawson, R.A. *The Neurobehavioral Treatment Manual: A Therapist Manual for Outpatient Cocaine Addiction Treatment.* Beverly Hills, CA: The Matrix Center, Inc., 1989.

This 250-page neurobehavioral model of cocaine dependency treatment establishes a clear timetable for recovery from cocaine dependency and focuses on four distinct areas of functioning. Strategies for addressing these areas include the use of relapse prevention methods and individual therapy procedures, which include education on the brain chemicals and the recovering brain and on emotional problems, family systems materials, 12-Step involvement, and urine testing. The model constructs a comprehensive framework for facilitating involvement in recovery activities that promote positive behavior change. The manual describes the relapse prevention component of the model, presents the use of a systematic relapse analysis procedure, and outlines plans for evaluating the model. The development of a comprehensive outpatient model for treating cocaine dependency provides a standardized structure within which other treatment interventions (e.g., medication and acupuncture) may be evaluated.

Schuckit, M.A. *Drug and Alcohol Use: A Clinical Guide to Diagnosis and Treatment, 3d.* New York, NY: Plenum Medical Book Company, 1989.

The third edition of this text has been modified to reflect the changes that have taken place in the field since the second edition, e.g., the introduction of new nonbenzodiazepine antianxiety drugs that are not true central nervous

system depressants and the increased knowledge with regard to the basic pharmacology of many of the drugs that are abused. This book includes a marked expansion of the discussion of dual diagnoses; a new section describing the nonbenzodiazepine antianxiety drugs; new data regarding the brain mechanisms of a variety of drugs, including opiates; and an extensive update on alcohol detoxification as well as drug and alcohol rehabilitation programs. Consistent with the overall goals of this work to help the student and clinician stay up to date, more than 60 percent of the references offered at the end of the chapters have been updated to reflect data published since the appearance of the second edition in 1984.

Additionally, anyone involved with the delivery of health care to patients with drug or alcohol problems uses the Diagnostic and Statistical Manual of Mental Disorders published by the American Psychiatric Association. Therefore, beginning in Chapter 3 and continuing throughout the text, the author refers the reader to relevant codes in the revised third edition of that manual.

Society for Neuroscience. *Brain Facts.* Woodlawn, MD: Wolk Press, Aug. 1991, second printing.

This 32-page illustrated booklet, designed for a lay audience, contains up-to-date information on the latest understanding of the brain and nervous system. It includes sections on the neuron, brain development, sensation and perception, learning and memory, movement, the major neurological and psychiatric disorders, new diagnostic methods, and potential therapies for brain disorders. The chapter on addiction discusses alcohol, psychostimulants, and opiates.

Stimel, B. (ed.) *Addiction Potential of Abused Drugs and Drug Classes.* New York, NY: The Haworth Press, 1990.

The papers in this volume clarify the state of addiction liability of the drugs that are abused most often. Nine drugs and drug classes have been chosen for review. The authors have meshed their research expertise with the available scientific literature to evaluate factors that contribute to the addictive qualities of drugs. Topics include the addictiveness of central stimulants, opioids, alcohol, barbiturates and other sedatives, benzodiazepines and nonbenzodiazepine anxiolytics, PCP and hallucinogens, and inhalants and anesthetics.

Washton, A., and Boundy, D. *Willpower's Not Enough.* New York, NY: Harper Collins Publishers, 1990.

This book presents a model for understanding and recovering from the source of addictions. It addresses the addictive personality, addictive family, and addictive society and explains why it is essential for clients to adopt less addictive lifestyles to avoid vulnerability. Although the authors state that this is not a quick-fix book, they describe a strategy for embarking on a recovery path that will significantly change the lives of those suffering from addictions of every kind.

Zweben, J.E., and Smith, D.E. (eds.) "Pharmacological Adjuncts and Nutritional Supplements in the Treatment of Drug Dependence." *Journal of Psychoactive Drugs*, 20(3), July-Sept. 1988.

Since the inception of this journal, more has been learned about brain chemistry as it relates to alcohol and other drug dependence than in the entire history of science. This explosion of knowledge has provided the foundation for a better understanding of the biochemical basis of alcoholism and has set the stage for the study of a range of pharmacological adjuncts and nutritional supplements in the treatment of drug dependence. This journal edition examines a wide variety of topics that concern an understanding of how the brain works and an identification of specific receptors in the brain that led to the discovery of neurotransmitters (biochemicals that are produced by the brain). Articles such as "A Primer on Neurotransmitters and Cocaine and Improvement of Cocaine-Induced Neuromodulator Deficits by the Neuronutrient Tropamine" add to the knowledge base in these areas.

VIDEOTAPE MATERIALS

Uppers, Downers, All Arounders (60 minutes), Haight-Ashbury. (Cinemed, Inc.)

Part I, The Effects, examines how and why the physical and emotional centers of the brain are affected by psychoactive drugs. It gives a general classification of drugs; discusses and illustrates tolerance, dependence, and withdrawal; and examines the various levels of drug-seeking behavior (e.g., experimentation, social use, habituation, abuse, and addiction).

Part II, The Drugs, identifies the most commonly used psychoactive drugs (e.g., alcohol, cocaine, heroin, inhalants, look-alikes, marijuana, and Valium), classifies them by effect, and shows how they are absorbed and metabolized. It also gives a short history on drug use.

The Haight-Ashbury Cocaine Film: Physiology, Compulsion and Recovery (35 minutes), Haight-Ashbury. (Cinemed, Inc.)

This video demonstrates how cocaine manipulates brain chemistry using animation, computer graphics, live action, and interviews with recovering abusers. The video demonstrates how cocaine forces the release of neurotransmitters—such as dopamine, epinephrine, serotonin, and acetylcholine—and how that release exhausts and disrupts the brain chemistry to the point of exhaustion, paranoia, and even convulsions. The video also shows how the sex, hunger, and thirst drives are artificially satiated, causing the user to be truly hungry, thirsty, unable to feel pleasure, and yet harbor a voracious drug hunger.

Fires of the Mind (57.44 minutes), WQED/Pittsburgh and The National Academy of Sciences. (NAS Film Committee)

This video addresses the following three questions: (1) Which is more powerful—a computer or a human brain?

(2) Are people born with special talents or are these talents acquired? and (3) Do children's brains use as much energy as adults' brains? The video introduces the viewer to scientists investigating the human brain and the mystery of thought.

Prisoners of the Brain (60 minutes), WQED/Pittsburgh and the National Academy of Sciences. (NAS Film Committee)

This video reports on the progress being made in treating mental illness. The video delves into the sociological issues related to the use of mind-altering drugs and explores what ultimately determines thinking and behavior and how we can control them.

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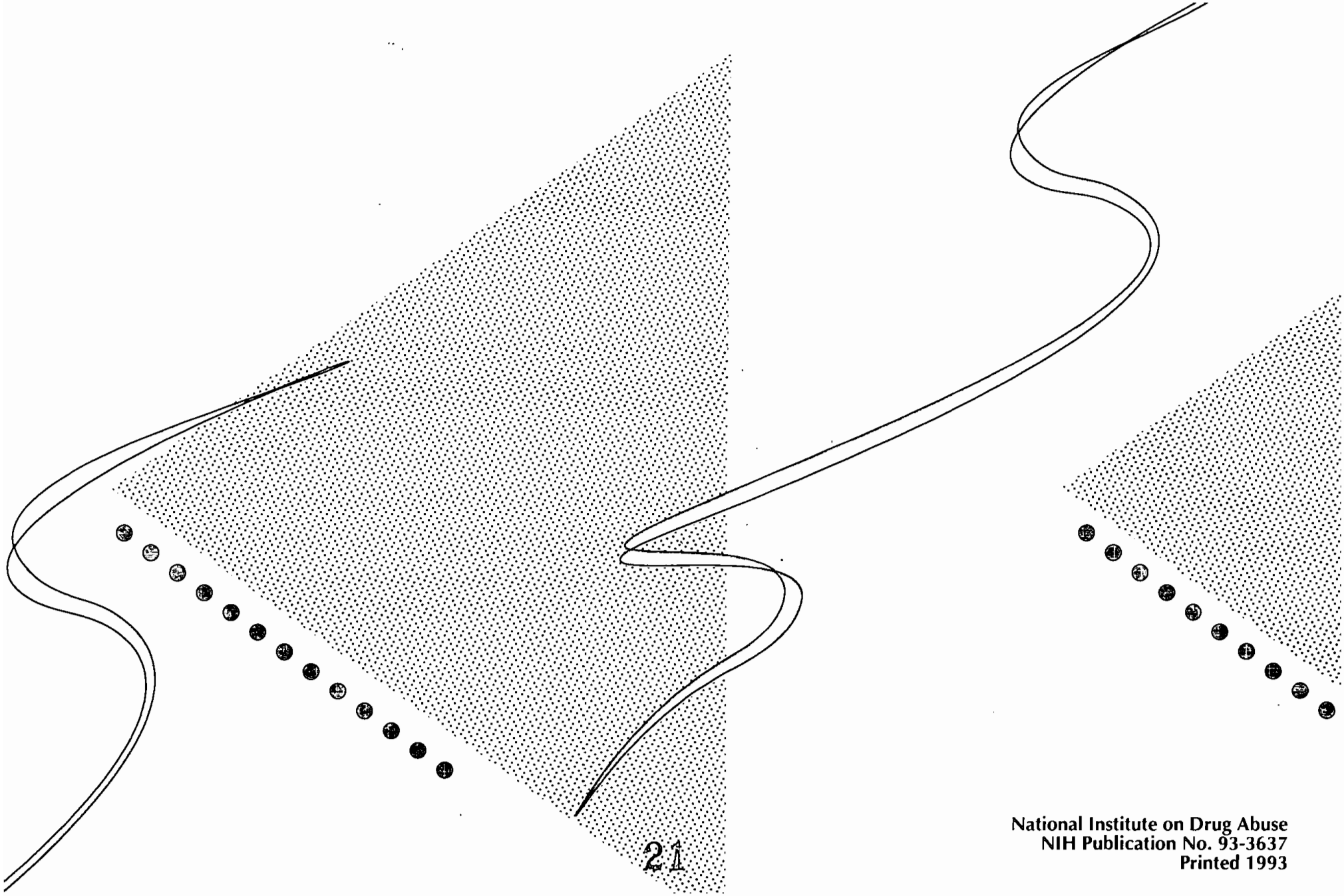

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