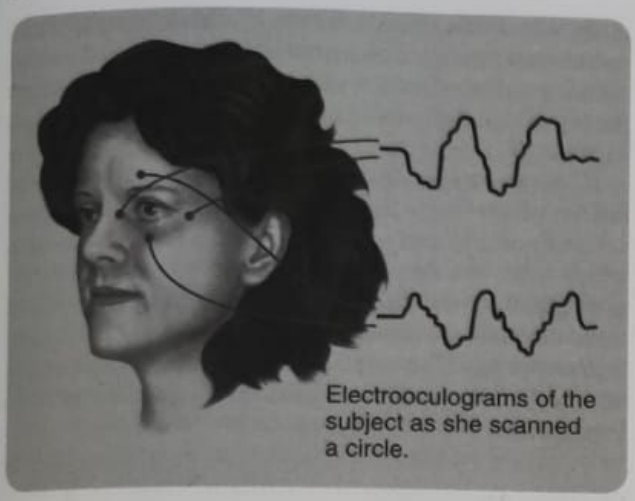


FIGURE 5.13 The typical placement of electrodes around the eye for electrooculography. The two electrooculogram traces were recorded as the volunteer scanned a circle.

its horizontal movements and between two electrodes placed above and below the eye to measure its vertical movements (see Figure 5.13).

SKIN CONDUCTANCE

Emotional thoughts and experiences are associated with increases in the ability of the skin to conduct electricity. The two most commonly employed indexes of *electrodermal activity* are the **skin conductance level** (**SCL**) and the **skin conductance response** (**SCR**). The SCL is a measure of the background level of skin conductance that is associated with a particular situation, whereas the SCR is a measure of the transient changes in skin conductance that are associated with discrete experiences.

The physiological bases of skin conductance changes are not fully understood, but there is considerable evidence implicating the sweat glands. Although the main function of sweat glands is to cool the body, these glands tend to become active in emotional situations. Sweat glands are distributed over most of the body surface; but, as you are almost certainly aware, those of the hands, feet, armpits, and forehead are particularly responsive to emotional stimuli.

CARDIOVASCULAR ACTIVITY

The presence in our language of phrases such as *chicken-hearted*, *white with fear*, and *blushing bride* indicates that modern psychophysiologists were not the first to recognize the relationship between *cardiovascular activity* and emotion. The cardiovascular system has two parts: the blood vessels and the heart. It is a system for distributing oxygen and nutrients to the tissues of the body, removing metabolic wastes, and transmitting chemical messages. Three different measures of cardiovascular activity are frequently employed in psychophysiological research: heart rate, arterial blood pressure, and local blood volume.

Heart Rate The electrical signal associated with each heartbeat can be recorded through electrodes placed on the chest. The recording is called an **electrocardiogram** (abbreviated either **ECG**, for obvious reasons, or **EKG**, from the original German). The average resting heart rate of a healthy adult is about 70 beats per minute, but it increases abruptly at the sound, or thought, of a dental drill.

Blood Pressure Measuring arterial blood pressure involves two independent measurements: a measurement of the peak pressure during the periods of heart contraction, the *systoles*, and a measurement of the minimum pressure during the periods of relaxation, the *diastoles*. Blood pressure is usually expressed as a ratio of systolic over diastolic blood pressure in millimeters of mercury (mmHg). The normal resting blood pressure for an adult is about 130/70 mmHg. A chronic blood pressure of more than 140/90 mmHg is viewed as a serious health hazard and is called **hypertension.**

You have likely had your blood pressure measured with a *sphygmomanometer*—a crude device composed of a hollow cuff, a rubber bulb for inflating it, and a pressure gauge for measuring the pressure in the cuff (*sphygmos* means "pulse"). More reliable, fully automated methods are used in research.

Blood Volume Changes in the volume of blood in particular parts of the body are associated with psychological events. The best-known example of such a change is the engorgement of the genitals associated with sexual arousal in both males and females. **Plethysmography** refers to the various techniques for measuring changes in the volume of blood in a particular part of the body (*plethysmos* means "an enlargement").

One method of measuring these changes is to record the volume of the target tissue by wrapping a strain gauge around it. Although this method has utility in measuring blood flow in fingers or similarly shaped organs, the possibilities for employing it are somewhat limited. Another plethysmographic method is to shine a light through the tissue under investigation and to measure the amount of the light absorbed by it. The more blood there is in a structure, the more light it will absorb.

5.3 Invasive Physiological Research Methods

We turn now from a consideration of the noninvasive techniques employed in research on living human brains to a consideration of more direct techniques, which are commonly employed in biopsychological studies of laboratory animals. Most physiological techniques used

in biopsychological research on laboratory animals fall into one of three categories: lesion methods, electrical stimulation methods, and invasive recording methods. Each of these three methods is discussed in this section of the chapter, but we begin with a description of *stereotaxic surgery*.

STEREOTAXIC SURGERY

Stereotaxic surgery is the first step in many biopsychological experiments. *Stereotaxic surgery* is the means by which experimental devices are precisely positioned in the depths of the brain. Two things are required in stereotaxic surgery: an atlas to provide directions to the target site and an instrument for getting there.

The **stereotaxic atlas** is used to locate brain structures in much the same way that a geographic atlas is used to locate geographic landmarks. There is, however, one important difference. In contrast to the surface of the earth, which has only two dimensions, the brain has three. Accordingly, the brain is represented in a stereotaxic atlas by a series of individual maps, one per page, each representing the structure of a single, two-dimensional frontal brain slice. In stereotaxic atlases, all distances are given in millimeters from a designated reference point. In some rat atlases, the reference point is **bregma**—the point on the top of the skull where two of the major *sutures* (seams in the skull) intersect.

The **stereotaxic instrument** has two parts: a *head holder*, which firmly holds each subject's brain in the prescribed position and orientation; and an *electrode holder*, which holds the device to be inserted. A system of precision gears allows the electrode holder to be moved in three dimensions: anterior–posterior, dorsal–ventral, and lateral–medial. The implantation by stereotaxic surgery of an electrode in the amygdala of a rat is illustrated in Figure 5.14.

LESION METHODS

Those of you with an unrelenting drive to dismantle objects to see how they work will appreciate the lesion methods. In those methods, a part of the brain is removed, damaged, or destroyed; then, the behavior of the subject is carefully assessed in an effort to determine the functions of the lesioned structure. Four types of lesions are discussed here: aspiration lesions, radio-frequency lesions, knife cuts, and cryogenic blockade.

Aspiration Lesions When a lesion is to be made in an area of cortical tissue that is accessible to the eyes and instruments of the surgeon, **aspiration** is frequently the method of choice. The cortical tissue is drawn off by suction through a fine-tipped handheld glass pipette. Because the underlying white matter is slightly more resistant to suction than the cortical tissue itself, a skilled surgeon can delicately peel off the layers of cortical tissue from the surface of the brain, leaving the underlying white matter and major blood vessels undamaged.

Radio-Frequency Lesions Small subcortical lesions are commonly made by passing *radio-frequency current* (high-frequency current) through the target tissue from the tip of a stereotaxically positioned electrode. The heat from the current destroys the tissue. The size and shape of the lesion are determined by the duration and intensity of the current and the configuration of the electrode tip.

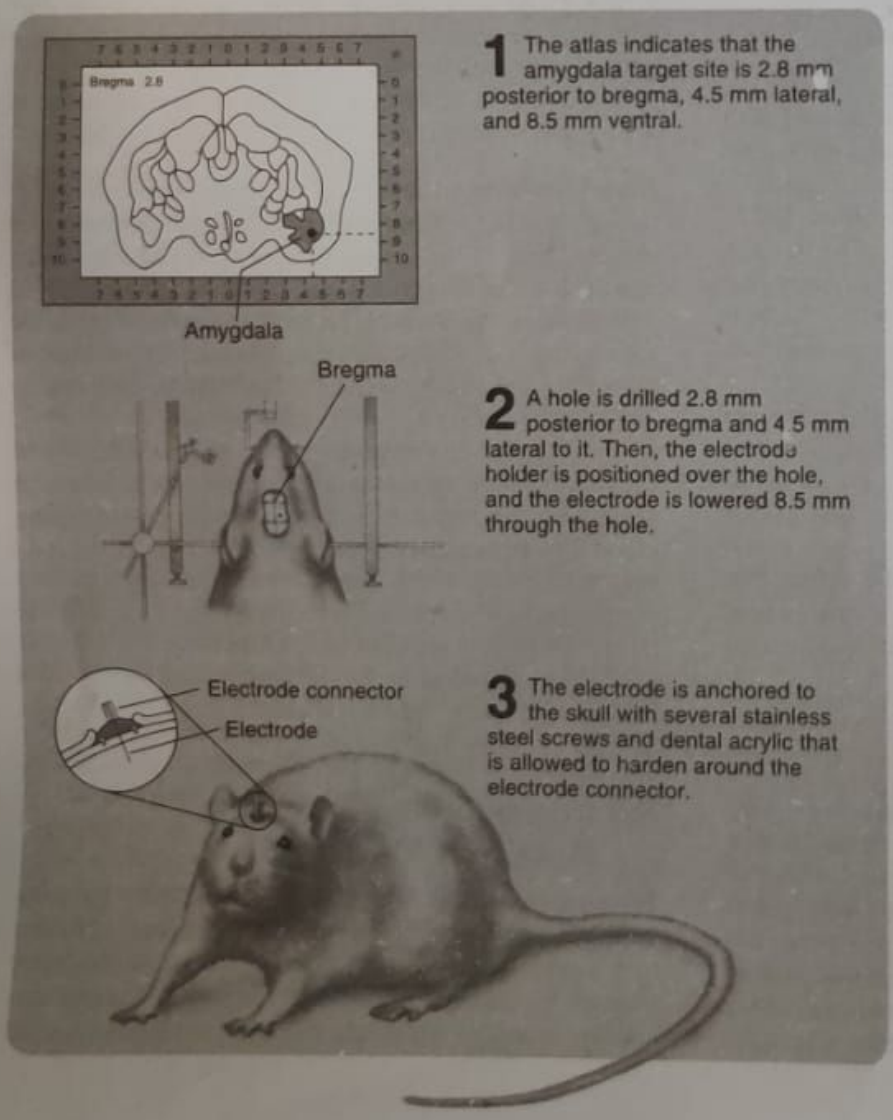


FIGURE 5.14 Stereotaxic surgery: implanting an electrode in the rat amygdala.

Knife Cuts *Sectioning* (cutting) is used to eliminate conduction in a nerve or tract. A tiny, well-placed cut can unambiguously accomplish this task without producing extensive damage to surrounding tissue. How does one insert a knife into the brain to make a cut without severely damaging the overlying tissue? One method is depicted in Figure 5.15.

Reversible Lesions Reversible lesions are useful alternatives to *destructive lesions*. **Reversible lesions** are methods for temporarily eliminating the activity in a particular area of the brain while tests are being conducted. The advantage of reversible lesions is that the same subjects can be repeatedly tested in both the lesion and control conditions. Reversible lesions can be produced by cooling the target structure or by injecting an anesthetic (e.g., *lidocaine*) into it.

Interpreting Lesion Effects Before you leave this section on lesions, a word of caution is in order. Lesion effects are deceptively difficult to interpret. Because the structures of the brain are small, convoluted, and tightly packed together, even a highly skilled surgeon cannot completely destroy a structure without producing significant damage to adjacent structures. There is, however, an unfortunate tendency to lose sight of this fact. For example, a lesion that leaves major portions of the amygdala intact and damages an assortment of neighboring structures comes to be thought of simplistically as an *amygdala lesion*. Such an apparently harmless abstraction can be misleading in two ways. If you believe that all lesions referred to as "amygdala lesions" include damage to no other brain structure, you may incorrectly attribute all of their behavioral effects to amygdala damage; conversely, if you believe that all lesions referred to as "amygdala lesions" include the entire amygdala, you may incorrectly conclude that the amygdala does not participate in behaviors uninfluenced by the lesion.

Thinking Creatively

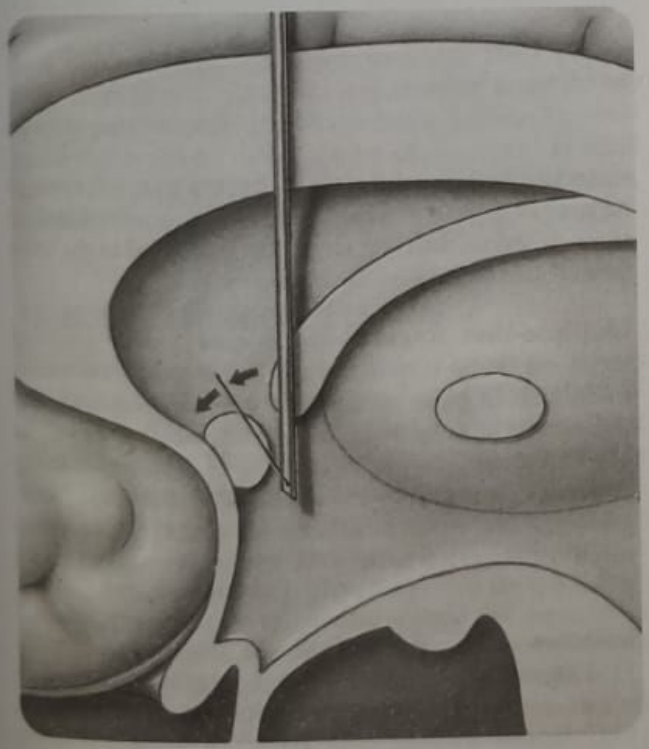


FIGURE 5.15 A device for performing subcortical knife cuts. The device is stereotaxically positioned in the brain; then, the blade swings out to make the cut. Here, the anterior commissure is being sectioned.

Bilateral and Unilateral Lesions As a general principle—but one with several notable exceptions—the behavioral effects of *unilateral lesions* (lesions restricted to one half of the brain) are much milder than those of symmetrical *bilateral lesions* (lesions involving both sides of the brain), particularly in nonhuman species. Indeed, behavioral effects of unilateral lesions to some brain structures can be difficult to detect. As a result, most experimental studies of lesion effects are studies of bilateral, rather than unilateral, lesions.

ELECTRICAL STIMULATION

Clues about the function of a neural structure can be obtained by stimulating it electrically. Electrical brain stimulation is usually delivered across the two tips of a *bipolar electrode*—two insulated wires wound tightly together and cut at the end. Weak pulses of current produce an immediate increase in the firing of neurons near the tip of the electrode.

Electrical stimulation of the brain is an important biopsychological research tool because it often has behavioral effects, usually opposite to those produced by a lesion to the same site. It can elicit a number of behavioral sequences, including eating, drinking, attacking, copulating, and sleeping. The particular behavioral response elicited depends on the location of the electrode tip, the parameters of the current, and the test environment in which the stimulation is administered.

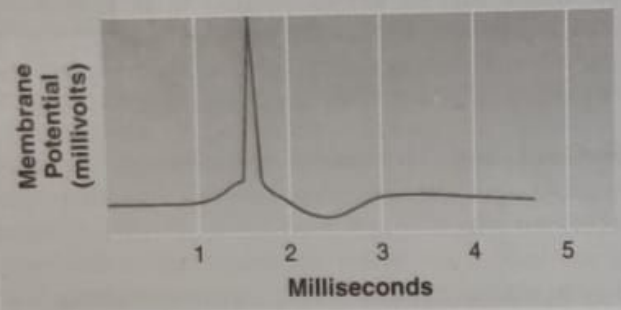
Because electrical stimulation of the brain is an invasive procedure, its use is usually limited to nonhumans. However, there are situations in which it is administered to conscious human patients (Borchers et al., 2012).

INVASIVE ELECTROPHYSIOLOGICAL RECORDING METHODS

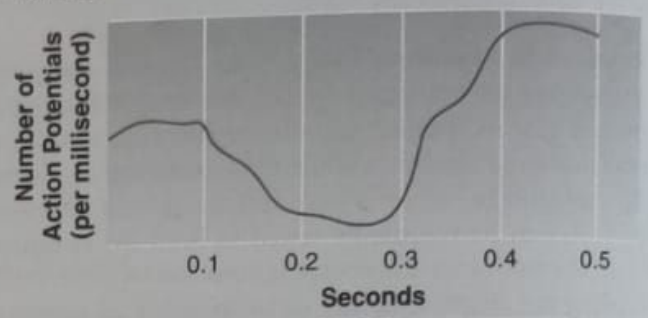
This section describes four invasive electrophysiological recording methods: intracellular unit recording, extracellular unit recording, multiple-unit recording, and invasive EEG recording. See Figure 5.16 for an example of each method.

Intracellular Unit Recording This method, whose findings were discussed at length in Chapter 4, provides a moment-by-moment record of the graded fluctuations

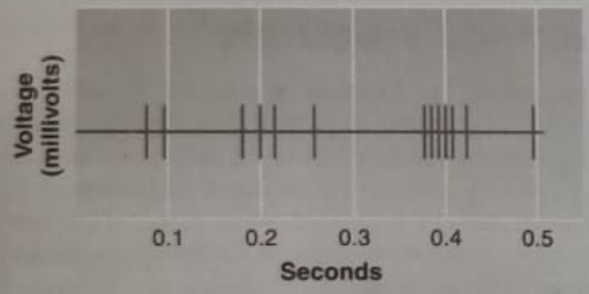
An Intracellular Unit Recording
An intracellular microelectrode records the membrane potential from one neuron as it fires.



A Multiple-Unit Recording
A small electrode records the action potentials of many nearby neurons. These are added up and plotted. In this example, firing in the area of the electrode tip gradually declined and then suddenly increased.



An Extracellular Unit Recording
An extracellular microelectrode records the electrical disturbance that is created each time an adjacent neuron fires.



An Invasive EEG Recording
A large implanted electrode picks up general changes in electrical brain activity. The EEG signal is not related to neural firing in any obvious way.

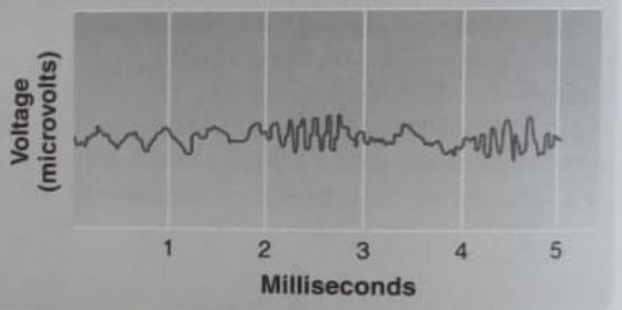


FIGURE 5.16 Four methods of recording electrical activity of the nervous system.

in one neuron's membrane potential. Most experiments using this recording procedure are performed on chemically immobilized animals because it is difficult to keep the tip of a microelectrode positioned inside a neuron of a freely moving animal (see Gilja et al., 2010; Long & Lee, 2012).

Extracellular Unit Recording It is possible to record the action potentials of a neuron through a microelectrode whose tip is positioned in the extracellular fluid next to it—each time the neuron fires, there is an electrical disturbance and a blip is recorded at the electrode tip. Accordingly, *extracellular unit recording* provides a record of the firing of a neuron but no information about the neuron's membrane potential. It is difficult to record extracellularly from a single neuron in a freely moving animal without the electrode tip shifting away from the neuron, but it can be accomplished with special flexible microelectrodes that can shift slightly with the brain. Initially, extracellular unit recording involved recording from one neuron at a time, each at the tip of a separately implanted electrode. However, it is now possible to simultaneously record extracellular signals from up to about 100 neurons by analyzing the correlations among the signals picked up through several different electrodes implanted in the same general area (e.g., Nicolelis & Ribeiro, 2006).

Multiple-Unit Recording In *multiple-unit recording*, the electrode tip is much larger than that of a microelectrode; thus, it picks up signals from many neurons, and slight shifts in its position due to movement of the subject have little effect on the overall signal. The many action potentials picked up by the electrode are fed into an integrating circuit, which adds them together. A multiple-unit recording is a graph of the total number of recorded action potentials per unit of time (e.g., per 0.1 second).

Invasive EEG Recording In laboratory animals, EEG signals are recorded through large implanted electrodes rather than through scalp electrodes. Cortical EEG signals are frequently recorded through stainless steel skull screws, whereas subcortical EEG signals are typically recorded through stereotaxically implanted wire electrodes.

5 5.4 Pharmacological Research Methods

In the preceding section, you learned how physiological psychologists study the brain by manipulating it and recording from it using surgical and electrical methods. In this section, you will learn how psychopharmacologists manipulate and record from the brain using chemical methods.

The major research strategy of psychopharmacology is to administer drugs that either increase or decrease the effects of particular neurotransmitters and to observe the behavioral consequences. You learned in Chapter 4 how agonists and antagonists affect neurotransmitter systems. Described here are routes of drug administration, methods of using chemicals to make selective brain lesions, methods of measuring the chemical activity of the brain that are particularly useful in biopsychological research, and methods for locating neurotransmitter systems.

ROUTES OF DRUG ADMINISTRATION

In most psychopharmacological experiments, drugs are administered in one of the following ways: (1) they are fed to the subject; (2) they are injected through a tube into the stomach (*intragastrically*); or (3) they are injected hypodermically into the peritoneal cavity of the abdomen (*intraperitoneally, IP*), into a large muscle (*intramuscularly, IM*), into the fatty tissue beneath the skin (*subcutaneously, SC*), or into a large surface vein (*intravenously, IV*). A problem with these peripheral routes of administration is that many drugs do not readily pass through the blood–brain barrier. To overcome this problem, drugs can be administered in small amounts through a fine, hollow tube, called a **cannula,** that has been stereotaxically implanted in the brain.

SELECTIVE CHEMICAL LESIONS

The effects of surgical, electrolytic, and cryogenic lesions are frequently difficult to interpret because they affect all neurons in the target area. In some cases, it is possible to make more selective lesions by injecting **neurotoxins** (neural poisons) that have an affinity for certain components of the nervous system. There are many selective neurotoxins. For example, when either *kainic acid* or *ibotenic acid* is administered by microinjection, it is preferentially taken up by cell bodies at the tip of the cannula and destroys those neurons, while leaving neurons with axons passing through the area largely unscathed.

Another selective neurotoxin that has been widely used is *6-hydroxydopamine* (*6-OHDA*). It is taken up by only those neurons that release the neurotransmitter *norepinephrine* or *dopamine*, and it leaves other neurons at the injection site undamaged.

MEASURING CHEMICAL ACTIVITY OF THE BRAIN

There are many procedures for measuring the chemical activity of the brains of laboratory animals. Two techniques that have proved particularly useful in biopsychological research are the 2-deoxyglucose technique and cerebral dialysis.

2-Deoxyglucose Technique The *2-deoxyglucose (2-DG) technique* entails placing an animal that has been injected with radioactive 2-DG in a test situation in which it engages in the activity of interest. Because 2-DG is similar in structure to glucose—the brain's main source of energy—neurons active during the test absorb it at a high rate but do not metabolize it. Then the subject is killed, and its brain is removed and sliced. The slices are then subjected to **autoradiography**; they are coated with a photographic emulsion, stored in the dark for a few days, and then developed much like film. Areas of the brain that absorbed high levels of the radioactive 2-DG during the test appear as black spots on the slides. The density of the spots in various regions of the brain can then be color-coded (see Figure 5.17).

Cerebral Dialysis **Cerebral dialysis** is a method of measuring the extracellular concentration of specific neurochemicals in behaving animals (see Robinson & Justice, 1991)—most other techniques for measuring neurochemicals require that the subjects be killed so that tissue can be extracted. Cerebral dialysis involves the implantation in the brain of a fine tube with a short semipermeable section. The semipermeable section is positioned in the brain structure of interest so that extracellular chemicals from the structure will diffuse into the tube. Once in the tube, they can be collected for freezing, storage, and later analysis; or they can be carried in solution directly to a *chromatograph* (a device for measuring the chemical constituents of liquids or gases).

LOCATING NEUROTRANSMITTERS AND RECEPTORS IN THE BRAIN

A key step in trying to understand the psychological function of a particular neurotransmitter or receptor is finding out where it is located in the brain. Two of the techniques available for this purpose are immunocytochemistry and in situ hybridization. Each involves exposing brain slices to a labeled *ligand* of the molecule under investigation (the ligand of a molecule is another molecule that binds to it).

Immunocytochemistry When a foreign protein (an *antigen*) is injected into an animal, the animal's body creates *antibodies* that bind to it and help the body remove or destroy it; this is known as the body's *immune reaction*. Neurochemists have created stocks of antibodies to

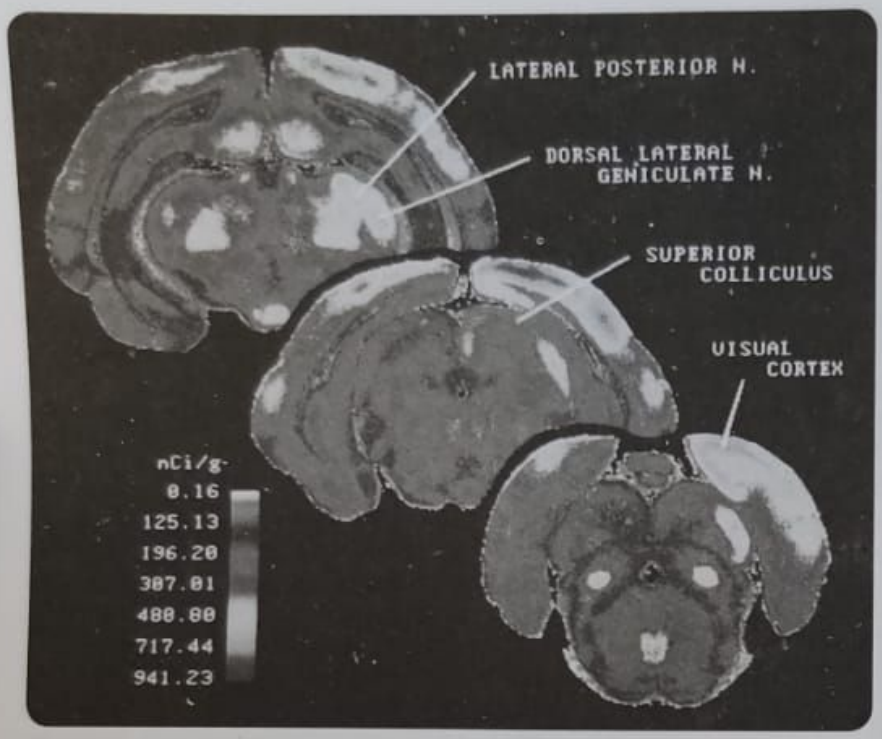


FIGURE 5.17 The 2-deoxyglucose technique. The accumulation of radioactivity is shown in three frontal sections taken from the brain of a Richardson's ground squirrel. The subject was injected with radioactive 2-deoxyglucose; then, for 45 minutes, it viewed brightly illuminated black and white stripes through its left eye while its right eye was covered. Because the ground squirrel visual system is largely crossed, most of the radioactivity accumulated in the visual structures of the right hemisphere (the hemisphere on your right). (Courtesy of Rod Cooper, Department of Psychology, University of Calgary.)

the brain's peptide neurotransmitters (neuropeptides; see Chapter 4) and their receptors. **Immunocytochemistry** is a procedure for locating particular neuroproteins in the brain by labeling their antibodies with a dye or radioactive element and then exposing slices of brain tissue to the labeled antibodies. Regions of dye or radioactivity accumulation in the brain slices mark the locations of the target neuroprotein.

Because all enzymes are proteins and because only those neurons that release a particular neurotransmitter are likely to contain all the enzymes required for its synthesis, immunocytochemistry can be used to locate neurotransmitters by binding to their enzymes. This is done by exposing brain slices to labeled antibodies that bind to enzymes located in only those neurons that contain the neurotransmitter of interest (see Figure 5.18).

In Situ Hybridization Another technique for locating peptides and other proteins in the brain is **in situ hybridization.** This technique takes advantage of the fact that all peptides and proteins are transcribed from sequences of nucleotide bases on strands of messenger RNA (see Chapter 2). The nucleotide base sequences that direct the synthesis of many neuroproteins have been identified, and hybrid strands of mRNA with the complementary base sequences have been artificially created. In situ hybridization (see Figure 5.19) involves the following steps. First, hybrid RNA strands with the base sequence complementary to that of the mRNA that directs the synthesis of the target neuroprotein are obtained. Next, the hybrid RNA strands are labeled with a dye or radioactive element. Finally, the brain slices are exposed to the labeled hybrid RNA

FIGURE 5.18 Immunocytochemistry. This section through a rat's substantia nigra reveals dopaminergic neurons that have taken up the antibody for tyrosine hydroxylase, the enzyme that converts tyrosine to L-dopa. (Courtesy of Mark Klitenick and Chris Fibiger, Department of Psychiatry, University of British Columbia.)

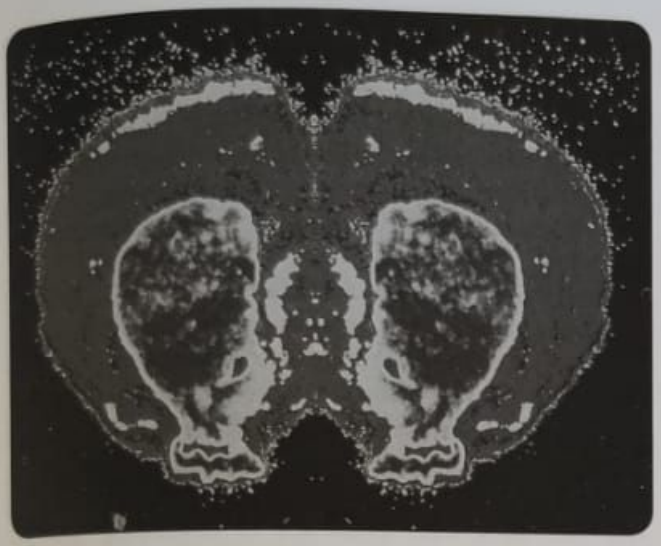


FIGURE 5.19 In situ hybridization. This color-coded frontal section through a rat brain reveals high concentrations of mRNA expression for an endorphin in the striatum (in red and yellow). (Courtesy of Ningning Guo and Chris Fibiger, Department of Psychiatry, University of British Columbia.)

strands; they bind to the complementary mRNA strands, marking the location of neurons that release the target neuroprotein.

5.5 Genetic Engineering

Genetics is a science that has made amazing progress in the last two decades, and biopsychologists are reaping the benefits. Modern genetic methods are now widely used in biopsychological research, which just a few years ago would have seemed like science fiction.

GENE KNOCKOUT TECHNIQUES

Gene knockout techniques are procedures for creating organisms that lack a particular gene under investigation (see Eisener-Dorman, Lawrence, & Bolivar, 2008). Mice (the favored mammalian subjects of genetic research) that are the products of gene knockout techniques are referred to as *knockout mice*. (This term often makes me smile, as images of little mice with boxing gloves flit through my mind.)

Many gene knockout studies have been conducted to clarify the neural mechanisms of behavior. For example, Ruby and colleagues (2002) and Hattar and colleagues (2003) used *melanopsin knockout mice* (mice in whom the gene for the synthesis of melanopsin has been deleted) to study the role of melanopsin in regulating the light–dark cycles that control circadian (about 24 hours) rhythms of bodily function—for example, daily cycles of sleep, eating, and body temperature. *Melanopsin* is a protein found in some neurons in the mammalian *retina* (the receptive layer of the eye), and it had been implicated in the control of circadian rhythms by light. Knockout of the gene for synthesizing melanopsin impaired, but did not eliminate, the ability of mice to adjust their circadian rhythms in response to changes in the light–dark cycle. Thus, melanopsin appears to contribute to the control of circadian rhythms by light, but it is not the only factor.

This type of result is typical of gene knockout studies of behavior: Many genes have been discovered that contribute to particular behaviors, but invariably other mechanisms are involved. It may be tempting to think that each behavior is controlled by a single gene, but the reality is much more complex. Each behavior is controlled by many genes interacting with one another and with experience through epigenetic mechanisms.

Thinking Creatively

GENE REPLACEMENT TECHNIQUES

It is now possible to replace one gene with another. **Gene replacement techniques** have created interesting possibilities for research and therapy. Pathological genes from human cells can be inserted in other animals such as mice—mice that contain the genetic material of another species are called **transgenic mice.** For example, Shen and colleagues (2008) created transgenic mice by inserting a defective human gene that had been found to be associated with schizophrenia in a Scottish family with a particularly high incidence of the disorder. The transgenic mice displayed a variety of cerebral abnormalities (e.g., reduced cerebral cortex and enlarged ventricles) and abnormal behaviors reminiscent of human schizophrenia. Treating neurological disease by replacing faulty genes in patients suffering from genetic disorders is an exciting, but as yet unrealized, goal.

Clinical Implications

In another gene replacement technique, a gene is replaced with one that is identical except for the addition of a few bases that can act as a switch, turning the gene off or on in response to particular chemicals or light (Deisseroth, 2010, Dieterich, 2010, Rana & Dolmetsch, 2010). As a result, the gene can be activated or suppressed at a particular point in development.

FANTASTIC FLUORESCENCE AND THE BRAINBOW

Green fluorescent protein (GFP) is a protein that exhibits bright green fluorescence when exposed to blue light. First isolated by Shimomura, Johnson, and Saiga (1962), from a species of jellyfish found off the west coast of North America, GFP is currently stimulating advances in many fields of biological research. Martin Chalfie, Osamu Shimomura, and Roger Y. Tsien were awarded the 2008 Nobel Prize in chemistry for its discovery and study.

Evolutionary Perspective

The utility of GFP as a research tool in the biological sciences could not be realized until its gene was

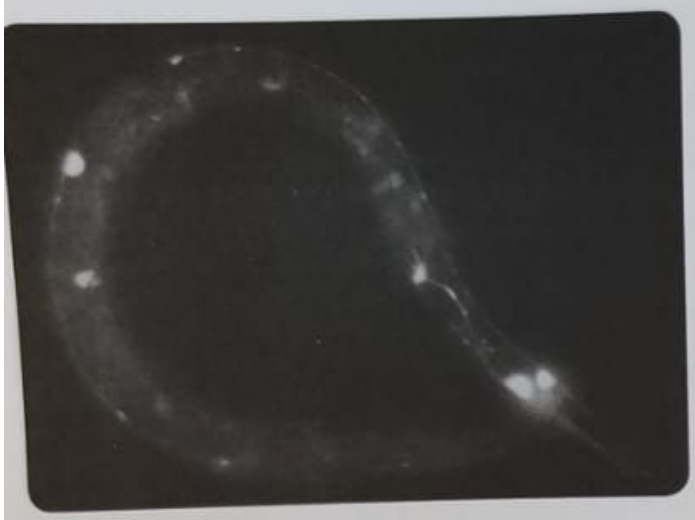


FIGURE 5.20 Touch receptor neurons of the transparent *Caenorhabditis elegans* labeled by green fluorescent protein.

identified and cloned in the early 1990s. The general strategy is to activate the GFP gene in only the particular cells under investigation so that they can readily be visualized. This can be accomplished in two ways: by inserting the GFP gene in only the target cells or by introducing the GFP gene in all cells of the subject but expressing the gene in only the target cells. Chalfie and colleagues (1994) were the first to use GFP to visualize neurons. They introduced the GFP gene into a small transparent roundworm, *Caenorhabditis elegans*, in an area of its chromosomes that controls the development of touch receptor neurons. Figure 5.20 shows the glowing touch receptor neurons. The GFP gene has now been expressed in the cells of many plant and animal species, including humans.

Livet and colleagues took the very useful GFP technique one step further—one big step. First, Tsien (1998) found that making minor alterations to the GFP gene resulted in the synthesis of proteins that fluoresced in different colors. Livet and colleagues (2007) then introduced the mutated genes for cyan, yellow, and blue fluorescent proteins into the genomes of developing mice in such a way that they were expressed in developing neurons. Each neuron produced different amounts of the three proteins, giving it a distinctive color—in the same way that a color printer can make any color by mixing only three colored inks in differing proportions. Because each neuron was labeled with its own distinctive color, the pathways of neural axons could be traced to their destinations through the cellular morass. This technique has been dubbed **brainbow** for obvious reasons—see Figure 5.21.

Thinking Creatively

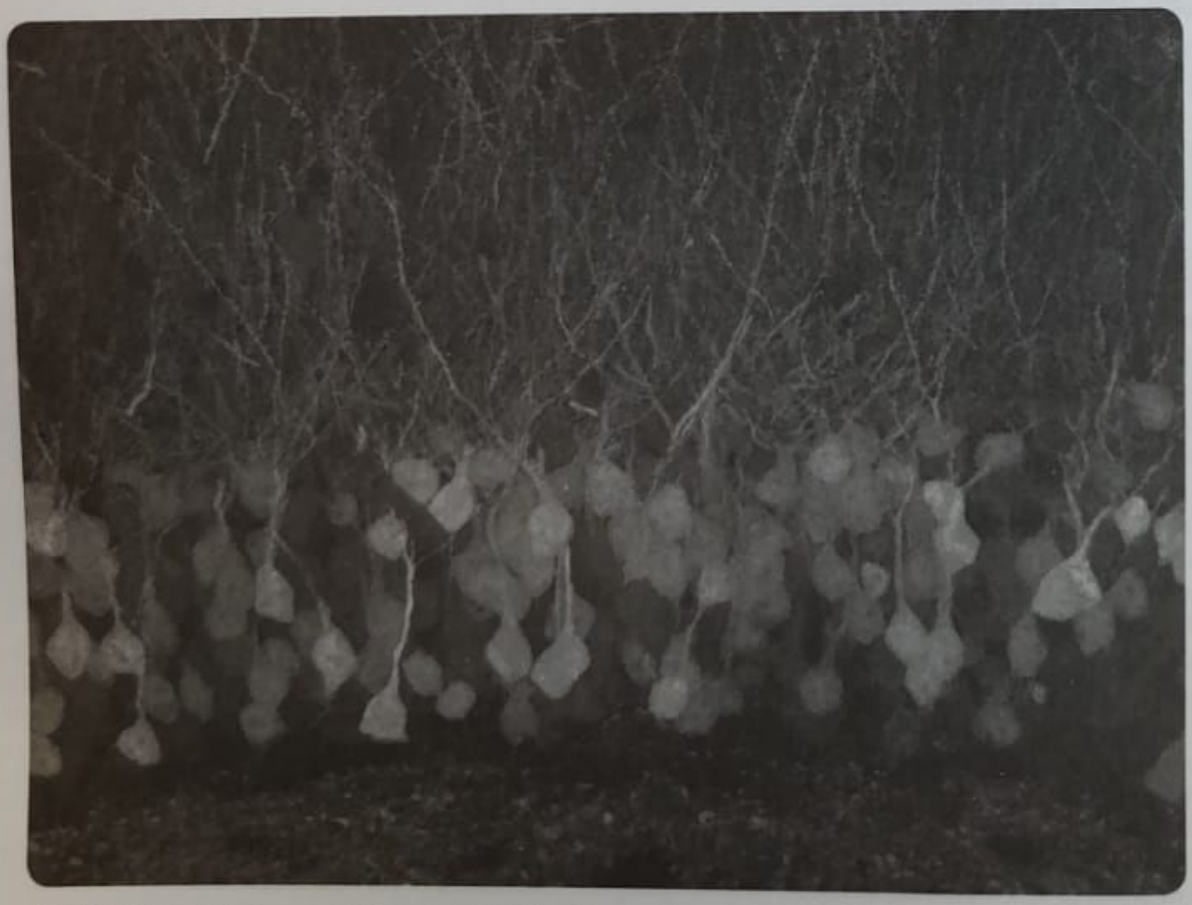


FIGURE 5.21 With the research technique called *brainbow*, each neuron is labeled with a different color, facilitating neuron tracing.

SCAN YOUR BRAIN

The research methods of biopsychology illustrate a psychological disorder suffered by many scientists. I call it "unabbreviaphobia"—the fear of leaving any term unabbreviated. To determine whether you have mastered Part One of this chapter and are ready for Part Two, supply the full term for each of the following abbreviations. The correct answers are provided at the end of the exercise. Before proceeding, review material related to your incorrect answers and omissions.

1. CT: _____
2. MRI: _____
3. PET: _____
4. 2-DG: _____
5. fMRI: _____
6. MEG: _____
7. TMS: _____
8. EEG: _____
9. ERP: _____
10. AEP: _____
11. EMG: _____
12. EOG: _____
13. SCL: _____
14. SCR: _____
15. ECG: _____
16. EKG: _____
17. IP: _____
18. IM: _____
19. IV: _____
20. SC: _____
21. 6-OHDA: _____
22. GFP: _____

Scan Your Brain answers: (1) computed tomography, (2) magnetic resonance imaging, (3) positron emission tomography, (4) 2-deoxyglucose, (5) functional MRI, (6) magnetoencephalography, (7) transcranial magnetic stimulation, (8) electroencephalogram, (9) event-related potential, (10) average evoked potential, (11) electromyogram, (12) electrooculogram, (13) skin conductance level, (14) skin conductance response, (15) electrocardiogram, (16) electrocardiogram, (17) intraperitoneal, (18) intramuscular, (19) intravenous, (20) subcutaneous, (21) 6-hydroxydopamine, (22) green fluorescent protein.

PART TWO
Behavioral Research Methods of Biopsychology

We turn now from methods used by biopsychologists to study the nervous system to those that deal with the behavioral side of biopsychology. Because of the inherent invisibility of neural activity, the primary objective of the methods used in its investigation is to render the unobservable observable. In contrast, the major objectives of behavioral research methods are to control, to simplify, and to objectify.

A single set of procedures developed for the investigation of a particular behavioral phenomenon is commonly referred to as a **behavioral paradigm**. Each behavioral paradigm normally comprises a method for producing the behavioral phenomenon under investigation and a method for objectively measuring it.

5.6 Neuropsychological Testing

A patient suspected of suffering from some sort of nervous system dysfunction is usually referred to a *neurologist*, who assesses simple sensory and motor functions. More subtle changes in perceptual, emotional, motivational, or cognitive functions are the domain of the *neuropsychologist*.

Clinical Implications

Because neuropsychological testing is so time consuming, it is typically prescribed for only a small portion of brain-damaged patients. This is unfortunate; the results of neuropsychological testing can help brain-damaged patients in three important ways: (1) by assisting in the diagnosis of neural disorders, particularly in cases in which brain imaging, EEG, and neurological testing have proved equivocal; (2) by serving as a basis for counseling and caring for the patients; and (3) by providing a basis for objectively evaluating the effectiveness of the treatment and the seriousness of its side effects.

MODERN APPROACH TO NEUROPSYCHOLOGICAL TESTING

The nature of neuropsychological testing has changed radically since the 1950s (see Stuss & Levine, 2002). Indeed, the dominant approach to psychological testing has evolved through three distinct phases: the *single-test approach*, the *standardized-test-battery approach*, and the modern *customized-test-battery approach*.

Single-Test Approach Before the 1950s, the few existing neuropsychological tests were designed to detect the presence of brain damage; in particular, the goal of these early tests was to discriminate between patients with psychological problems resulting from structural brain damage and those with psychological problems resulting from functional, rather than structural, changes to the brain. This approach proved unsuccessful, in large part because no single test could be developed that would be sensitive to all the varied and complex psychological symptoms that could potentially occur in a brain-damaged patient.

Standardized-Test-Battery Approach The standardized-test-battery approach to neuropsychological

testing grew out of the failures of the single-test approach, and by the 1960s, it was predominant. The objective stayed the same—to identify brain-damaged patients—but the testing involved standardized batteries (sets) of tests rather than a single test. The most widely used standardized test battery has been the *Halstead-Reitan Neuropsychological Test Battery*. The Halstead-Reitan is a set of tests that tend to be performed poorly by brain-damaged patients in relation to other patients or healthy control subjects; the scores on each test are added together to form a single aggregate score. An aggregate score below the designated cutoff leads to a diagnosis of brain damage. The standardized-test-battery approach proved only marginally successful; standardized test batteries discriminate effectively between neurological patients and healthy patients, but they are not so good at discriminating between neurological patients and psychiatric patients.

The Customized-Test-Battery Approach The customized-test-battery approach began to be used routinely in a few elite neuropsychological research institutions in the 1960s. This approach proved highly successful in research, and it soon spread to clinical practice. It now predominates in both the research laboratory and the neurological ward.

The objective of current neuropsychological testing is not merely to identify patients with brain damage; the objective is to characterize the nature of the psychological deficits of each brain-damaged patient. So how does the customized-test-battery approach to neuropsychological testing work? It usually begins in the same way for all patients: with a common battery of tests selected by the neuropsychologist to provide an indication of the general nature of the neuropsychological symptoms. Then, depending on the results of the common test battery, the neuropsychologist selects a series of tests customized to each patient in an effort to characterize in more detail the general symptoms revealed by the common battery. For example, if the results of the test battery indicated that a patient had a memory problem, subsequent tests would include those designed to reveal the specific nature of the memory problem.

The tests used in the customized-test-battery approach differ in three respects from earlier tests. First, the newer tests are specifically designed to measure aspects of psychological function that have been spotlighted by modern theories and data. For example, modern theories, and the evidence on which they are based, suggest that the mechanisms of short-term and long-term memory are totally different; thus, the testing of patients with memory problems virtually always involves specific tests of both short-term and long-term memory. Second, the interpretation of the test results often does not rest entirely on how well the patient does; unlike early neuropsychological tests, currently used tests often require the neuropsychologist to assess the cognitive strategy that the patient employs in performing the test. Third, the customized-test-battery approach requires more skill and knowledge on the part of the neuropsychologist to select just the right battery of tests to expose a particular patient's deficits and to identify qualitative differences in cognitive strategy.

TESTS OF THE COMMON NEUROPSYCHOLOGICAL TEST BATTERY

Because the customized-test-battery approach to neuropsychological testing typically involves two phases—a battery of general tests given to all patients followed by a series of specific tests customized to each patient—the following examples of neurological tests are presented in two subsections. First are some tests that are often administered as part of the initial common test battery, and second are some tests that might be used by a neuropsychologist to investigate in more depth particular problems revealed by the common battery.

Clinical Implications

Intelligence Although the overall *intelligence quotient* (*IQ*) is a notoriously poor measure of brain damage, a test of general intelligence is nearly always included in the battery of neuropsychological tests routinely given to all patients. Many neuropsychological assessments begin with the **Wechsler Adult Intelligence Scale** (**WAIS**), first published in 1955 and standardized in 1981 on a sample of 1,880 U.S. citizens between 16 and 71. The WAIS is often the first test because knowing a patient's IQ can help a neuropsychologist interpret the results of subsequent tests. Also, a skilled neuropsychologist can sometimes draw inferences about a patient's neuropsychological dysfunction from the pattern of deficits on the 15 subtests of the WAIS. For example, low scores on subtests of verbal ability tend to be associated with left hemisphere damage, whereas right hemisphere damage tends to reduce scores on performance subtests. The 11 original subtests of the WAIS are described in Table 5.1.

Memory One weakness of the WAIS is that it often fails to detect memory deficits, despite including subtests specifically designed to test memory function. For example, the information subtest of the WAIS assesses memory for general knowledge (e.g., "Who is Queen Elizabeth?"), and the **digit span** subtest (the most widely used test of short-term memory) identifies the longest sequence of random digits that a patient can repeat correctly 50% of the time; most people have a digit span of 7. However, these two forms of memory are among the least likely to be disrupted by brain damage—patients with seriously disturbed memories often show no deficits on either the information or the digit span

TABLE 5.1 The 11 Original Subtests of the Wechsler Adult Intelligence Scale (WAIS).

Verbal Subtests
Information The subject is asked 29 questions of general information—for example "Who is the president of the United States?"
Digit Span Three digits are read to the subject at 1-second intervals, and the subject is asked to repeat them in the same order. Two trials are given at three digits, four digits, five digits, and so on until the subject fails both trials at one level.
Vocabulary The subject is asked to define a list of 35 words that range in difficulty.
Arithmetic The subject is presented with 14 arithmetic questions and must answer them without the benefit of pencil and paper.
Comprehension The subject is asked 16 questions that test the ability to understand general principles—for example, why should people vote?
Similarities The subject is presented with pairs of items and is asked to explain how the items in each pair are similar.
Performance Subtests
Picture Completion The subject must identify the important part missing from 20 drawings—for example, a drawing of a squirrel with no tail.
Picture Arrangement The subject is presented with 10 sets of cartoon drawings and is asked to arrange each set so that it tells a sensible story.
Block Design The subject is presented with blocks that are red on two sides, white on two sides, and half red and half white on the other two. The subject is shown pictures of nine patterns and is asked to duplicate them by arranging the blocks appropriately.
Object Assembly The subject is asked to put together the pieces of four simple jigsaw puzzles to form familiar objects.
Digit Symbol The subject is presented with a key that matches each of a series of symbols with a different digit. On the same page is a series of digits and the subject is given 90 seconds to write the correct symbol, according to the key, next to as many digits as possible.

subtest. Be that as it may, memory problems rarely escape unnoticed because they are usually reported by the patient or the family of the patient.

Language If a neuropsychological patient has taken the WAIS, deficits in the use of language can be inferred from a low aggregate score on the verbal subtests. A patient who has not taken the WAIS can be quickly screened for language-related deficits with the **token test.** Twenty tokens of two different shapes (squares and circles), two different sizes (large and small), and five different colors (white, black, yellow, green, and red) are placed on a table in front of the patient. The test begins with the examiner reading simple instructions—for example, "Touch a red square"—and the patient trying to follow them. Then, the test progresses to more difficult instructions, such as "Touch the small, red circle and then the large, green square." Finally, the patient is asked to read the instructions aloud and follow them.

Language Lateralization It is usual for one hemisphere to participate more than the other in language-related activities. In most people, the left hemisphere is dominant for language, but in some, the right hemisphere is dominant (see Chapter 16). A test of language lateralization is often included in the common test battery because knowing which hemisphere is dominant for language is often useful in interpreting the results of other tests. Furthermore, a test of language lateralization is virtually always given to patients before any surgery that might encroach on the cortical language areas. The results are used to plan the surgery, trying to avoid the language areas if possible.

There are two widely used tests of language lateralization. The sodium amytal test (Wada, 1949) is one, and the dichotic listening test (Kimura, 1973) is the other.

The **sodium amytal test** involves injecting the anesthetic sodium amytal into either the left or right carotid artery in the neck. This temporarily anesthetizes the *ipsilateral* (same-side) hemisphere while leaving the *contralateral* (opposite-side) hemisphere largely unaffected. Several tests of language function are quickly administered while the ipsilateral hemisphere is anesthetized. Later, the process is repeated for the other side of the brain. When the injection is on the side dominant for language, the patient is completely mute for about 2 minutes. When the injection is on the nondominant side, there are only a few minor speech problems. Because the sodium amytal test is invasive, it can be administered only for medical reasons—usually to determine the dominant language hemisphere prior to brain surgery.

In the standard version of the **dichotic listening test,** sequences of spoken digits are presented to subjects through stereo headphones. Three digits are presented to one ear at the same time that three different digits are presented to the other ear. Then the subjects are asked to report as many of the six digits as they can. Kimura (1973) found that subjects correctly report more of the digits heard by the ear contralateral to their dominant hemisphere for language, as determined by the sodium amytal test.

TESTS OF SPECIFIC NEUROPSYCHOLOGICAL FUNCTION

Following analysis of the results of a neuropsychological patient's performance on the common test battery, the neuropsychologist selects a series of specific tests to clarify

Clinical Implications the nature of the general problems exposed by the common battery. There are thousands of tests that might be selected. This section describes a few of them and mentions some of the considerations that might influence their selection.

Memory Following the discovery of memory impairment by the common test battery, at least four fundamental questions about the memory impairment must be answered (see Chapter 11): (1) Does the memory impairment involve *short-term memory*, *long-term memory*, or both? (2) Are any deficits in long-term memory *anterograde* (affecting the retention of things learned after the damage), *retrograde* (affecting the retention of things learned before the damage), or both? (3) Do any deficits in long-term memory involve *semantic memory* (memory for knowledge of the world) or *episodic memory* (memory for personal experiences)? (4) Are any deficits in long-term memory deficits of *explicit memory* (memories of which the patient is aware and can thus express verbally), *implicit memory* (memories demonstrated by the improved performance of the patient without the patient being conscious of them), or both?

Many amnesic patients display severe deficits in explicit memory with no deficits at all in implicit memory (Curran & Schacter, 1997). **Repetition priming tests** have proven instrumental in the assessment and study of this pattern. Patients are first shown a list of words and asked to study them; they are not asked to remember them. Then, at a later time, they are asked to complete a list of word fragments, many of which are fragments of words from the initial list. For example, if "purple" had been in the initial test, "pu_p_ _" could be one of the test word fragments. Amnesic patients often complete the fragments as accurately as healthy control subjects. But—and this is the really important part—they often have no conscious memory of any of the words in the initial list or even of ever having seen the list. In other words, they display good implicit memory of experiences without explicit memories of them.

Language If a neuropsychological patient turns out to have language-related deficits on the common test battery, a complex series of tests is administered to clarify the nature of the problem (see Chapter 16). For example, if a patient has a speech problem, it may be one of three fundamentally different problems: problems of *phonology* (the rules governing the sounds of the language), problems of *syntax* (the grammar of the language), or problems of *semantics* (the meaning of the language). Because brain-damaged patients may have one of these problems but not the others, it is imperative that the testing of all neuropsychological patients with speech problems include tests of each of these three capacities (Saffran, 1997).

Reading aloud can be disrupted in different ways by brain damage, and follow-up tests must be employed that can differentiate between the different patterns of disruption (Coslett, 1997). Some *dyslexic* patients (those with reading problems) remember the rules of pronunciation but have difficulties pronouncing words that do not follow these rules, words such as *come* and *tongue*, whose pronunciation must be remembered. Other dyslexic patients pronounce simple familiar words based on memory but have lost the ability to apply the rules of pronunciation—they cannot pronounce nonwords such as *trapple* or *fleeming*.

FRONTAL-LOBE FUNCTION

Injuries to the frontal lobes are common, and the **Wisconsin Card Sorting Test** (see Figure 5.22) is a component of many customized test batteries because performance on it is sensitive to frontal-lobe damage (see Eling, Derckx, & Maes, 2008). On each Wisconsin card is either one symbol or two, three, or four identical symbols. The symbols are all either triangles, stars, circles, or crosses; and they are all either red, green, yellow, or blue. At the beginning of the test, the patient is confronted with four stimulus cards that differ from one another in the form, color, and number of symbols they display. The task is to correctly sort cards from a deck into piles in front of the stimulus cards. However, the

FIGURE 5.22 The Wisconsin Card Sorting Test. This woman is just starting the test. If she places the first card in front of the stimulus card with the three green circles, she is sorting on the basis of color. She must guess until she can learn which principle—color, shape, or number—should guide her sorting. After she has placed a card, she is told whether or not her placement is correct.

patient does not know whether to sort by form, by color, or by number. The patient begins by guessing and is told after each card has been sorted whether it was sorted correctly or incorrectly. At first, the task is to learn to sort by color. But as soon as the patient makes several consecutive correct responses, the sorting principle is changed to shape or number without any indication other than the fact that responses based on color become incorrect. Thereafter, each time the patient learns a new sorting principle, the principle is changed.

Patients with damage to their frontal lobes often continue to sort on the basis of one sorting principle for 100 or more trials after it has become incorrect (Demakis, 2003). They seem to have great difficulty learning and remembering that previously appropriate guidelines for effective behavior are no longer appropriate, a problem called *perseveration*.

5.7 Behavioral Methods of Cognitive Neuroscience

Cognitive neuroscience is predicated on two related assumptions. The first premise is that each complex cognitive process results from the combined activity of simple cognitive processes called **constituent cognitive processes.** The second premise is that each constituent cognitive process is mediated by neural activity in a particular area of the brain. One of the main goals of cognitive neuroscience is to identify the parts of the brain that mediate various constituent cognitive processes.

With the central role played by PET and fMRI in cutting-edge cognitive neuroscience research, the **paired-image subtraction technique** has become one of the key behavioral research methods in such research (see Posner & Raichle, 1994; Kriegeskorte, 2010). Let me illustrate this technique with the classic PET study of single-word processing by Petersen and colleagues (1988). Petersen and his colleagues were interested in locating the parts of the brain that enable a person to make a word association (to respond to a printed word by saying a related word). You might think this would be an easy task to accomplish by having a volunteer perform a word-association task while a PET image of the volunteer's brain is recorded. The problem with this approach is that many parts of the brain that would be active during the test period would have nothing to do with the constituent cognitive process of forming a word association; much of the activity recorded would be associated with other processes such as seeing the words, reading the words, and speaking. The paired-image subtraction technique was developed to deal with this problem.

The paired-image subtraction technique involves obtaining functional brain images during several different cognitive tasks. Ideally, the tasks are designed so that pairs of them differ from each other in terms of only a single constituent cognitive process. Then, the brain activity associated with that process can be estimated by subtracting the activity in the image associated with one of the two tasks from the activity in the image associated with the other. For example, in one of the tasks in the study by Petersen and colleagues, volunteers spent a minute reading aloud printed nouns as they appeared on a screen; in another, they observed the same nouns on the screen but responded to each of them by saying aloud an associated verb (e.g., *truck—drive*). Then, Petersen and his colleagues subtracted the activity in the images they recorded during the two tasks to obtain a *difference image*. The difference image illustrated the areas of the brain specifically involved in the constituent cognitive process of forming the word association; the activity associated with fixating on the screen, seeing the nouns, saying the words, and so on was eliminated by the subtraction (see Figure 5.23).

Interpretation of difference images is complicated by the fact that there is substantial brain activity when humans sit quietly and let their minds wander—this level

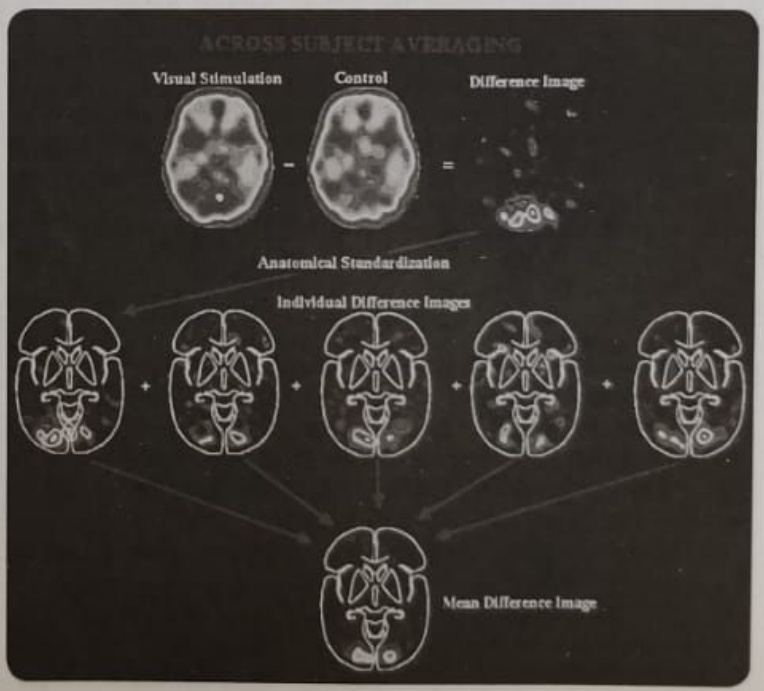


FIGURE 5.23 The paired-image subtraction technique, which is commonly employed in cognitive neuroscience. Here we see that the brain of a subject is generally active when the subject looks at a flickering checkerboard pattern (visual stimulation condition). However, if the activity that occurred when the subject stared at a blank screen (control situation) is subtracted, it becomes apparent that the perception of the flashing checkerboard pattern was associated with an increase in activity that was largely restricted to the occipital lobe. The individual difference images of five subjects were averaged to produce the mean difference image. (PET scans courtesy of Marcus Raichle, Mallinckrodt Institute of Radiology, Washington University Medical Center.)

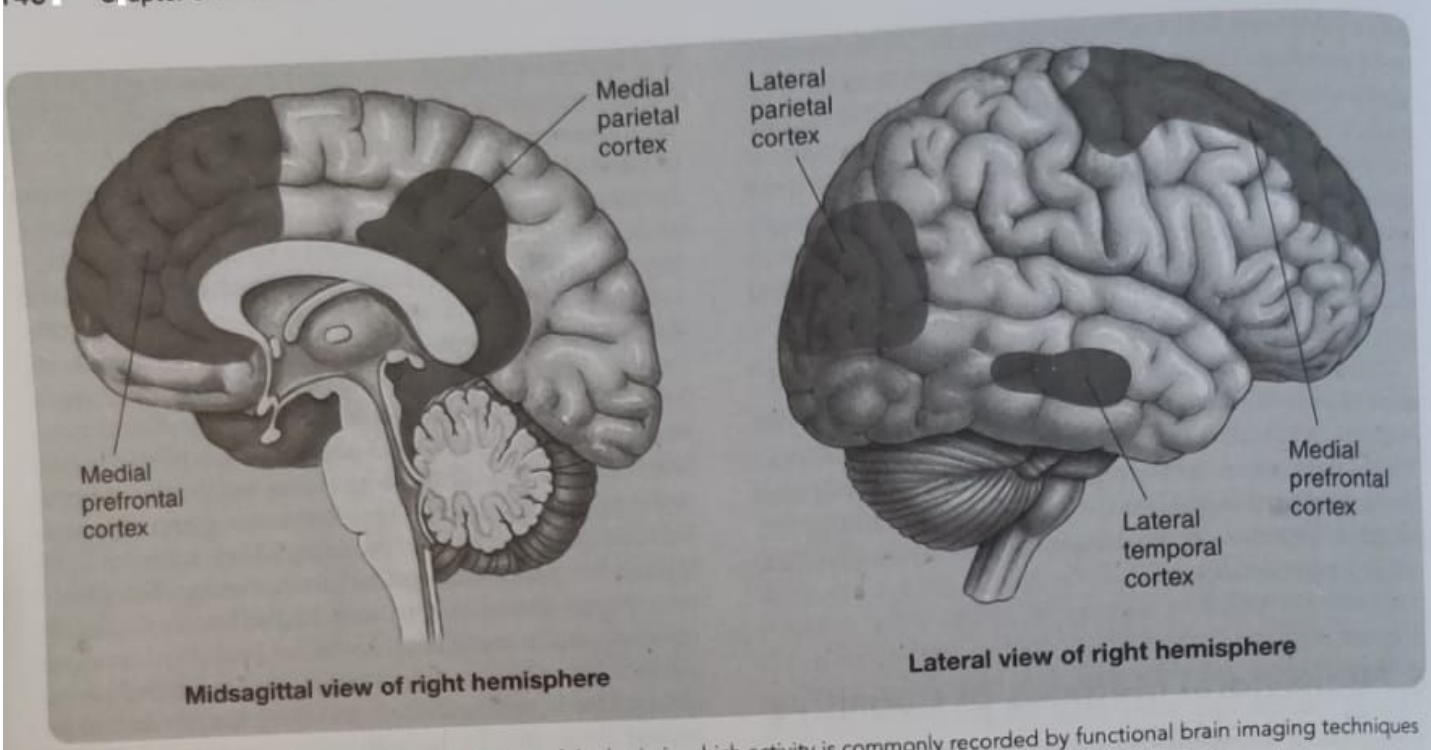


FIGURE 5.24 The default mode network: areas of the brain in which activity is commonly recorded by functional brain imaging techniques when the mind wanders, but not when it is actively engaged.

of activity has been termed the brain's **default mode** (Raichle, 2010). Brain structures typically active in the default mode and less active during cognitive or behavioral tasks are collectively referred to as the **default mode network.** The default mode network comprises many neural structures (Northoff, Qin, & Nakao, 2010) including the following four cortical areas: medial parietal cortex, lateral parietal cortex, medial frontal cortex, and lateral temporal cortex. See Figure 5.24.

Another difficulty in using PET and fMRI to locate constituent cognitive processes results from the *noise* associated with random cerebral events that occur during the test—for example, thinking about a sudden pang of hunger, noticing a fly on the screen, or wondering whether the test will last much longer (see Mason et al., 2007). The noise created by such events can be significantly reduced with a technique discussed earlier in this chapter: *signal averaging*. By averaging the difference images obtained from repetitions of the same tests, the researchers can greatly increase the *signal-to-noise ratio*. It is standard practice to average the images obtained from several volunteers; the resulting mean (averaged) difference image emphasizes areas of activity that are common to many volunteers and deemphasizes areas of activity that are peculiar to a few of them (see Figure 5.23). However, this averaging procedure can lead to a serious problem: If two volunteers had specific but different patterns of cortical activity, the average image derived from the two would reveal little about either.

Thinking Creatively Because people differ substantially from one another in the cortical localization of cognitive abilities, this is a serious problem (see Braver, Cole, & Yarkoni, 2010; Kanai & Rees, 2011; Lichtman & Denk, 2011). Moreover, the area of cortex that controls a particular ability can change in an individual as a result of experience.

Neuroplasticity

5.8 Biopsychological Paradigms of Animal Behavior

Noteworthy examples of the behavioral paradigms used to study the biopsychology of laboratory species are provided here under three headings: (1) paradigms for the assessment of species-common behaviors, (2) traditional conditioning paradigms, and (3) seminatural animal learning paradigms. In each case, the focus is on methods used to study the behavior of the laboratory rat, the most common subject of biopsychological research.

PARADIGMS FOR ASSESSMENT OF SPECIES-COMMON BEHAVIORS

Many of the behavioral paradigms used in biopsychological research are used to study species-common behaviors. **Species-common behaviors** are those displayed by virtually all members of a species, or at least by all those of the same age and sex. Commonly studied species-common behaviors include grooming, swimming, eating, drinking, copulating, fighting, and nest building. Described here are the open-field test, tests of aggressive and defensive behavior, and tests of sexual behavior.

Open-Field Test In the **open-field test,** the subject is placed in a large, barren chamber, and its activity is recorded (see Brooks & Dunnett, 2009). It is also common in the open-field test to count the number of *boluses* (pieces of excrement) that were dropped by an animal during the test. Low activity scores and high bolus counts are frequently used as indicators of fearfulness. Fearful rats are highly **thigmotaxic**; that is, they rarely venture away from the walls of the test chamber and rarely engage in such activities as rearing and grooming. Rats are often fearful when they are first placed in a strange open field, but this fearfulness usually declines with repeated exposure to the same open field.

Tests of Aggressive and Defensive Behavior Typical patterns of aggressive and defensive behavior can be observed and measured during combative encounters between the dominant male rat of an established colony and a smaller male intruder (see Blanchard & Blanchard, 1988). This is called the **colony-intruder paradigm**. The behaviors of the dominant male are considered to be aggressive and those of the hapless intruder defensive. The dominant male of the colony (the *alpha male*) moves sideways toward the intruder, with its hair erect. When it nears the intruder, it tries to push the intruder off balance and to deliver bites to its back and flanks. The defender tries to protect its back and flanks by rearing up on its hind legs and pushing the attacker away with its forepaws or by rolling onto its back. Thus, piloerection, lateral approach, and flank- and back-biting indicate conspecific aggression in the rat; freezing, boxing (rearing and pushing away), and rolling over indicate defensiveness.

Some tests of rat defensive behavior assess reactivity to the experimenter rather than to another rat. For example, it is common to rate the resistance of a rat to being picked up—no resistance being the lowest category and biting the highest—and to use the score as one measure of defensiveness.

The **elevated plus maze**, a four-armed, plus-sign-shaped maze typically mounted 50 centimeters above the floor, is a test of defensiveness commonly used to study in rats the *anxiolytic* (anxiety-reducing) effects of drugs. Two of the arms of the maze have sides, and two do not. The measure of defensiveness, or anxiety, is the proportion of time the rats spend in the protected closed arms rather than on the exposed arms. Many established anxiolytic drugs significantly increase the proportion of time that rats spend on the open arms, and, conversely, new drugs that prove to be effective in reducing rats' defensiveness on the maze often turn out to be effective in the treatment of human anxiety.

Clinical Implications

Tests of Sexual Behavior Most attempts to study the physiological bases of rat sexual behavior have focused on the copulatory act itself. The male mounts the female from behind and clasps her hindquarters. If the female is receptive, she responds by assuming the posture called **lordosis**; that is, she sticks her hindquarters in the air, she bends her back in a U, and she deflects her tail to the side. During some mounts, the male inserts his penis into the female's vagina; this act is called **intromission.** After intromission, the male dismounts by jumping backwards. He then returns a few seconds later to mount and intromit once again. Following about 10 such cycles of mounting, intromitting, and dismounting, the male mounts, intromits, and **ejaculates** (ejects his sperm).

Three common measures of male rat sexual behavior are the number of mounts required to achieve intromission, the number of intromissions required to achieve ejaculation, and the interval between ejaculation and the reinitiation of mounting. The most common measure of female rat sexual behavior is the **lordosis quotient** (the proportion of mounts that elicit lordosis).

TRADITIONAL CONDITIONING PARADIGMS

Learning paradigms play a major role in biopsychological research for three reasons. The first is that learning is a phenomenon of primary interest to psychologists. The second is that learning paradigms provide an effective technology for producing and controlling animal behavior. Because animals cannot follow instructions from the experimenter, it is often necessary to train them to behave in a fashion consistent with the goals of the experiment. The third reason is that it is possible to infer much about the sensory, motor, motivational, and cognitive state of an animal from its ability to learn and perform various responses.

If you have taken a previous course in psychology, you will likely be familiar with the Pavlovian and operant conditioning paradigms. In the **Pavlovian conditioning paradigm,** the experimenter pairs an initially neutral stimulus called a *conditional stimulus* (e.g., a tone or a light) with an *unconditional stimulus* (e.g., meat powder)—a stimulus that elicits an *unconditional* (reflexive) *response* (e.g., salivation). As a result of these pairings, the conditional stimulus eventually acquires the capacity, when administered alone, to elicit a *conditional response* (e.g., salivation)—a response that is often, but not always, similar to the unconditional response.

In the **operant conditioning paradigm,** the rate at which a particular voluntary response (such as a lever press) is emitted is increased by *reinforcement* or decreased by *punishment*. One of the most widely used operant conditioning paradigms in biopsychology is the self-stimulation paradigm. In the **self-stimulation paradigm,** animals press a lever to deliver electrical

stimulation to particular sites in their own brains; those structures in the brain that support self-stimulation are often called *pleasure centers*.

SEMINATURAL ANIMAL LEARNING PARADIGMS

In addition to Pavlovian and operant conditioning paradigms, biopsychologists use animal learning paradigms that have been specifically designed to mimic situations that an animal might encounter in its natural environment (see Gerlai & Clayton, 1999). Development of these paradigms stemmed in part from the reasonable assumption that forms of learning tending to benefit an animal's survival in the wild are likely to be more highly developed and more directly related to innate neural mechanisms. The following are four common seminatural learning paradigms: the conditioned taste aversion, radial arm maze, Morris water maze, and conditioned defensive burying.

Evolutionary Perspective

Conditioned Taste Aversion A **conditioned taste aversion** is the avoidance response that develops to tastes of food whose consumption has been followed by illness (see Garcia & Koelling, 1966). In the standard conditioned taste aversion experiment, rats receive an *emetic* (a nausea-inducing drug) after they consume a food with an unfamiliar taste. On the basis of this single conditioning trial, the rats learn to avoid the taste.

The ability of rats to readily learn the relationship between a particular taste and subsequent illness unquestionably increases their chances of survival in their natural environment, where potentially edible substances are not routinely screened by government agencies. Rats and many other animals are *neophobic* (afraid of new things); thus, when they first encounter a new food, they consume it in only small quantities. If they subsequently become ill, they will not consume it again. Conditioned aversions also develop to familiar tastes, but these typically require more than a single trial to be learned.

Humans also develop conditioned taste aversions. Cancer patients have been reported to develop aversions to foods consumed before nausea-inducing chemotherapy (Bernstein & Webster, 1980). Many of you will be able to testify on the basis of personal experience about the effectiveness of conditioned taste aversions. I still have vivid memories of a batch of red laboratory punch that I overzealously consumed after eating two pieces of blueberry pie. But that is another story—albeit a particularly colorful one.

The discovery of conditioned taste aversion challenged three widely accepted principles of learning (see Revusky & Garcia, 1970) that had grown out of research on traditional operant and Pavlovian conditioning paradigms. First, it challenged the view that animal conditioning is always a gradual step-by-step process; robust taste aversions can be established in only a single trial. Second, it showed that *temporal contiguity* is not essential for conditioning; rats acquire taste aversions even when they do not become ill until several hours after eating. Third, it challenged the *principle of equipotentiality*—the view that conditioning proceeds in basically the same manner regardless of the particular stimuli and responses under investigation. Rats appear to have evolved to readily learn associations between tastes and illness; it is only with great difficulty that they learn relations between the color of food and nausea or between taste and footshock.

Radial Arm Maze The radial arm maze taps the well-developed spatial abilities of rodents. The survival of rats in the wild depends on their ability to navigate quickly and accurately through their environment and to learn which locations in it are likely to contain food and water. This task is much more complex for a rodent than it is for us. Most of us obtain food from locations where the supply is continually replenished; we go to the market confident that we will find enough food to satisfy our needs. In contrast, the foraging rat must learn, and retain, a complex pattern of spatially coded details. It must not only learn where morsels of food are likely to be found but must also remember which of these sites it has recently stripped of their booty so as not to revisit them too soon. Designed by Olton and Samuelson (1976) to study these spatial abilities, the **radial arm maze** (see Figure 5.25) is an array of arms—usually eight or more—radiating from a central starting area. At the end of each arm is a food cup, which may or may not be baited, depending on the purpose of the experiment.

In one version of the radial arm maze paradigm, rats are placed each day in a maze that has the same arms baited each day. After a few days of experience, rats rarely

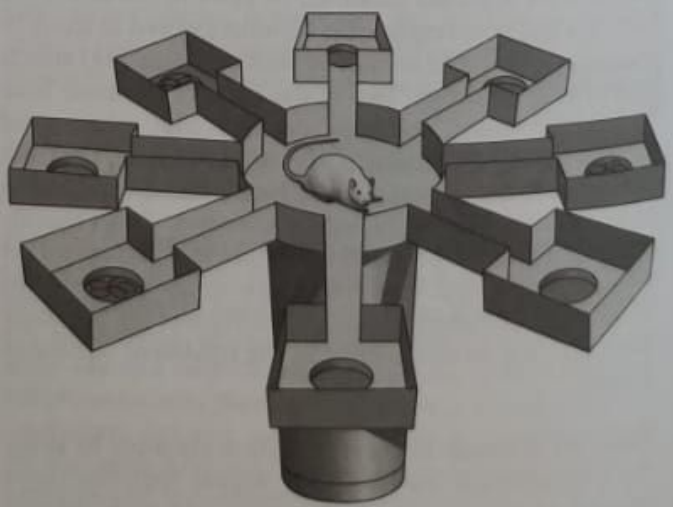


FIGURE 5.25 A radial arm maze.

visit unbaited arms at all, and they rarely visit baited arms more than once in the same day—even when control procedures make it impossible for them to recognize odors left during previous visits to an arm or to make their visits in a systematic sequence. Because the arms are identical, rats must orient themselves in the maze with reference to external room cues; thus, their performance can be disrupted by rotation of the maze or by changes in the appearance of the room.

Morris Water Maze Another seminatural learning paradigm that has been designed to study the spatial abilities of rats is the **Morris water maze** (Morris, 1981). The rats are placed in a circular, featureless pool of cool milky water, in which they must swim until they discover the escape platform—which is invisible just beneath the surface of the water. The rats are allowed to rest on the platform before being returned to the water for another trial. Despite the fact that the starting point is varied from trial to trial, the rats learn after only a few trials to swim directly to the platform, presumably by using spatial cues from the room as a reference. The Morris water maze is useful for assessing the navigational skills of brain-lesioned or drugged animals.

Conditioned Defensive Burying Yet another seminatural learning paradigm useful in biopsychological research is conditioned defensive burying (e.g., Pinel & Mana, 1989; Pinel & Treit, 1978). In studies of **conditioned defensive burying,** rats receive a single aversive stimulus (e.g., a shock, air blast, or noxious odor) from an object mounted on the wall of the chamber just above the floor, which is littered with bedding material. After a single trial, almost every rat learns that the test object is a threat and responds by flinging bedding material at the test object with its head and forepaws (see Figure 5.26). Antianxiety drugs reduce the amount of conditioned defensive burying, and thus the paradigm is used to study the neurochemistry of anxiety (e.g., Treit, 1987).

Before moving on to the next chapter, you need to appreciate that to be effective, the research methods you have encountered in this chapter must be used together; seldom, if ever, is an important biopsychological issue resolved by use of a single method. The reason for this is that neither the methods used to manipulate the brain nor the methods used to assess the behavioral consequences of these manipulations are totally selective; there are no methods

Thinking Creatively

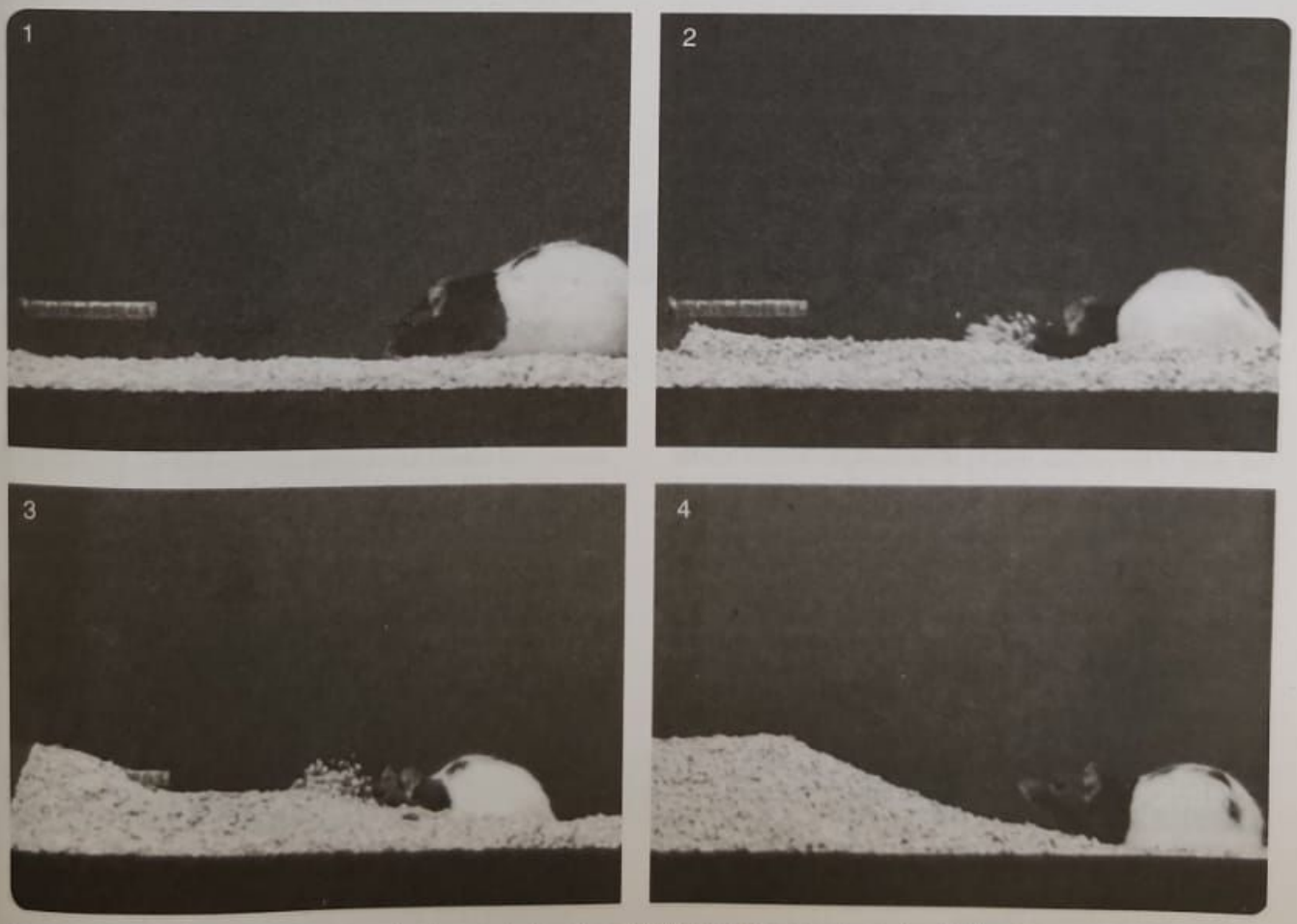


FIGURE 5.26 These photos show a rat burying a test object from which it has just received a single mild shock.

Ethics

Ethics refers to the correct rules of conduct necessary when carrying out research. We have a moral responsibility to protect research participants from harm... The purpose of these codes of conduct is to protect participants, the reputation of the researchers and the dignity and sanctity of the subject itself.

5 principles of Ethics

A. : Beneficence and nonmaleficence.
B : Fidelity and Responsibility.
C : Integrity
D : Justice.
E : Respect for people's rights and dignity.
- Resolving ethical issues.
- Compliance
- Human relations

APA (American Psychological Association) Guidelines on Ethics of Study.

1) Discuss intellectual property frankly

2) Be conscious of multiple roles.

3) Follow informed-Consent rules.
   a) the voluntary participation of the individuals as "participant"