2 Neuroscience Approaches to Understanding Psychopathology

CHAPTER OUTLINE

LEARNING OBJECTIVES

2.1 Explain why neuroscience, genetics, and an evolutionary perspective are increasingly important in understanding psychopathology.

2.2 Describe how information is communicated within the human brain.

2.3 Describe the major techniques used to view the human brain at work and their related ethical implications.

2.4 Explain what brain networks are and how they influence human behavior.

2.5 Explain the function of genes, epigenetics, and endophenotypes.

2.6 Ask critical questions about psychopathology from an evolutionary perspective.

The neuroscientist V. S. Ramachandran (1998) told about an individual, David, who came to see him at the medical center in San Diego, California. David appeared completely normal. He had no problems with memory, engaged easily in conversation, expressed emotions, and

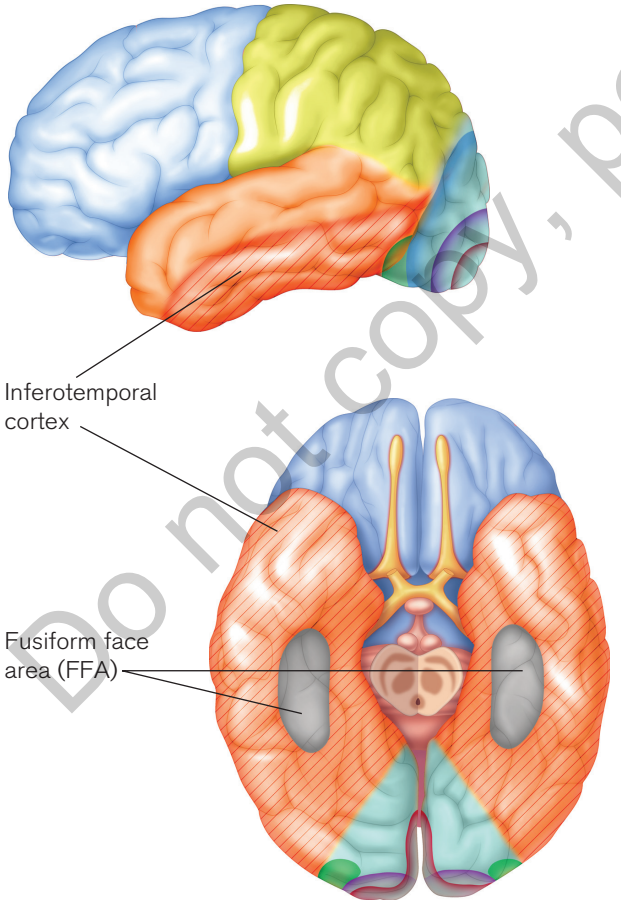
otherwise appeared as anyone you might meet any day. However, he did one very puzzling thing. When he saw his mother in any context, he would say, "That woman looks exactly like my mother, but she is not my mother!"

As a clinician, how might you understand this? You might ask if this was some type of psychosis in which David had the delusion that his mother was not his mother. However, David showed no other signs of disorganization or problems with functioning. You might also ask if David had any type of emotional conflict with his mother. The answer was no. After more information gathering, it was discovered that David, at times, also thought his father was not his real father. Additional information revealed that David did indeed experience his parents as his parents when talking to them on the phone.

The formal name for this condition is *Capgras syndrome,* named after the physician who first described the symptoms in the 1920s. However, the mechanisms involved are still not clear today. Since David had previously had a motorcycle accident, it was possible that normal brain processes were not functioning correctly. In order to understand David, Ramachandran asked himself what was missing in David's experience of his mother. His answer was that there was no emotional response.

FIGURE 2.1 The Fusiform Face Area in the Brain, Activated When Humans Look at Faces

The fusiform face area is part of the human visual system located in the temporal and occipital lobes. If this area is damaged, individuals cannot recognize faces. They see the parts but cannot put them together into a whole face.



The normal emotional response to seeing someone like our parents occurs as follows: Our visual system gives us the experience of seeing the person. In humans, one particular part of the temporal lobe is sensitive to seeing faces (see *Figure 2.1*).

In turn, this information goes to a variety of areas including the limbic system, which is involved in emotional processing. One particular structure, the amygdala, is involved in perceptions that are emotionally important to us (see *Figure 2.2*). The amygdala has rich connections with other cortical areas, which together give us the experience of emotion.

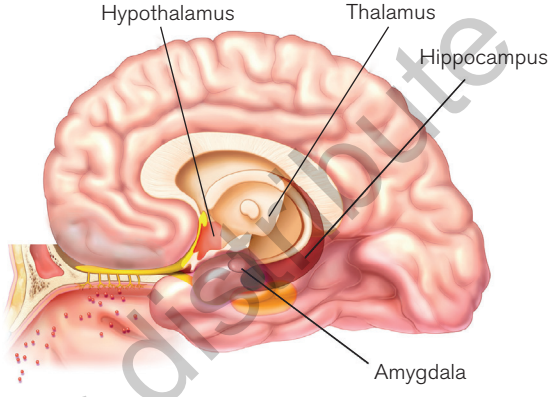
If David had no emotional response to seeing a face, how might this be tested? Emotion is processed not only in the brain but also in the *autonomic nervous system (ANS),* which prepares the body for dangerous situations. If we see a bear and run away, it is the *sympathetic* part of the ANS that makes us feel excited and moves blood to our muscles for a quick getaway. One easy way to measure the sympathetic nervous system is to pass a small electrical current along the skin, usually between the palm and the finger, to assess *electrodermal activity (EDA).* If we are excited, then our skin sweats slightly. This, in turn, makes it easier for the electrical current to pass between the two electrodes. Whenever we have an emotional response to what we see, we get changes in the EDA. David did not show any EDA differences when viewing pictures of those close to him. This suggested to Ramachandran that there was a disconnection

between his visual face perception areas and the emotional centers of the brain. Since the auditory system is wired differently, that would also explain why David did not have the same experience when talking with his parents on the phone. The point of David's story, as strange as it may seem, is to suggest that one important way to understand our mental processes is through their underlying mechanisms.

We can discuss David on different levels. We can consider his actual behavior of saying his mother was not his mother. We can also ask David to tell us what he experiences when he sees his parents. In this case, David said that he sees them as nice people but that he does not expect from them what he expects from his parents. We can discuss how this affects other people, such as his parents, to be told they are not his parents. We can also look at the interaction between him and his parents. From another standpoint, we can consider cognitive and emotional mechanisms involved such as the memory of his mother and his emotional feeling for her. In other chapters of this book, discussions of mental illness from the levels just described will be discussed. The present chapter will focus on current neuroscience approaches to understanding mental illness with an emphasis on brain imaging, genetics, and evolutionary perspectives.

FIGURE 2.2 Amygdala and Other Areas of the Brain Associated With Emotion

The amygdala is an almond-shaped structure on each side of the brain connected to other structures in the limbic system. These areas are involved in processing of emotions such as fear.



The Growing Importance of Neuroscience, Genetics, and an Evolutionary Perspective

The historical considerations of psychopathology emphasized careful observation and interaction with the afflicted individuals as important methods for understanding the nature of the disorder. However, with progress in the neurosciences, brain imaging, and genetics, other levels of analysis have become possible. The new levels offer different perspectives for the field of mental illness, but because many of these discoveries are so new, it is not surprising that our understanding of the field of mental illness is currently in flux. Neuroscience research has been used to find more objective markers in the diagnosis and treatment of mental disorders. It has also helped describe cognitive, emotional, and motor processes in both health and illness. This has resulted in a better articulation of what underlies these processes such as problems in setting goals, having relationships with others, thinking, and feeling, as well as deficits in the memory system and the reward system.

The past 40 years have brought forth new technologies that allow us to study human behavior and experience in ways not previously possible. As you will see with many of the techniques described in this chapter, sampling brain processes or genetic material is basically simple and painless for the people involved. In terms of psychopathology, by using brain imaging techniques it is possible to see how individuals with a particular mental disorder perform cognitive and emotional tasks differently from those without the disorder. We can also examine genetic differences between those with a certain disorder and those who do not show the signs and symptoms of the disorder. Further, to understand the brain and genetic levels, it is important to consider the role that evolution has played. These three approaches will be emphasized in this chapter.

Modern brain imaging techniques help researchers discover how mental disorders appear in the brain.

One word of warning before we continue—currently, we have no neuroscience technique that can definitively diagnose a given individual in terms of mental disorders. What we can say is that a group of individuals with a particular disorder appear to differ on certain measures compared to a group of individuals without the disorder. Even those with the same disorder may show differences in how the disorder is manifested.

To understand mental illness as a brain disease, we need methods for showing how the brain is involved in psychopathology (Andreasen, 2001). Within the past four decades, a variety of research techniques have been developed or significantly improved that allow us to better specify the nature of mental disorders from the standpoint of the brain. In this quest, there has been a strong emphasis on brain imaging, genetics, and an evolutionary perspective. In general, these approaches have allowed researchers to study individuals with mental disorders on a number of levels simultaneously.

Historically, what we now consider to be neuroscience approaches to psychopathology were limited. For example, Paul Broca in the 1800s needed to wait until his patients died before he could study the nature of their brains. In the early part of the twentieth century, work with animals was the major way of understanding how the various structures of the brain influenced behavior. Some scholars such as Carl Jung added EDA to reaction time research. Jung used the word association test developed by Wilhelm Wundt to better understand psychopathology and how individuals with different disorders process cognitive and emotional information. The second part of the twentieth century expanded a tradition that used psychophysiological measures such as *electroencephalography (EEG)* and EDA to study psychopathology. In this century, a variety of noninvasive techniques have allowed researchers and clinicians to obtain a better view of how the brain and other physiological systems function in psychopathology (see Raichle, 2011, 2015, for overviews). These will be reviewed in this chapter.

One common conviction of neuroscientists is that there is something unusual, both in complexity and ability, about the human brain that leads to our abilities to perform a variety of tasks (Northcutt & Kaas, 1995; Preuss & Kaas, 1999). The human brain has been estimated to contain 86 billion neurons and more than 100,000 kilometers of interconnections (Hofman, 2001; Goldstone, Pestilli, & Börner, 2015). Estimates in mammals suggest that a given neuron would directly connect to at least 500 other neurons and probably more. This, in turn, would suggest there are 50 trillion different connections in the human brain!

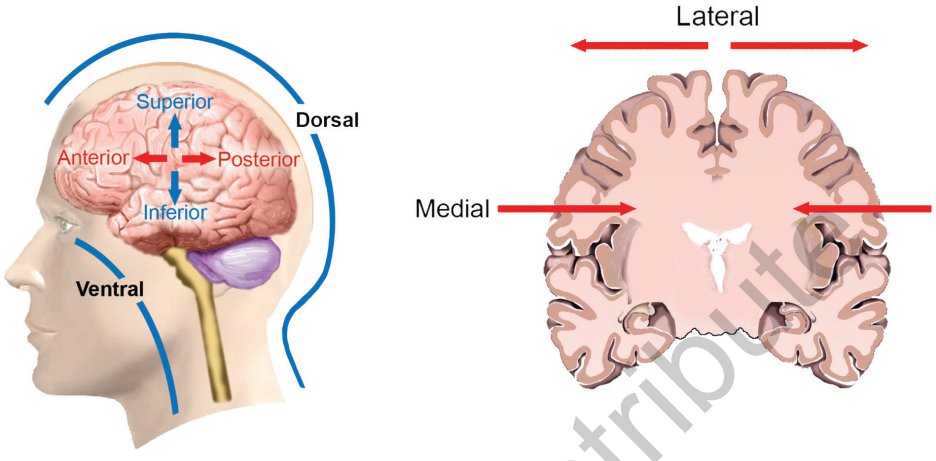
Regardless of how exact this estimate may be, the conclusion is that the human brain has an extremely complex set of networks. Neurons created before birth follow chemical or other pathways in the brain to create the necessary connections to allow for vision, hearing, and other processes. In addition, we know that neurons are also created in humans after birth. A 1-year-old infant has more neurons than she will have throughout her life. After that, neurons are gained and lost depending on use. The genetic and brain mechanisms that create and remove neurons from the developing brain play an important role in the development of mental disorders. Let us now turn to the brain itself.

Brain Anatomy, Neurons, and Neurotransmitters

In this section, you will be introduced to the basic mechanism of the brain, the neuron. Over millions and even billions of years of evolution, the neuron has served as the basic building

FIGURE 2.3 Terms Used to Describe Location of Brain Areas

Traditionally, Latin terms are used to describe orientation in the brain such as above (superior) and below (inferior) as well as front (anterior) and back (posterior).



block of many organisms ranging from jellyfish to humans. Many of the topics covered in this chapter such as parts of the brain, neurotransmitters, and the function of neurons are available in 2-minute videos at www.neurochallenged.com.

Now, let's briefly examine some basic descriptions of brain anatomy.

A Quick Review of Brain Anatomy and Function

Let's begin with some simple terms. Structures closer to the front of the brain are referred to as *anterior,* whereas those closer to the back are called *posterior*. You will also see the terms *dorsal,* which is toward the back side, and *ventral,* which is toward the belly side (see *Figure 2.3*).

The brain appears symmetrical from the top with *left and right hemispheres*. Structures closer to the midline dividing the left and right hemispheres are referred to as *medial,* whereas those farther away from the midline are called *lateral.*

Brain areas can be described both in terms of location and function. Looking at the left hemisphere from the side, we can describe four lobes of the brain (see *Figure 2.4*). In addition to structure, we can also describe areas of the brain that are associated with different functions (see *Figure 2.5*). The *frontal lobe* is located at the front of the cortex and is involved in planning, higher-order cognitive processes such as thinking and problem solving, as well as moral and social judgments.

There is a cavity referred to as the *central sulcus* that separates the frontal lobe from the parietal lobe. The brain area behind the central sulcus receives sensory information from our body including the experience of touch. The area in front of the central sulcus allows the muscles of our bodies to make movements such as picking up a glass. The *parietal lobe*, which is toward the back and at the top of the cortex, is involved in spatial processes such as knowing where you are in space and performing spatial problems. The *occipital lobe* is located near the back of the brain and toward the bottom. The occipital lobe is involved with the processing of visual information and receives information from our eyes. Below the frontal and parietal lobes is the *temporal lobe*. Looking at the brain, you can see that the

FIGURE 2.4 The Left Hemisphere of the Brain From the Left Side Noting the Major Anatomical Structures

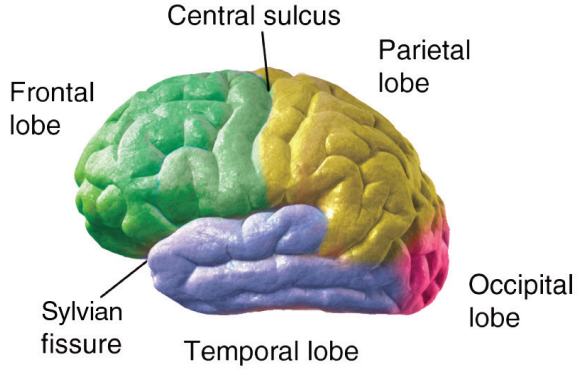
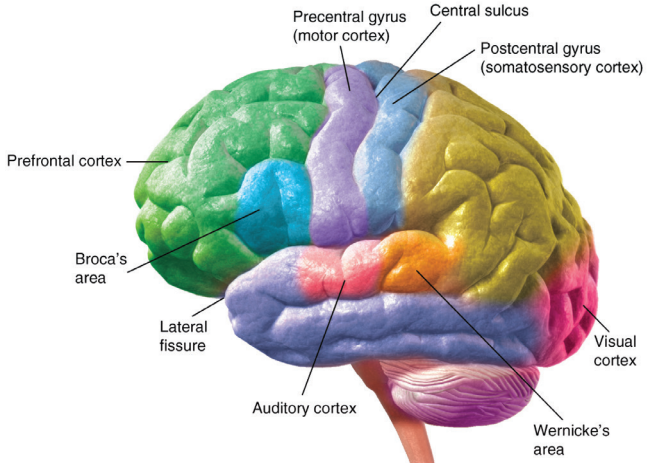


FIGURE 2.5 The Brain in Terms of Structural and Functional Anatomy



frontal and temporal lobes are separated by a deep groove, which is called the *Sylvian fissure*. The temporal lobe receives information from our ears and is involved in hearing as well as aspects of language. Other parts of the temporal lobe are involved in the naming of objects from visual information processed in the occipital lobes. Let us now turn to the manner in which information moves throughout the brain with an emphasis on the neuron.

Neurons and Neural Transmission

The brain's function involves one basic element, the *neuron*. Although neurons come in a variety of sizes and shapes, there are some basic characteristics as shown in *Figure 2.6*:

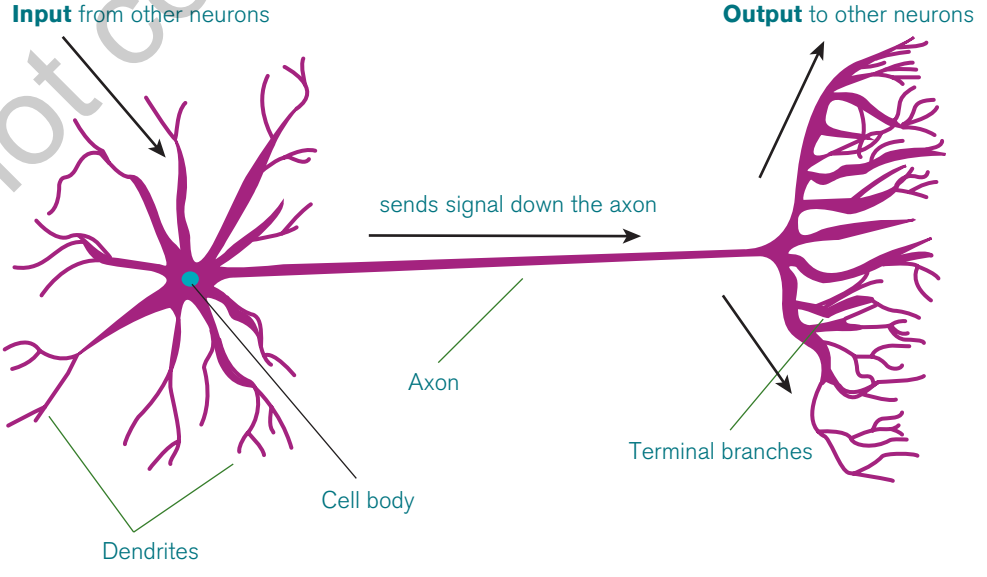
1. The cell body contains a nucleus, which includes *deoxyribonucleic acid (DNA)* and other elements including mitochondria, which are involved in supplying energy.
2. The axon is a slender nerve that conducts electrical impulses away from the cell body. Axons can be fairly short, as found in the human brain, or 4 or 5 feet in length, such as those that go from the spinal cord to the arms and legs.
3. The dendrites receive information from other cells.

The dendrites receive information from other neurons, which connect at different locations on the dendrites. Although illustrations in textbooks usually show only a few connections between neurons, there are generally thousands of them. The terminal branches from

FIGURE 2.6 Basic Characteristics of a Neuron

Input from other neurons comes through the dendrites to the cell body. Movement of the signal goes down the axon, with output to other neurons.

Source: Sobel & Li (2013).



these other neurons do not actually touch but make a biochemical connection through a small gap filled with fluid, which is referred to as a synapse. These biochemical connections can release molecules (ions) with an electrical charge.

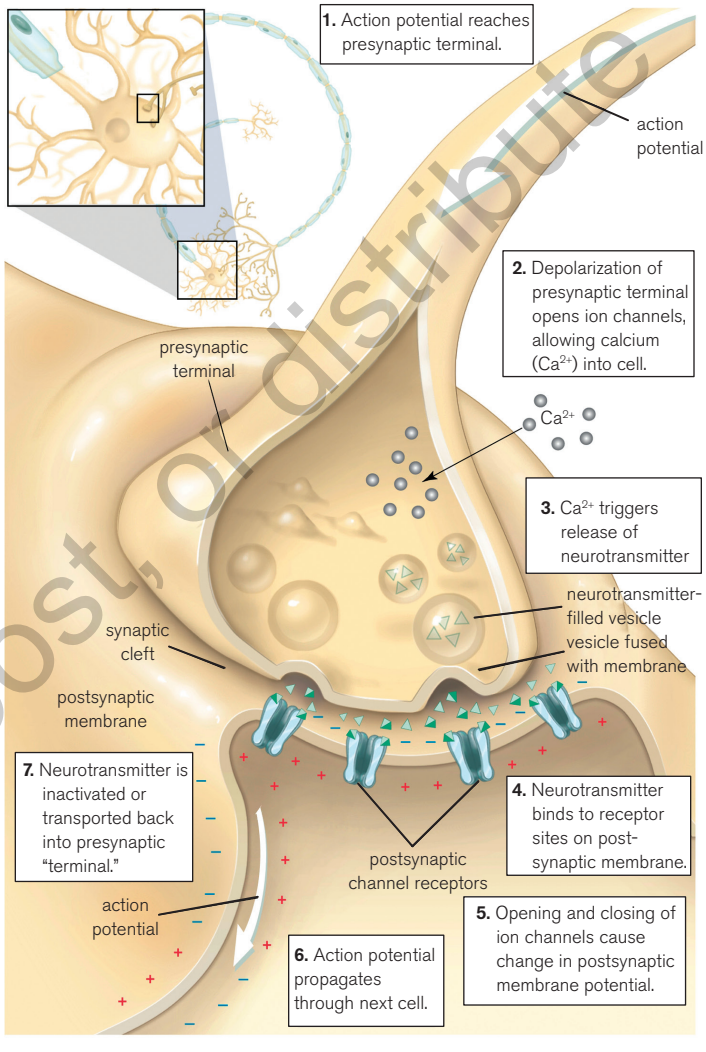
As more of these electrical charges add together, it increases the size of the electrical potential. At a critical point, an action potential is produced at a location near the cell body, which travels quickly down the axon in one direction. An action potential is referred to as an "all or none" signal, since above the critical value an action potential is produced, whereas below the critical value, no electrical activity is sent down the axon.

The speed at which the action potential travels down the axon depends on two factors. The first is the width of the axon. For example, action potentials travel faster in larger diameter axons. The second factor relates to whether the axon is covered with an insulating material called the *myelin sheath*. Action potentials travel faster in axons surrounded by myelin. Thus, an axon with a larger diameter and wrapped in myelin would have the fastest conduction times. Disorders such as multiple sclerosis and autism show deficits in axonal connections.

It should be noted that there are two major types of synapses. One type, referred to as a chemical synapse, involves secretion from the previous neuron of various types of neurotransmitters. These neurotransmitters create a current flow. This changes the physiological state of the next (postsynaptic) neuron such that it is more likely (excitatory) or less likely (inhibitory) to create an action potential (see *Figure 2.7*). The second type of synapse is electrical in nature. Current flows through special channels that connect the gap between the two neurons.

FIGURE 2.7 Depiction of the Structures and Processes of Synapses

This figure shows seven steps of activation, beginning with an action potential.



HOW DOES THE NEURON PASS INFORMATION?

Passing information from one neuron to another involves a number of steps:

1. Neurotransmitters need to be created and stored.
2. An action potential travels down the axon to the terminal.
3. Through a variety of processes, a neurotransmitter is released into the gap between the two neurons.
4. The neurotransmitter then binds with specific proteins in the next neuron.

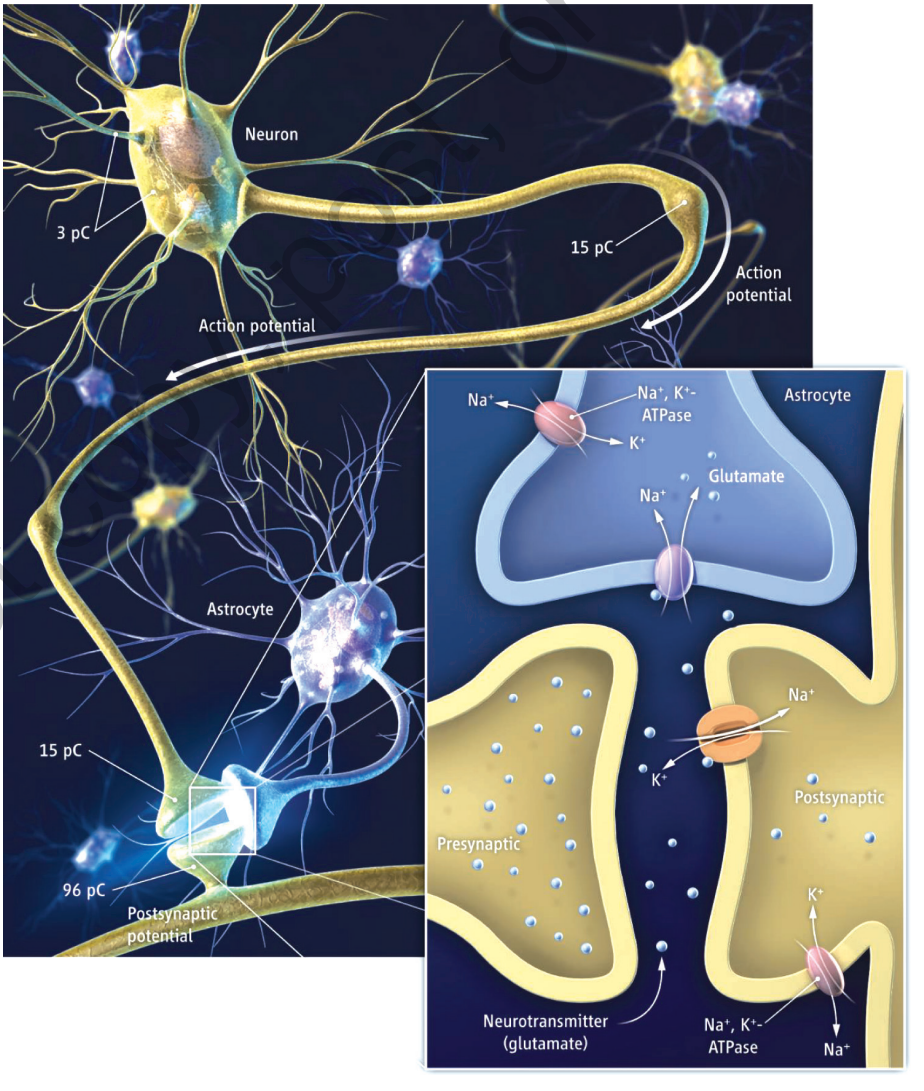
5. This either increases (excitatory) or decreases (inhibitory) the possibility that the next neuron will create an action potential.
6. The gap between the two neurons must be made neutral at this point by any of a number of mechanisms including making the neurotransmitter inactive, having the neurotransmitter taken up by the first neuron (referred to as reuptake), and removing the neurotransmitter from the gap between the two neurons.

It is these neurotransmitters that lead to anxiety processes in some cases but depression in others. Most medications used for treating mental illness influence the neurotransmitters at the synapses. It is also true that going to psychotherapy and learning new skills can also influence the structure and function of synaptic processes. In terms of disorders, Alzheimer's disease, which results in memory loss, is caused by destruction of individual neurons throughout the brain (Nath et al., 2012). Most addictive drugs increase the amount of dopamine in the gap between the neurons. Thus, having an understanding of the role of neurotransmitters is important.

FIGURE 2.8 The Role of Neurotransmitters in Synaptic Processes

Neurotransmitters transmit signals from one neuron to another.

Source: Magistretti, P. J. (2009). Low-cost travel in neurons. *Neuroscience Science, 325*(5946), 1349–1351. doi:10.1126/science.118102. Retrieved from http://www.sciencemag.org/content/325/5946/1349.short. Reprinted with permission from American Association for the Advancement of Science (AAAS).



MAJOR NEUROTRANSMITTERS

In the chemical synapse, **neurotransmitters** play a critical role. Neurotransmitters transmit signals from one neuron to another (see *Figure 2.8*). It is also the case that psychotropic medications largely have their influence at the site of the synapse. To date, more than 100 different neurotransmitters have been identified. Neurotransmitters have been classified both in terms of structure and function. Most neurons utilize more than one type of neurotransmitter for their functioning.

Regarding their structure, neurotransmitters can be classified in terms of size (Purves et al., 2013). This results in two broad categories. The first type is small molecule neurotransmitters such as *glutamate,* which is excitatory, and *GABA* (gamma-aminobutyric acid), which is inhibitory. They are often composed of single amino acids. These small molecule neurotransmitters tend to be involved in rapid synaptic functions.

Glutamate is considered to be the most important neurotransmitter in terms of normal brain function. In abnormal conditions, the firing of rapid glutamate neurons can lead to seizures in a number of areas of the brain. GABA is inhibitory, and drugs that increase the amount of GABA available are used to treat such disorders as anxiety.

TABLE 2.1 Some Representative Neurotransmitters

NEUROTRANSMITTER	FUNCTION
Acetylcholine	Transmitter at muscles; in brain, involved in learning, etc.
Monoamines	
Serotonin	Involved in mood, sleep and arousal, aggression, depression, obsessive-compulsive disorder, and alcoholism.
Dopamine	Contributes to movement control and promotes reinforcing effects of food, sex, and abused drugs; involved in schizophrenia and Parkinson's disease.
Norepinephrine	A hormone released during stress. Functions as a neurotransmitter in the brain to increase arousal and attentiveness to events in the environment; involved in depression.
Epinephrine	A stress hormone related to norepinephrine; plays a minor role as a neurotransmitter in the brain.
Amino Acids	
Glutamate	The principal excitatory neurotransmitter in the brain and spinal cord. Vitally involved in learning and implicated in schizophrenia.
Gamma-aminobutyric acid (GABA)	The predominant inhibitory neurotransmitter. Its receptors respond to alcohol and the class of tranquilizers called benzodiazepines. Deficiency in GABA or receptors is one cause of epilepsy.
Glycine	Inhibitory transmitter in the spinal cord and lower brain. The poison strychnine causes convulsions and death by affecting glycine activity.
Neuropeptides	
Endorphins	Neuromodulators that reduce pain and enhance reinforcement.
Substance P	Transmitter in neurons sensitive to pain.
Neuropeptide Y	Initiates eating and produces metabolic shifts.
Gas	
Nitric oxide	One of two known gaseous transmitters, along with carbon monoxide. Can serve as a retrograde transmitter, influencing the presynaptic neuron's release of neurotransmitters. Viagra enhances male erections by increasing nitric oxide's ability to relax blood vessels and produce penile engorgement.

Most medications used for treating mental illness influence the neurotransmitters at the synapses.

(c) iStockphoto.com/BCFC

The second type of neurotransmitter in terms of size is larger protein molecules referred to as *neuropeptides.* These can be made up of three to 36 amino acids. Neuropeptides tend to be involved in slower, ongoing synaptic functions.

In terms of function, neurotransmitters can also be categorized into three broad groups (Nadeau, 2004). The first group includes those neurotransmitters that mediate communication between neurons, such as glutamate and GABA. The second group includes those neurotransmitters that influence the communication of information, such as opioid peptides in the pain system. The third group includes those neurotransmitters that influence the activity of large populations of neurons, such as dopamine, adrenaline, noradrenaline, and serotonin. For example, cocaine blocks the ability of a neuron to remove the neurotransmitter dopamine from the synapse, which increases the experience of addiction. (See *Table 2.1* for a description of various neurotransmitters.)

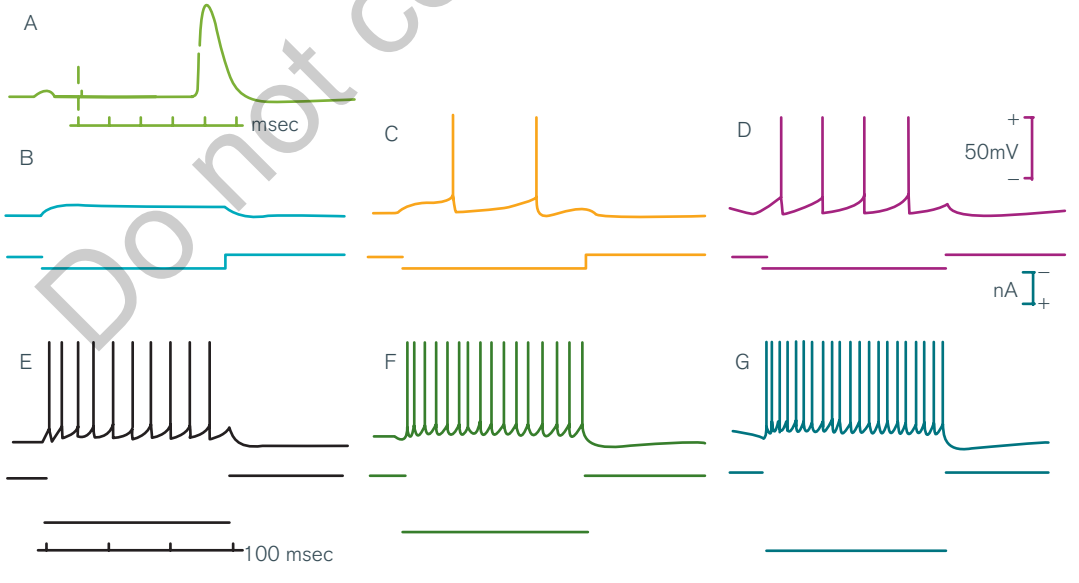
ENCODING INFORMATION

Information is encoded by means of action potentials in terms of frequency. That is, a loud sound would be encoded by a series of action potentials from the cells sensitive to sound intensity. A soft sound would result in fewer action potentials being fired. When observed in relation to a stimulus, action potentials are also referred to as spikes, and a number of spikes over time are referred to as *spike trains*. *Figure 2.9* shows different levels of firing.

FIGURE 2.9 Spike Trains Produced by Different Levels of Firing of Neurons

Neurons fire in relation to the intensity of the signal. A loud noise, for example, would produce a larger number of spike trains than a soft noise. Each of the spikes in the figure represents a single neuron firing.

Source: Spencer, W. (2011). The Physiology of Supraspinal Neurons in Mammals. *Supplement 1: Handbook of Physiology, The Nervous System, Cellular Biology of Neurons*, pp. 969–1021. First published in print, 1977.



Understanding the nature of spikes and how they relate to information in the brain has been an important question since the beginning of the twentieth century when they were first recorded (Rieke, Warland, van Steveninck, & Bialek, 1999).

Let us now move from the consideration of neurons and neurotransmission to an overview of some of the specific neuroscience techniques that are used to understand psychopathological processes. Following an examination of these neuroscience techniques, we will move to a discussion of the networks of the brain.

CONCEPT CHECK

- What are the four major lobes of the brain, and what is the primary role of each?
- "The brain's function involves one basic element, the neuron." What are the different parts that form the structure of the neuron, and what roles do they play?
- How does the neuron pass information on to other neurons, and how is that information encoded?

How Do We Observe the Brain at Work?

With 86 billion neurons and 50 to 200 trillion connections between neurons in the human brain, understanding these connections on a neuronal level would be an impossible task. However, scientists have been able to use the manner in which neurons work as a window into their function. A variety of techniques for observing activity in the brain have been developed.

Currently, the major types of brain imaging techniques are *electroencephalography (EEG)*, *magnetoencephalography (MEG)*, *positron emission tomography (PET)*, and *functional magnetic resonance imaging (fMRI)*. EEG is a technique for recording electrical activity from the scalp related to cortical activity. MEG measures the small magnetic field gradients exiting and entering the surface of the head that are produced when neurons are active. PET is a measure related to blood flow in the brain, which reflects cognitive processing. fMRI is based on the fact that blood flow increases in active areas of the cortex. It is also possible to use the magnetic resonance imaging (MRI) magnet to measure cortical connections in the brain, which is referred to as *diffusion tensor imaging (DTI)*. Let's take a look at each of these techniques, and consider the strengths and weaknesses of each type.

Electroencephalography

Electroencephalography (EEG) is a technique for recording electrical activity from the scalp related to cortical activity. It reflects the electrical activity of the brain at the level of the synapse (Nunez & Srinivasan, 2006). It records the product of the changing excitatory and inhibitory currents. Action potentials contribute very little to the EEG. However, since changes at the synapse do influence the production of action potentials, there is an association of EEG with spike trains (Whittingstall & Logothetis, 2009).

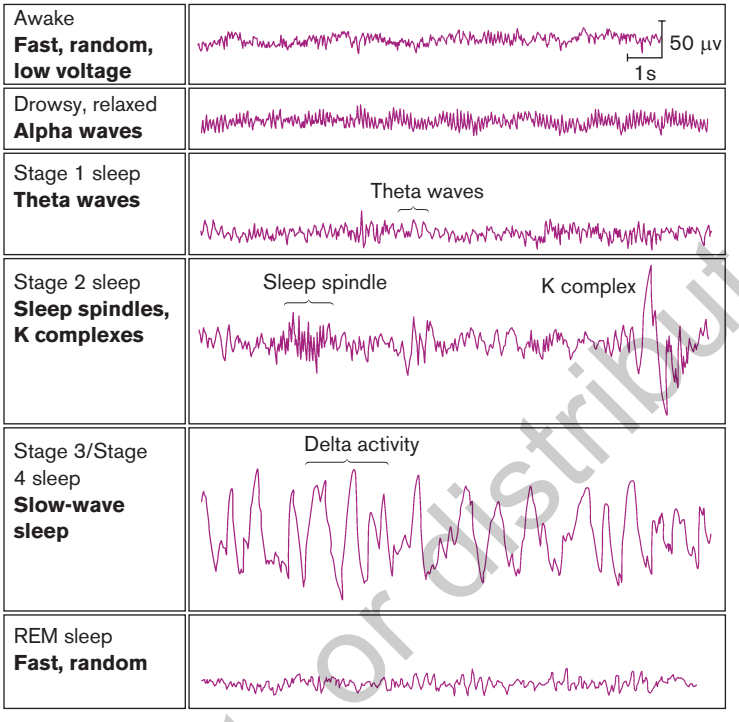
The EEG was first demonstrated in humans by Hans Berger in 1924, and results were published 5 years later (Berger, 1929/1969). Since the neurons of the brain and their connections are constantly active, EEG can be measured during both waking hours and sleep. In fact, EEG serves as an objective measure of depth of sleep (see *Figure 2.10*).

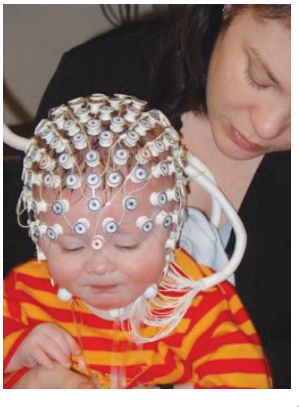
EEG can be measured with only two electrodes or as a high-density array of more than 200 electrodes. EEG activity has been used to infer brain processing. The actual measure of EEG is the difference between the signals at any two electrodes. Traditionally, the second or reference electrode was placed at a location not considered to produce electrical signals, for

FIGURE 2.10 Electroencephalogram as an Objective Measure of Sleep Stages

EEG can be used to determine the stage of sleep that is present. Being awake reflects low-amplitude, faster EEG activity. During the night, the EEG becomes of a lower frequency as the person goes into deeper sleep. A person generally goes through three or four cycles of sleep during the night in which they move from stage 1 to stage 4 and back again.

Source: P. Hauri, *Current Concepts: The Sleep Disorders*, 1982, Kalamazoo, MI: Upjohn.





An EEG "cap" that holds the electrodes is placed over the subject's head.

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example, the ear lobe. Today, a common practice is to average the signals in all of the electrodes available and compare that with each specific electrode.

Some aspects of the EEG signal may appear almost random, while other fluctuations appear periodic. Using signal processing techniques, it is possible to determine the major frequency and amplitude seen in the signal. Amplitude refers to how large the signal is, and frequency refers to how fast the signal cycles, measured in cycles per second, or Hertz (Hz). Over the years, researchers have noticed that specific patterns of EEG activity were associated with a variety of psychological states (see *Figure 2.11*). When an individual is relaxed with his or her eyes closed, high-amplitude regular activity is seen in the EEG at a frequency of 8 to 12 Hz. Alpha activity in the 8 to 12 Hz range was the first pattern of EEG activity Hans Berger noted. If the person begins to perform some mental activity such as mental arithmetic, lower-amplitude EEG is seen at a higher frequency, above 20 Hz, and is referred to as beta activity.

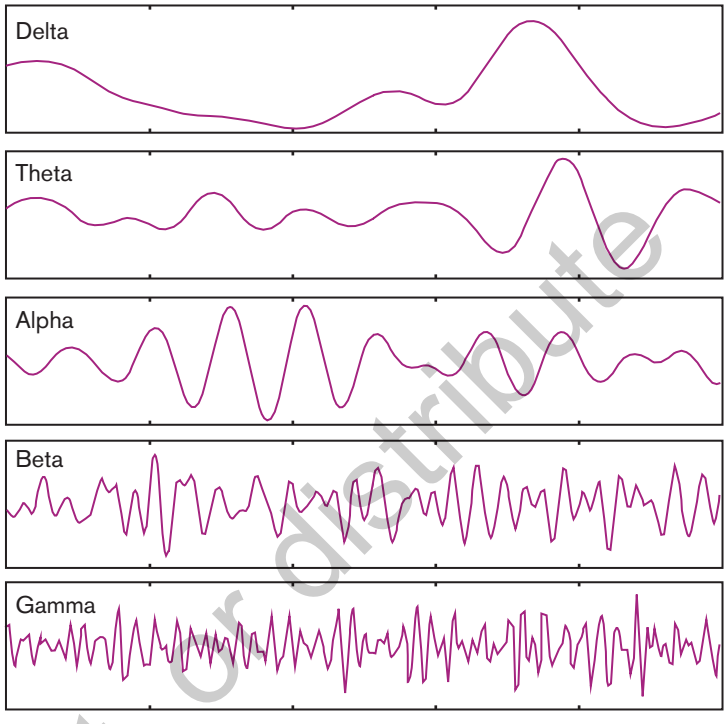
EEG oscillations are one way in which information is transferred in the brain (Knyazev, 2007). For example, theta oscillations are associated with memory performance (Liebe, Hoerzer, Logothetis, & Rainer, 2012). Theta is also involved in coordinating emotional information between the limbic areas and the frontal areas of the brain. Delta oscillations are seen in sleep and motivational processes such as drug use. Drugs such as cocaine produce changes in a number of EEG frequency bands. Alpha oscillations, on the other hand, are involved in inhibiting the activity of various brain areas.

In recent years, researchers have become interested in the processing of a percept (Singer, 2009; Singer & Gray, 1995; Tallon-Baudry & Bertrand, 1999). For example, when one sees a black and white spotted Dalmatian dog against a black and white background, there is usually a subjective experience of having the image "pop out." Associated with this perception is a burst of EEG gamma activity. *Figure 2.12* compares the amount of EEG gamma activity in those individuals trained to see the Dalmatian as compared with those who were not trained.

FIGURE 2.11 Depiction of Specific Patterns of Electroencephalography Activity

EEG activity is named in terms of its frequency and amplitude. Delta (0–4 hz) is seen in deep sleep, theta (4–8 hz) is seen as one goes to sleep, alpha (8–13 hz) is seen during periods of relaxation, beta (13–30 hz) is seen when a person is actively thinking, and gamma (about 30 hz) is seen in perceptual processes.

Source: Hugo Gambo (2005), Wikipedia.



EVOKED POTENTIALS

Event-related potentials (ERPs), also known as **evoked potentials (EP)**, show EEG activity in relation to a particular event. Imagine taking a continuous EEG signal during which a picture or tone is presented to an individual a number of times. If we were to take the EEG in the half-second following the stimulus presentation and average these together, we would have the brain response to the stimulus (see *Figure 2.13*).

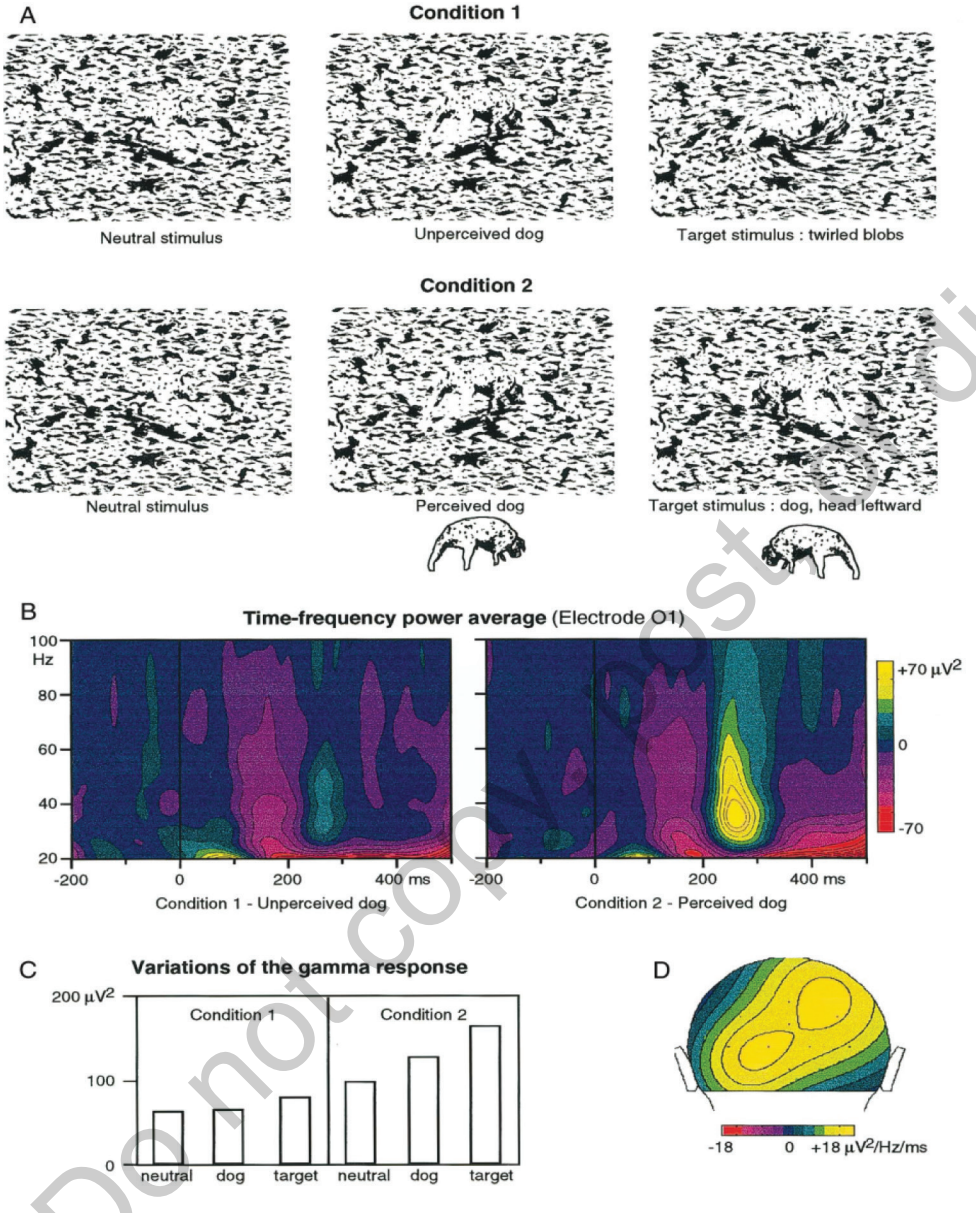
The waveform of the ERP is described in terms of positive and negative peaks and the time elapsed from the stimulus presentation. Thus, a P300 waveform is a peak in the ERP in the positive direction occurring 300 milliseconds after the stimulus presentation. Based on early recording equipment characteristics, positive peaks are often shown pointing downward and negative peaks upward. For simplicity, P300 is sometimes referred to as P3, since it represents the third positive peak following a stimulus presentation. Thus, one may see both N1 or P3 as well as N100 or P300 used in the literature.

Evoked potentials offer a view of cognitive and emotional processing that takes place in the brain outside of awareness. They are also useful in groups such as infants who cannot respond verbally. In one study, evoked potentials were recorded from 7-month-old infants as they saw faces with emotional expressions. A stronger reaction was seen at around 400 milliseconds when they saw a fearful face as opposed to a happy face (Taylor-Colls & Pasco Fearon, 2015). A common use of evoked potential research in terms of mental disorders has been to show how cognitive and emotional processing differs for those with a disorder and those without. Evoked potentials have also been used to distinguish those with schizophrenia from those without (Laton et al., 2014). In addition, evoked potentials have shown that children with ADHD (attention deficit/hyperactivity disorder) show different types of evoked potential components from those with autism spectrum disorder (Tye et al., 2014).

FIGURE 2.12 Wavelet Analysis Associated With Seeing the Dalmatian Dog

When the person recognizes that there is a dog in the picture, there is a burst of EEG gamma activity (yellow in the graph), as seen in the right wavelet analysis in panel B.

Source: Reprinted from Catherine Tallon-Baudry & Olivier Bertrand, Oscillatory Gamma Activity in Humans and Its Role in Object Representation, *Trends in Cognitive Sciences*, Vol. 3, pp. 151–162, Copyright © 1999, with permission from Elsevier.



Magnetoencephalography

Magnetoencephalography (MEG) measures the small magnetic field gradients exiting and entering the surface of the head that are produced when neurons are active. It uses a SQUID (superconducting quantum interference device) to detect small magnetic activity that results from the activity of neurons. As shown in the photo, the person simply puts his head in a device that contains magnetic sensors.

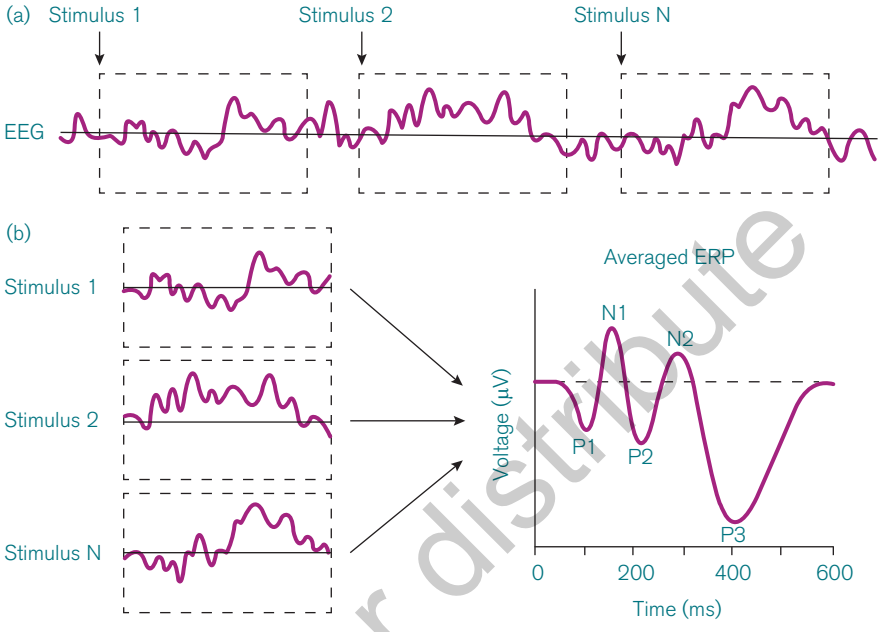


FIGURE 2.13 Evoked Potentials Are Created by Averaging Periods of EEG

Ongoing EEG is shown in (a). Responses to a stimulus are then averaged together (b) to create the evoked potential. Event-related potential waveforms come from the ongoing electroencephalography.

Source: Reprinted from Steven J. Luck, Geoffrey F. Woodman, & Edward K. Vogel, Event-Related Potential Studies of Attention, *Trends in Cognitive Sciences*, Vol. 4, pp. 432–440, Copyright © 2000, with permission from Elsevier.

MEG signals are similar to EEG signals but have one important advantage that stems from the fact that magnetic fields are not distorted when they pass through the cortex and the skull. This makes it possible to be more accurate in terms of spatial location of the signal with MEG. For example, youth with bipolar disorder show greater activation in the frontal gyrus and less in the insula following negative feedback than do control participants (Rich et al., 2011).

Positron Emission Tomography

Positron emission tomography (PET) is a measure related to blood flow in the brain that reflects cognitive processing. PET systems measure variations in cerebral blood flow that are correlated with brain activity. It is through blood flow that the brain obtains the oxygen and glucose from which it gets its energy. By measuring changes in blood flow in different brain areas, it is possible to infer which areas of the brain are more or less active during particular tasks. Blood flow using PET is measured after participants inhale, or are injected with, a tracer (a radioactive isotope) that travels in the bloodstream and is recorded by the PET scanner (a gamma ray detector). *Figure 2.14* depicts a PET scan in which individuals with schizophrenia show less metabolism in the frontal lobes as compared with healthy controls (Buchsbaum & Haier, 1987).

The general procedure is to make a measurement during a control task that is subtracted from the reading taken during an experimental task. Although it takes some time to make a PET reading, which reduces its value in terms of temporal resolution, it is possible to determine specific areas of the brain active during

Magnetoencephalography measures brain activity by measuring small magnetic fields produced in the brain.

National Institutes of Mental Health

FIGURE 2.14 Comparing Positron Emission Tomography Scans

Control subjects show more activity (brighter colors) than individuals with schizophrenia.

Source: Buchsbaum, M. S., & Haier, R. J. (1987), Functional and Anatomical Brain Imaging: Impact on Schizophrenia Research, *Schizophrenia Bulletin, 13*(1), 115–132.

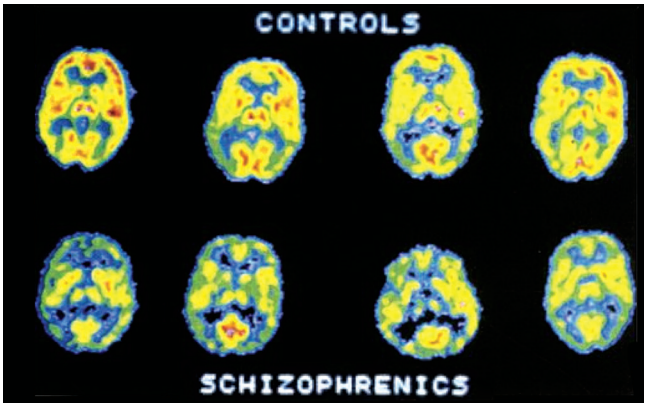
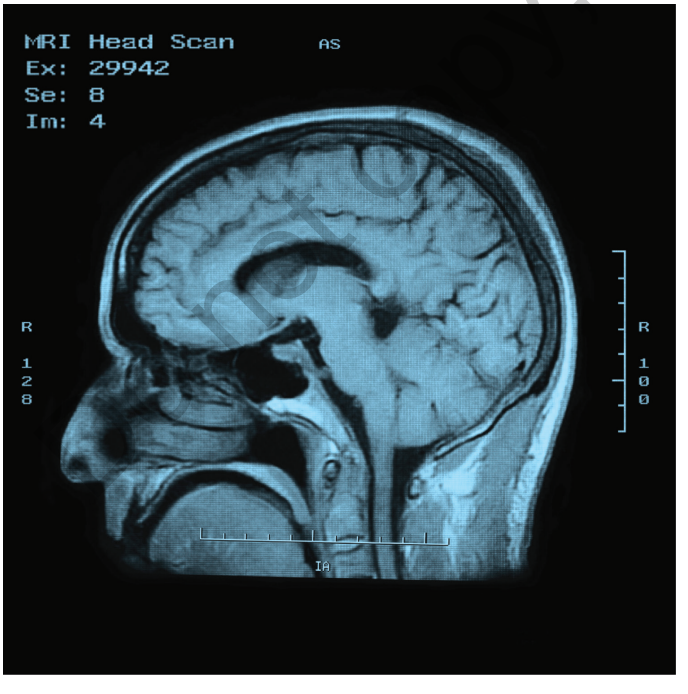


FIGURE 2.15 Magnetic Resonance Imaging (MRI) Shows the Anatomy of the Brain

Unlike fMRI, MRI does not reflect brain activity but only the structure of the brain.

Source: ©iStockphoto.com/CGinspiration.



different types of processing. Since PET can measure almost any molecule that can be radioactively labeled, it can be used to answer specific questions about perfusion, metabolism, and neurotransmitter turnover.

Some of PET's main disadvantages include expense; the need for a cyclotron to create radioactive agents; the injection of radioactive tracers, which limit the number of experimental sessions that can be run for a given individual; and limited temporal resolution. Due to risks associated with exposure to the radioactive tracer elements in a PET study, participants typically do not participate in more than one study per year, which limits the degree to which short-term treatment efficacy can be studied. With the development of fMRI, PET is no longer the technique of choice for research studies in psychopathology.

However, PET does offer an advantage for studying specific receptors such as dopamine receptors in the brain, which are particularly active in those with an addiction or inactive in those with Parkinson's disease. Another study used PET to examine serotonin in those with social anxiety disorder (A. Frick et al., 2015). An overactive serotonin system was found at the synaptic level in those with social anxiety disorder as compared to matched controls.

Functional Magnetic Resonance Imaging

Functional magnetic resonance imaging (fMRI) is based on the fact that blood flow increases in active areas of the cortex. Specifically, hemoglobin, which carries oxygen in the bloodstream, has different magnetic properties before and after oxygen is absorbed. Thus, by measuring the ratio of hemoglobin with and without oxygen, the fMRI is able to map changes in cortical blood and infer neuronal activity.

Measurements using fMRI are made by having a person lie on his back inside a large magnet and radio frequency device, which measures changes in blood oxygen levels. Initially, a structural image of the brain is created (see *Figure 2.15*). In contrast, a structural image (MRI), like an X-ray, shows the *anatomy* of the brain but does not reflect *activity*. It is possible to measure brain areas with an MRI in terms of size. Often, measures of those with

a disorder are compared to those without the disorder. For example, reduction in brain volume is seen in a variety of disorders including schizophrenia. These measures can be determined from the MRI.

Brain activity can be determined with the fMRI, or functional MRI. A common procedure for showing brain activity is to take a baseline in which the patient just relaxes. Following this baseline period, the patient performs specific tasks. The fMRI response recorded during the task is subtracted from that during the baseline period. This shows which specific areas of the brain are involved in performing a task. This information is then placed on the structural MRI image of the brain as shown in *Figure 2.16*. The color used reflects the amount of activity seen in a particular brain area. As you will see throughout this book, fMRI has been used with almost every disorder discussed. You can also compare one group of individuals with another. For example, *Figure 2.17* shows that women with post-traumatic stress disorder (PTSD) activate different areas of the brain (the amygdala and insula) when processing emotional information compared with women without PTSD (Bruce et al., 2013).

Blood flow measurements in the brain using fMRI are made by having a person lie on his back inside a large magnet and radio frequency device.

©iStockphoto.com/Mark Kostich

DIFFUSION TENSOR IMAGING

It is also possible to use the MRI magnet to measure cortical connections in the brain, which is referred to as **diffusion tensor imaging (DTI)**. DTI is available with most MRI imaging systems (see Thomason & Thompson, 2011, for an overview of DTI and psychopathology). It is a procedure for showing fiber tracts (white matter) in the brain. This information can then be visualized by color coding it as shown in *Figures 2.18* and *2.19*. This allows one to map the white matter connections in the brain. In these figures, the connections between different parts of the brain can be seen.

Developmentally, after-infancy measures of white matter suggest a linear development until a person is in her thirties. Following a plateau, these gradually decline with age. Using DTI, it is possible to map the mild cognitive impairment seen in dementia and the more severe impairment seen in Alzheimer's disease. Disconnections are seen between the major areas involved in memory such as the hippocampus and the temporal lobes (Stebbins & Murphy, 2009). As would be expected, this loss of connectivity is greater in Alzheimer's than in mild cognitive impairment. Individuals with schizophrenia also exhibit problems with cortical connections (Phillips et al., 2011). It is also possible to compare the structure of pathways in the brain between humans and other primate species (Wedeen et al., 2012). DTI and other brain imaging techniques have also given us a better understanding of cultural differences as described in the *Cultural LENS: Using Brain Imaging to Understand Culture.*

FIGURE 2.16 Functional Magnetic Resonance Imaging (fMRI)

In these fMRI scans, the amount of color reflects the amount of activity seen in a particular brain area. The activity is related to the energy demands needed to perform a particular task.

Source: Philippe Psaila/Science Photo Library.

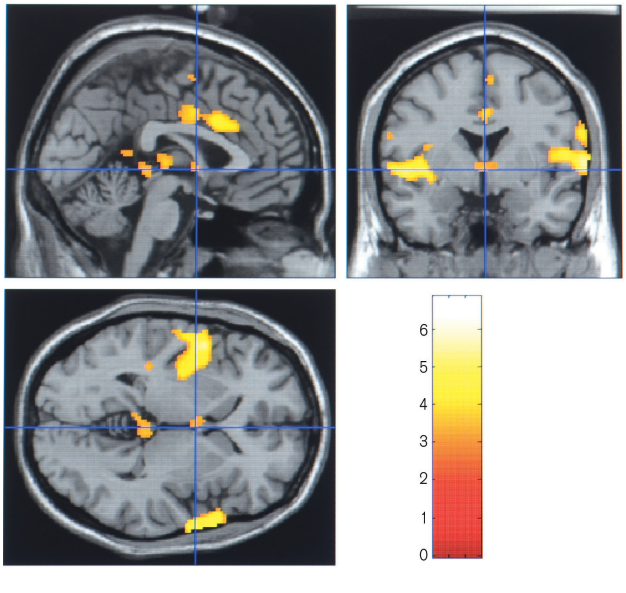


FIGURE 2.17 Brain Activation Differences in the Amygdala and Insula

This figure shows the fMRI scans of the brain at two different levels along the z-axis. Women with post-traumatic stress disorder (PTSD) activate the amygdala and insula more when processing emotional information compared with women without PTSD.

Source: Reprinted from Steven E. Bruce, Katherine R. Buchholz, Wilson J. Brown, Laura Yan, Anthony Durbin, & Yvette I. Sheline, Altered Emotional Interference Processing in the Amygdala and Insula in Women With Post-Traumatic Stress Disorder, *NeuroImage: Clinical*, Vol. 2, pp. 43–49. Copyright © 2013, with permission from Elsevier.

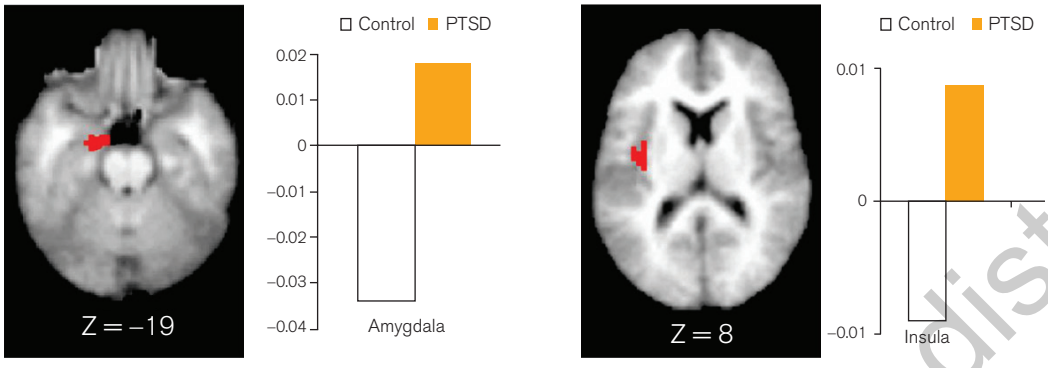


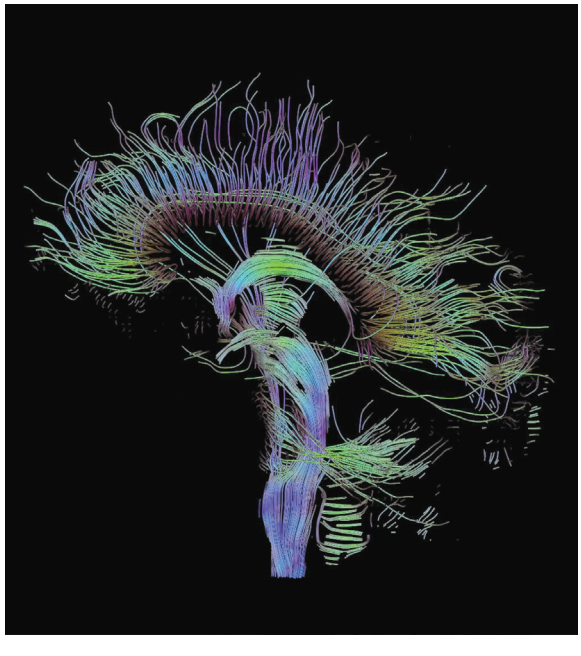
FIGURE 2.18 Mapping White Matter Connections in the Brain Using Color Coding

Source: © Zephyr/Science Source

FIGURE 2.19 Mapping White Matter Connections in the Brain Measured With Diffusion Tensor Imaging (DTI)

DTI reflects fiber tracts in the brain. This information can then be visualized by color coding the size of the tract.

Source: Thomas Schultz (2006), Wikipedia.



Spatial and Temporal Resolution

There are a number of trade-offs that researchers must consider when choosing a brain imaging technique (see *Table 2.2* for pros and cons of using the different techniques). It begins with the research question one is asking. If you wanted to know if the areas of the brain

TABLE 2.2 Pros and Cons of Different Neuroscience Techniques

TECHNIQUE	PROS	CONS
EEG	Reflects quick changes in the brain, inexpensive, not invasive, safe, little discomfort	Difficult to know which brain areas produced the EEG
MEG	Reflects quick changes in the brain, not invasive, safe, no discomfort	Basic equipment is expensive
MRI and fMRI	More exact location of structure and activity, safe, little discomfort	Basic equipment is expensive, cannot be used with people who have any metal in their body (heart pacemaker or metal pins), fMRI not able to measure short-term changes in the brain
PET	Able to measure specific neurotransmitters	Basic equipment is expensive, injection of radioactive tracers limits number of scans per year, not able to measure short-term changes in the brain

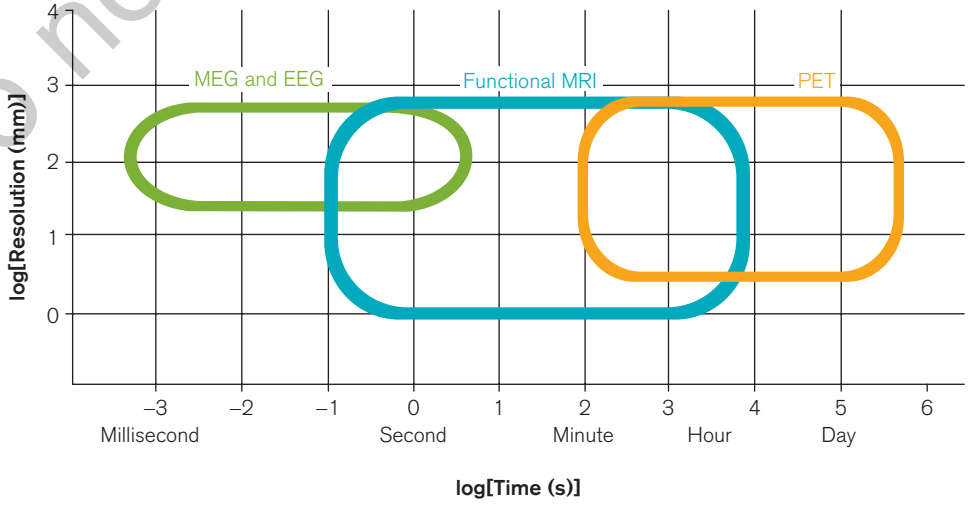
associated with memory, such as the hippocampus, are larger or smaller in those with PTSD, then you would want a measure of structure. If you wanted to know if those with autism quickly viewed different emotional faces in a different way, then you would want a measure that reflects changes in brain processes.

One important question is how fast a particular technique can measure change. This is referred to as *temporal resolution.* EEG and MEG, for example, can measure quick changes in the brain on the millisecond level. PET, on the other hand, can only record changes that take place in a period of a few minutes or more. Another consideration is spatial resolution—that is, what size of brain area a technique can measure. PET and fMRI are better able to pinpoint the location of activity in the brain, whereas with EEG it is less possible to know specifically where in the brain activity came from. The relationship between spatial and temporal resolution is shown in *Figure 2.20*.

FIGURE 2.20 Spatial and Temporal Resolution of Imaging Techniques

EEG and MEG have temporal resolution of less than a second. Using these techniques, it is possible to measure quick changes in the brain. PET takes a longer time to complete a measurement. Although MRI measurements are slower than EEG, the ability to image specific areas of the brain is better.

Source: Meyer-Lindenberg (2010, p. 194).



CULTURAL LENS

Using Brain Imaging to Understand Culture

A traditional healer in the Shona village in Harare, Zimbabwe.
Robert Fried/Alamy

For thousands of years, humans have traveled and been fascinated by the diversity of human behavior and thinking around the world. Historically, those interested in psychopathology and neuroscience research have focused more on the universality of human processing rather than the diversity found in different cultures. This is beginning to change with an integration of human diversity and neuroscience perspectives on human behavior and experience (see Chiao, 2009, 2011; Henderson, Vincenzi, Yeung, Fricchione, 2016; Kitayama & Cohen, 2007).

In terms of assessment and *classification* of mental disorders, it is critical when working with individuals from different cultures to understand the rules of expression as well as the labeling of mental disorders. This is especially true if the rules for expression of distress and emotion differ greatly from the interviewer's culture. It is also important to understand what would be considered a mental disorder in another culture. For example, in some cultures such as the Shona of Zimbabwe, there is a disorder referred to as thinking too much (*Kufungisisa*). Thinking too much is seen to cause anxiety and depression as well as headaches and dizziness. A common theme in Latin America is to speak of nerves (*nervios*) as a common idiom for psychological distress. People may say that they cannot function because of nerves. In Japan, there is a broad concept of social concern when interacting with others (*taijin kyofusho*). This can include concern that one is making too much or too little eye contact, has an unpleasant body odor, or is making inappropriate body movements (see Mezzich & Ruiperez, 2015, for an overview). Cultural displays of emotional expression vary. Individuals from different cultures may display their emotions differently even though the underlying experience of the emotion may be similar. Some of the early work on this topic was performed by Paul Ekman and his colleagues (Ekman & Oster, 1979). In these studies, individuals from North America and Asia were shown emotionally arousing films that brought forth feelings of disgust or happiness. Although in private, both cultural groups showed similar facial expression, the situation changed drastically when another person was present.

In that situation, those from Asia showed fewer facial expressions in reaction to the films than when they were alone. Western individuals, on the other hand, showed similar reactions to the films both alone and in the presence of another. Thus, different cultures have different display rules for the expression of similar underlying emotions.

Neuroscience research has shown that human reactions are also culturally sensitive. We know that the amygdala shows increased activity in response to emotional reactions—especially fear. Native Japanese and Caucasian Americans show greater amygdala responses to fear expressions of those of their own culture. To put it another way, a person shows less response when viewing an emotional expression of someone who is not part of his or her own culture (see *Figure 2.21*).

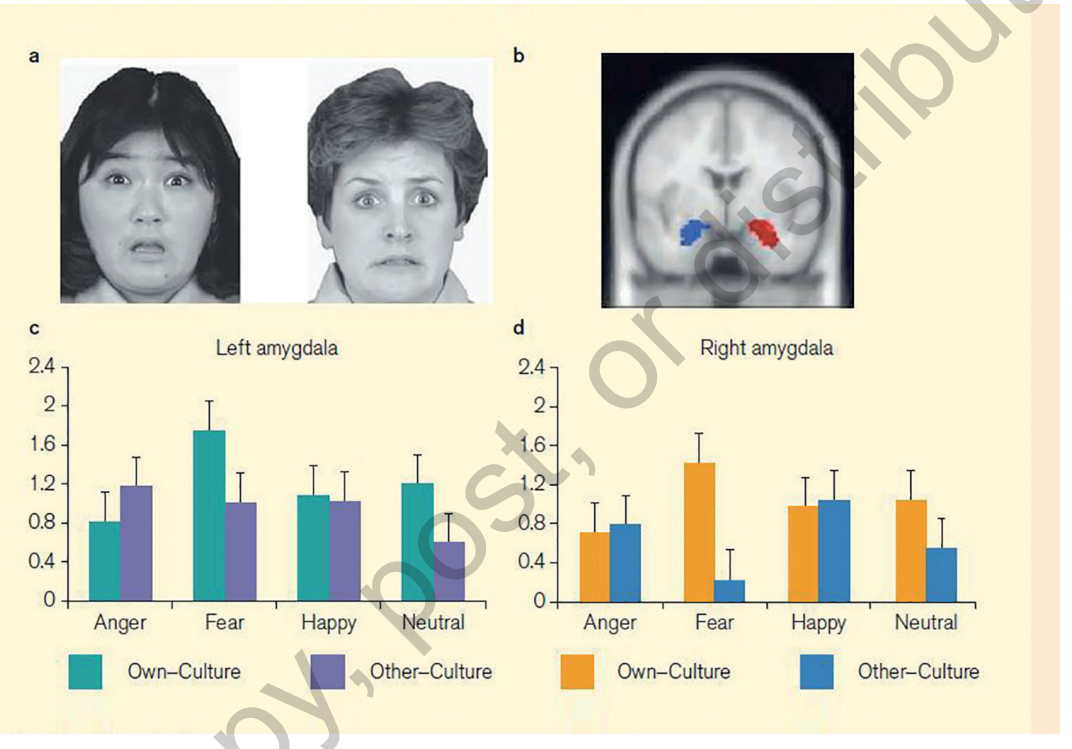
Thought Question: What cultural factors need to be considered in the assessment and classification of mental disorders? How could the failure to notice cultural differences lead to an incorrect assessment?

FIGURE 2.21 Cultural Specificity in Bilateral Amygdala Response to Fear Faces

Do we respond differently to those in our culture?

In terms of fear faces, people show more amygdala responses to the expression of such fear faces by those in one's own culture. Less response is seen to fear faces of those from cultures other than one's own. In the various panels in this figure, (a) portrays fear expressions on a Japanese person and a Caucasian American, and (b) shows an illustration of bilateral amygdala response to fear faces. As shown in the graphs, participants show greater left (c) and right (d) amygdala response to fear expressed by members of their own cultural group.

Source: Chiao (2009).



Neuroethics

When we read in the news about discoveries in the neurosciences, they are often presented in an optimistic manner. We are told they will help us treat medical disorders or learn more about how we think and feel. This is true. However, traditionally, societies have based codes of conduct and the law on observable behaviors. An important question currently being asked is who should have access to data and scans of your internal processes. *LENS: Neuroethics: Ethical Considerations When Using Neuroscience Techniques* examines the field of inquiry that is asking these questions. It is referred to as **neuroethics**.

CONCEPT CHECK

- Describe four major types of brain imaging techniques currently being used, and identify a psychological disorder for which each is especially valuable.
- What are some of the trade-offs that researchers and clinicians must consider when choosing a brain imaging technique? What questions help inform their decision?

LENS

Neuroethics: Ethical Considerations When Using Neuroscience Techniques

Safety and ethics are global concerns in the age of neuroscience.
AP Photo/Susan Walsh

Through genetics, brain imaging, and other neuroscience procedures, it is now possible to know not only about one's behaviors but also about one's internal processes. For example, predictions can be made from genetics about certain types of medical and psychological disorders that are more likely to develop in one's future. This raises ethical questions concerning who should have access to this information and how it may be used by a society.

In the first half of the twentieth century, certain Western societies attempted to make changes in future populations. This was referred to as *eugenics*. The basic idea was that it was possible to improve the human race by discouraging reproduction among those considered to be inferior and encouraging reproduction among those who were considered to be healthy or otherwise preferable. Individuals with mental disorders and mental disabilities were among those sterilized. The eugenics movement impacted policies in the United States, Britain, and elsewhere, then reached its extreme in Nazi Germany during World War II.

Although today eugenics is thought of as a disreputable crusade of the past, ethical issues in terms of one's own genetic information raise important questions. Should people who want to have children be told about the possible characteristics, including potential disorders such as autism, of their future child? Should an insurance company know whether you might have the potential to experience schizophrenia or depression in your lifetime? Should companies be able to patent human genes that could prevent disease? Should people be told early in their life which disorders they might develop 40 or 50 years in the future? These are just a few of the complex questions to be considered.

There are also a number of questions related to brain imaging techniques. For example, with millions of MRI scans being performed for research, scientists may discover what are referred to as *incidental findings*. Should an individual be told that he or she has a non-normal brain if a neurologist does not consider the findings related to the person's physical health?

At this point in time, brain imaging techniques cannot absolutely determine if one individual has a mental disorder or not. What neuroscientists *can* say is that a group of individuals with a particular disorder will show different patterns of brain activity than another group of individuals who do not have the disorder.

Neuroethics takes us beyond the questions of traditional research ethics and focuses on the ethical, legal, and social policy implications of neuroscience (Illes & Bird, 2006). Because of this, a number of scientific neuroscience groups and governmental agencies have sought to understand the ethical problems that neuroscience will bring our society.

Thought Question: Neuroethics focuses on the ethical, legal, and social policy implications of neuroscience and asks complex questions. Choose a position on one of the questions presented in this *LENS*, and present evidence to support your position.

Networks of the Brain

Given that the human brain has some 86 billion neurons with some 5,000 synapses, each resulting in trillions of synaptic connections, it is clear that a higher-level analysis of brain function is necessary (Goldstone et al., 2015). A variety of brain imaging techniques have

allowed for a network analysis that describes which areas of the brain are involved in specific tasks. The first step has been to describe the normal processing of networks such as those involved in rewards or fear. The next step is to understand how these networks become involved in more psychopathological states such as addiction and anxiety. The goal now is to better understand how the basic network becomes involved in psychopathological processes. Is it a lack of connections between brain areas, or is there a reorganization of normal processes that underlies specific psychopathologies? This is one question scientists are asking.

Following the discovery of brain areas involved in particular functions such as Broca's area in the 1800s, researchers searched for specific areas involved in particular cognitive, emotional, and motor processes. With the increased sophistication of brain imaging technologies came a greater ability to view the manner in which certain parts of the brain work together as well as large-scale turning off and on of various areas. Some processes involve a pathway using only a few neurons. Being startled by a loud noise or touching a hot stove are examples of processes that have short neuronal pathways. Other processes use a more complex series of connections. More voluntary and complex processes use a much larger series of neuronal connections referred to as *networks*.

Researchers examine how specific brain areas work together as networks. This search has also extended to psychopathology. Psychopathology can be seen in terms of problems involving either particular brain areas or the connections between areas that make up the network.

We all experience the brain organizing itself in terms of various networks throughout our day. One of the most familiar is sleep. Another is waiting for a lecture to start, when we just let our mind wander. Both of these cases are not responses to external stimuli but are self-organizing processes that occur. These types of processes are controlled by a large number of neurons working together in the form of a network.

Networks allow our brains to process information efficiently (Laughlin & Sejnowski, 2003; Sporns, 2011). Overall, cortical networks are influenced by experience and are designed to be efficient in terms of connections between neurons in the network. This efficiency allows for less use of energy. One way energy is conserved is through not having every neuron connect with every other neuron.

Neurons Connect in a Network

How are neurons connected in a network? The answer may seem strange. Neurons are neither totally random in their connections with other neurons nor totally patterned. It appears that neurons are connected to one another in the same way that all humans on this planet are socially connected.

In the 1960s, the social psychologist Stanley Milgram (Travers & Milgram, 1969) asked the question, "What is the probability that any two people randomly selected from a large population of individuals such as the United States would know each other?" He answered this question by giving an individual a letter addressed to another person somewhere in the United States. This individual was to send the letter to someone he knew who might know the other person. In turn, this person was to send the letter to someone she knew who might know the person. Surprisingly, it only required five or six different people for the letter to go from the first individual to the final individual. This phenomenon has been referred to as the small world problem; more recently, the phrase *six degrees of separation* has been used.

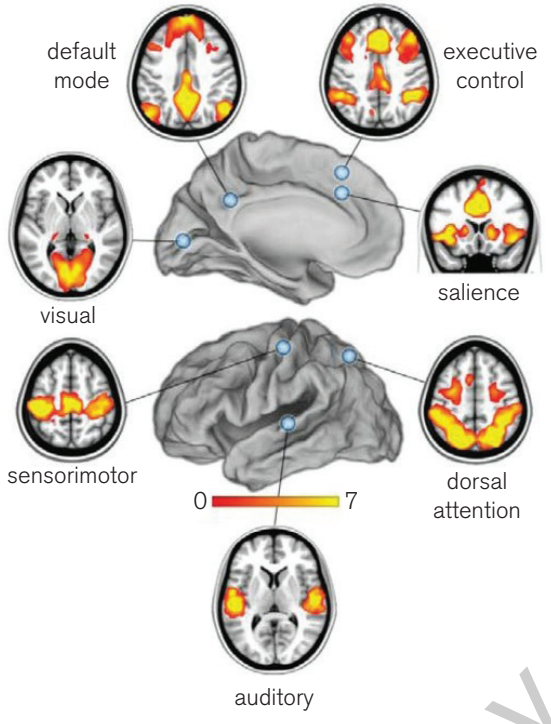
Various studies have shown that the neurons in the brain can also be considered within a **small world framework** (Sporns, 2011). Neurons have numerous short-distance local connections, which taken together can be considered as a hub or module. From these hubs extend more long-distance connections to other hubs.

Local hubs can be made up of neurons that connect with each other over very short distances. Such connections are seen in gray matter. Underlying this are the *axons,* which transfer information throughout the brain. Their myelin sheaths are lighter in color, and thus, these areas are referred to as white matter. Myelin is made up of fats and proteins. It wraps

FIGURE 2.22 Major Networks of the Brain

When someone is doing a task, it is possible to determine which areas of the brain are connected to each other. This figure shows those areas of the brain that work together when performing certain types of tasks.

Source: Raichle, M. E. (2015, March 30). The restless brain: How intrinsic activity organizes brain function. *Philosophical Transactions of the Royal Society B.*



around axons like insulation does around electrical cables and results in an increased speed in information transmissions. About 44% of the human brain is white matter. White matter generally represents longer connections between neurons. This allows for cortical networks over larger areas of the brain. Knowing this, it is possible to examine the network connections in individuals with a particular disorder and their matched controls. For example, individuals with schizophrenia have been shown to have disrupted global networks of the brain (O. Wang et al., 2012) as have those with depression (B. J. Li et al., 2018).

Networks have been studied in terms of a variety of cognitive and emotional tasks (Bressler & Menon, 2010; Raichle, 2015). These include separate networks involved in the processing of visual or auditory information, sensorimotor processes, attentional processes, executive control, salience, and default mode (see *Figure 2.22*).

Three of these networks have been examined in terms of psychopathology (Menon, 2011). These are the baseline or default network (also called the intrinsic network), the **central executive network**, and the **salience network**. The default network is active when an individual is not performing a particular task, such as when one's mind wanders or is processing internal information. The central executive network is involved in higher-order cognitive and attentional tasks. The salience network is important for monitoring critical external events as well as internal states. As will be described throughout this text, psychopathological disorders such as schizophrenia, depression, anxiety, dementia, and autism have been shown to involve problems in turning networks on or off as well as problems in the connections within the network itself.

The historical considerations of psychopathology emphasized careful observation and interaction with the afflicted individuals as important methods for understanding the nature of the disorder. However, with progress in the neurosciences, brain imaging, and genetics, other levels of analysis have become possible. The new levels offer different perspectives for the field of mental illness, but because many of these discoveries are so new, it is not surprising that our understanding of the field of mental illness is currently in flux. Neuroscience research has been used to find more objective markers in the diagnosis and treatment of mental disorders. It has also helped describe cognitive, emotional, and motor processes in both health and illness. This has resulted in a better articulation of what underlies these processes such as problems in setting goals; having relationships with others, thinking, and feeling; as well as deficits in the memory system and the reward system.

What Is the Brain's Default (Intrinsic) Network?

What does your brain do when you are just sitting and waiting or daydreaming or talking to yourself? This is a question that is just now beginning to be explored. In psychology, most of the research you read about involves a person *doing* something. Reacting to emotional pictures or solving cognitive problems are common examples. In these cases, one's attention is focused on a task in the external world.

In the same way that the brain is organized to process spatial and verbal material differently and involve different cortical networks, it also appears that different circuits are

involved with internal versus external information. A variety of studies have examined brain imaging procedures in which individuals performed internal tasks versus external tasks (e.g., Ray & Cole, 1985).

However, we all know that even without an external task to do, our mind is constantly working. It jumps from one thought to another. The psychologist William James called this process the *stream of consciousness*. Recent researchers refer to this process as mind wandering.

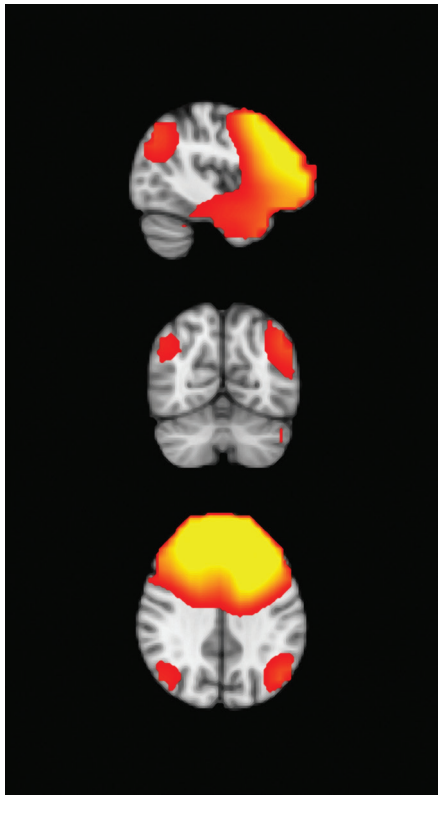
Those neural networks that are active during internal processing have come to be referred to as the brain's **default or intrinsic network** (Buckner, Andrews-Hanna, & Schacter, 2008; Raichle, 2011; Raichle & Snyder, 2007). It has been suggested that *intrinsic* is a better term than *default,* since a variety of internal tasks use this network (C. Kelly, Biswal, Craddock, Castellanos, & Milham, 2012). The default network is separate from, but can be understood as similar to, other networks such as those involved in visual perception or motor activities. It is made up of a set of interacting brain regions. Those areas involved are pictured in *Figure 2.23* and represent periods of brain imaging when individuals are not engaged in any active task.

Overall, the *default network* is involved during internal or private considerations that do not require processing external sensory information. In fact, it appears as if there is a negative correlation between activities in the default network versus networks associated with processing information from the environment. That is, when someone begins some cognitive activity, then new networks associated with that task become active and the default network becomes less active. This suggests that separate brain mechanisms evolved for dealing with information involving the external environment as opposed to considerations internal to the person. A variety of psychopathology disorders show problems with the default network in terms of being able to turn it off and engage in a more active external task. People with schizophrenia, ADHD, and autism are groups that have difficulty turning off the default network and moving to an active task that uses a different network.

FIGURE 2.23 The Brain's Default Network

Using a number of positron emission tomography studies, it is possible to determine those areas in the brain involved in the default network. Activity in these areas is seen during internal or private considerations that do not require processing external sensory information.

Source: James King-Holmes/Henry Luckhoo/Science Source



Different Networks Are Involved in Different Tasks

In addition to the default network, the executive and salience networks are dysfunctional in different psychopathologies (Menon, 2011). The *central executive network* is involved in performing such tasks as planning, goal setting, directing attention, performing, inhibiting the management of actions, and the coding of representations in working memory (Eisenberg & Berman, 2010). These are sometimes referred to as frontal lobe tasks, since damage to the frontal areas of the brain compromises performance of these tasks. These tasks are also referred to as **executive functions**, because they assist in planning, understanding new situations, and having cognitive flexibility. The *salience network,* as the name implies, is involved in monitoring and noting important (i.e., salient) changes in biological and cognitive systems.

The three networks—default, executive, and salience—show deficits in individuals with specific psychopathologies. Menon (2011) has reviewed the research literature and suggests that these networks play a prominent role in schizophrenia, depression, anxiety, dementia, and autism. As you will see throughout this book, the role of these networks may be dysfunctional in the network itself or in the ability to activate or deactivate specific networks in changing situations.

Figure 2.24 shows those areas of the brain that Menon (2011) found to be associated with each of these networks. The figure shows an MRI structural image of the brain in black and white. The areas that are activated during the task are displayed in color. The brain is shown in terms of a three-dimensional image along an x-, y-, and z-axis. The x-axis shows the brain from the side, the y-axis from the back, and the z-axis from above. The numbers below the image represent the location along each axis. Using these three numbers, brain imaging programs can identify the areas in relation to traditional anatomical structures.

In *Figure 2.24*, the central executive network, which is involved in higher-order cognitive and attentional demands including planning for the future and remembering concepts, is shown in blue. The salience network, which is important for monitoring critical external events and internal states, is shown in yellow. The default network, which is active during mind wandering and when the person is not engaged in active problem solving, is shown in red.

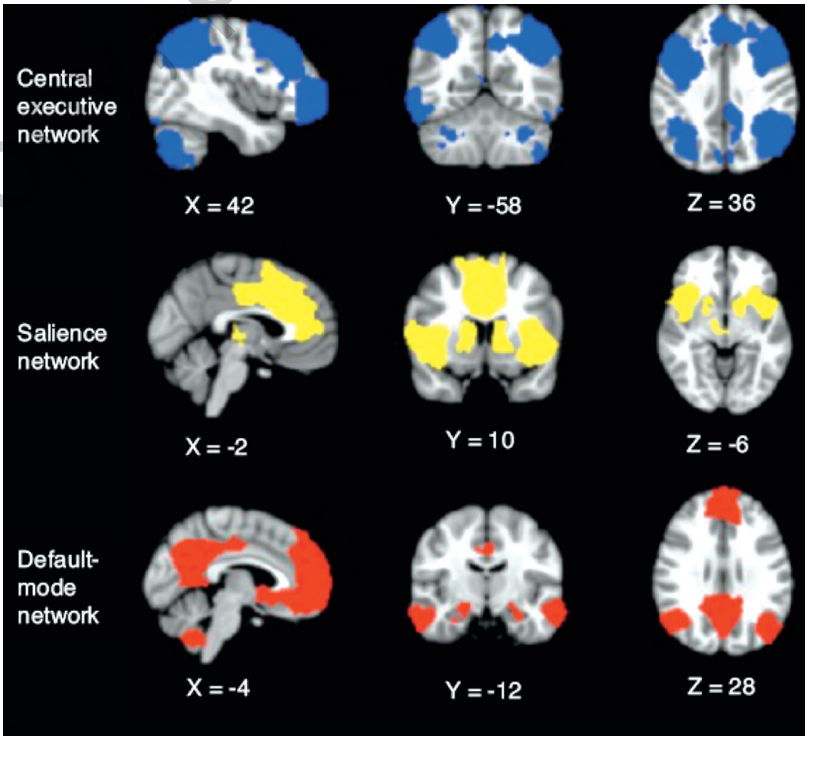
Let's take a moment to understand how researchers describe brain function in terms of networks. One important concept is **modularity**. *Modularity* describes how specific areas of the brain are dedicated to certain types of processing. For example, as discussed early in the chapter, we know that a particular part of the temporal lobe, the fusiform face area, is involved in processing responses to the human face. fMRI measures, for example, would show greater brain activation in this area when observing the human face as opposed to nonhuman faces.

Another important concept is **connectivity**. This asks how different areas of the brain work together in specific conditions. To determine connectivity, researchers examine fMRI or EEG measures from a large number of locations throughout the brain. It is assumed that those areas whose activity is correlated are in some way working together.

FIGURE 2.24 Structural Image of Three Brain Networks

In this figure using MRI technology, the executive network is shown in blue, the salience network in yellow, and the default network in red. Note that the x-, y-, and z-axis for each is different. That is, the three networks show different parts of the brain.

Source: Reprinted from Vinod Menon, Large-Scale Brain Networks and Psychopathology: A Unifying Triple-Network Model, *Trends in Cognitive Sciences*, Vol. 15, pp. 483–506, Copyright © 2011, with permission from Elsevier.



CONCEPT CHECK

- How does the brain operate as a "small world framework," and why is this significant?
- How is the brain's default or intrinsic network different from the central executive and salience networks?
- Researchers are concerned with modularity and connectivity in terms of neural networks. What are modularity and connectivity, and how are they important in thinking about psychopathology?

Genetics and Psychopathology

In this section, we consider the genetic level of analysis. This discussion includes a historical understanding of the study of genes as well as their structure. You will then learn about the role of DNA, how genes influence behavior, epigenetics, mitochondria, and endophenotypes.

Genes form the blueprint that determines what an organism is to become. Specific sets of genes have been associated with a variety of disorders, as will be described throughout this book. However, the original hope from the last century of finding a few genes that were involved in particular mental disorders has not panned out. Psychological disorders are related to many genetic differences, each having a small effect (Plomin, 2018). Many of these same genes that are related to problems of mental illness are also involved in normal development. What has become apparent is that there is a complex interaction of genetic and environmental factors involved in mental illness.

As the factors involved have become more complicated, there has been a search for particular processes related to psychopathology. For example, there exists a gene (SERT) that is involved in the removal of the neurotransmitter serotonin from the synapse. A variant of the SERT gene has been associated with depression, alcoholism, eating disorders, ADHD, and autism (Serretti, Calati, Mandelli, & De Ronchi, 2006). Likewise, a variant of the gene (DßH), which is associated with the synthesis of norepinephrine from dopamine, is associated with schizophrenia, cocaine-induced paranoia, depression, ADHD, and alcoholism (Cubells & Zabetian, 2004). It is suggested that the lower level of the *proteins* produced by the DßH gene is associated with a vulnerability to psychotic symptoms.

As researchers discover genes related to specific forms of mental illness, there may be a need to reorganize how we view mental illness in general. One study analyzed the genes from 33,332 individuals with a mental disorder in comparison with 27,888 without a disorder (Cross-Disorder Group of the Psychiatric Genomics Consortium et al., 2013). This research suggests that similar genetic risk factors involved in calcium channel signaling exist for what we have considered to be separate disorders. These five disorders are autism spectrum disorder, schizophrenia, bipolar disorder, major depressive disorder, and ADHD. This study implies that a particular genetic makeup may put some individuals at higher risk for developing a variety of disorders. There is also research that suggests that having certain mental disorders such as schizophrenia may actually protect these individuals from getting certain types of cancer (Tabarés-Seisdedos & Rubenstein, 2013).

Overall, current genetic research suggests a complicated relationship between genetic conditions and

There is a complex interaction of genetic and environmental factors involved in mental illness.

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environmental factors. For example, the MAOA gene, which is located on the X chromosome, makes the neurotransmitters serotonin, norepinephrine, and dopamine inactive and is associated with aggression in mice and humans. Caspi and his colleagues (2002) performed a longitudinal study and found that mistreatment as a child influenced some boys differently from others later in adulthood. Those boys who were mistreated in childhood and had a particular form of the MAOA gene were more likely to be violent and engage in a variety of antisocial behaviors as adults, as well as have problems with law enforcement officials. Those without this particular form of the gene did not display antisocial behaviors, even if they had been mistreated as children. Thus, environmental influences in terms of maltreatment modulate the expression of specific genetic structures but not the expression of others.

As researchers studied how genes turn on and off and what factors influence this, the story became even more complicated—the processes that determine which genes turn on and off could themselves be passed on to the next generation. Of course, which factors turn the genes on and off are largely influenced by the environment of the organism. Thus, although the genes themselves could not be influenced by the environment, it was possible for the environment to influence future generations through its changes to those processes that turn genes on and off. This is referred to as **epigenetics**.

The Study of Genetics

The study of genetics begins with the work of Gregor Mendel (1823–1884). Being curious as to how plants obtain atypical characteristics, Mendel performed a series of experiments with the garden pea plant. Peas are a self-fertilizing plant, which means that the male and female aspects needed for reproduction develop in different parts of the same flower. Therefore, successive generations of peas are similar to their parents in terms of particular traits such as their height or the color of their flowers.

Mendel found that when combining peas that have white flowers with those with purple flowers, the next generation had all purple flowers. Allowing this generation to self-fertilize brought forth plants that had purple flowers but also some that had white flowers. Mendel explained these findings by suggesting that a plant inherits information from each parent, the male and female aspects. Mendel was hypothesizing that information must be conveyed. He further suggested that one unit of information could be dominant in comparison to the other, which we now call a recessive trait. In this case, the unit of information that coded for purple would be dominant.

Mendel did not know about genes but hypothesized the existence of a specific structure he called elements. From his experiments, he determined the basic principle that there are two elements of heredity for each trait (e.g., color in the previous example). Mendel also assumed that one of these elements can dominate the other and if the dominant element is present, then the trait will also be present. In addition, Mendel suggested that these elements can be nondominant, or recessive. For the trait to appear, both of these nondominant elements must be present. These ideas are referred to as **Mendel's first law or the law of segregation**.

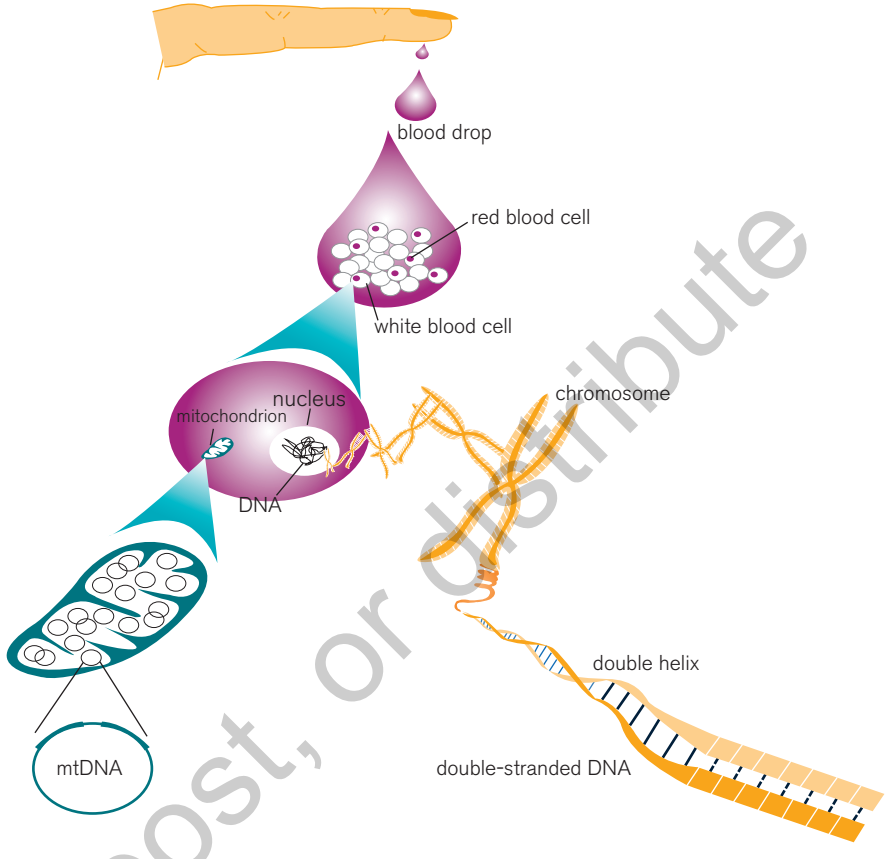
Put in today's language, Mendel suggested that variants of a specific gene exist, which account for variations in inherited characteristics, and that an organism receives one of these from each parent. Further, one of these can be dominant or recessive, which determines which characteristics are expressed. Mendel also realized that the inheritance of the gene for one trait is not affected by the inheritance of the gene for another trait. In the previous example illustrating the inheritance of color and height, those factors influencing color do not affect height, and vice versa. That is, the probability for each occurs separately. This is known as **Mendel's second law or the law of independent assortment**.

Since Mendel's time, we have learned a great deal about the process of inheritance. What he referred to as elements or units of information, we now call *genes* (see *Figure 2.25*). We also know that genes can have alternative forms, which we call alleles. Independent

FIGURE 2.25 Genetic Components Found in a Drop of Blood

A drop of blood contains red and white blood cells. From this, one can determine the person's DNA. The DNA is contained in 23 pairs of chromosomes in humans. Located at specific sites on those chromosomes are some 20,000 genes in each human. One part of the cell nucleus related to energy production is mtDNA (discussed later) and is passed on from the mother.

Source: Courtesy of National Human Genome Research Institute.



researchers, Walter Sutton and Theodore Boveri, in 1903 put forth a theory we now accept as fact, that genes are carried on **chromosomes**. We now know that each of the approximately 20,000 human genes occurs at a specific site, called a locus, on one of our 23 different pairs of chromosomes. As genetics progressed in the twentieth century, it was necessary to go beyond the two laws suggested by Mendel to a more complex understanding of how traits are passed from generation to generation. For example, if two genes are located close to one another on the same chromosome, then the result is different from that predicted by Mendel's second law.

What Do Genes Do?

Genes form the blueprint to describe what an organism is to become. Over our evolutionary history, a majority of human genes reflect little variation. In fact, you are the same as every other human being in over 99% of your genes (Plomin, 2018). This is why all humans have two eyes and one nose and one mouth. However, perhaps one fourth of all genes allow for variation. What makes things interesting is that the two genes of these pairs are usually slightly different. The technical name for the unique molecular form of the same gene is an **allele**. It has been estimated that of our approximately 20,000 to 21,000 genes, some 6,000 exist in different versions or alleles (Zimmer, 2001). Current research suggests that the high heritability of mental disorders is related to many genetic differences, each having a small effect (Plomin, 2018).

When a person has two copies of the same allele, they are said to be **homozygotes or homozygous** for that allele. If, on the other hand, they have two different alleles for a

particular gene, they are said to be **heterozygotes or heterozygous** for those alleles. Given that the alleles that come from your mother may not result in exactly the same characteristics as those from your father, variation is possible. It is these variations that allow for the process of natural selection to have its effect.

The job of a gene is to lay out the process by which a particular protein is made. That is, each gene is able to **encode** a protein, influencing its production. **Proteins**, which do the work of the body, are involved in a variety of processes. Functionally, proteins in the form of enzymes are able to make metabolic events speed up, whereas structural proteins are involved in building body parts. Proteins are diverse and complex and are found in the foods we eat as well as made by our cells from some 20 amino acids. Proteins serve as signals for changes in cell activity as illustrated by hormones. Proteins are also involved in health and disease as well as in development and aging.

Although the cells in the body carry the full set of genetic information, only a limited amount is expressed at any one time related to the function of the cell. That is to say, although a large variety of proteins could be produced at any one time, there is selectivity as to what is produced relative to internal and external conditions. Further, the location of the genes makes a difference in that cells in the brain produce different proteins from those in the muscles, liver, or heart.

A gene is turned on (produces the protein) or turned off (does not produce the protein) relative to specific events. Just because a person has a specific gene does not mean that it will necessarily be expressed. The environment in which a person develops and lives plays an important role in gene expression. Even identical twins with the same *genotype* can display different *phenotypes* (defined below) if their environmental conditions differ during their development. For example, if one was to grow up in a high mountain range and the other in a desert below sea level, important physiological differences such as lung capacity and function would be apparent. There are few factors other than blood type in terms of human processes that can be explained totally by genetic factors alone. It is equally true that few human processes can be explained totally by the environment.

DNA

With the discovery of the structure of DNA by Watson and Crick in 1953, specifying the method by which genetic material was copied became possible. **Deoxyribonucleic acid (DNA)** provides information necessary to produce proteins. Proteins can be viewed as a link between the **genotype** (complete genetic composition of an organism) and the **phenotype** (an organism's observable characteristics). Moving the genotype to the phenotype initially begins in two steps. First, the information in DNA is encoded in **ribonucleic acid (RNA)**. Second, this information in RNA determines the sequence of amino acids, which are the building blocks of proteins. Technically, the DNA synthesis of RNA is called *transcription,* whereas the step from RNA to protein is called *translation.* RNA is like DNA except its structure is a single strand, whereas DNA has a double strand. Once encoded, the RNA goes to a part of the cell capable of producing proteins. Proteins are produced by putting together amino acids.

To be more specific, DNA represents the chemical building blocks, or nucleotides, that store information. There are only four types of bases for this coding. DNA molecules are composed of two strands that twist together in a spiral manner. The strands consist of a sugar phosphate backbone to which the bases are attached. Each strand consists of four types of nucleotides that are the same except for one component, a nitrogen-containing base. The four bases are adenine, guanine, thymine, and cytosine. These are generally referred to as A, G, T, and C. To give you some sense of size, each full twist of the DNA double helix is 3.4 nanometers (i.e., one billionth of a meter). Said in other terms, if we took the DNA in the 46 chromosomes of a single human cell and stretched it out, it would be around 6 feet long. This measurement gives you some idea of the thinness of DNA.

DNA, which is the information storage molecule, transfers information to RNA, which is the information transfer molecule, to produce a particular protein. Further, change in the rate at which RNA is transcribed controls the rate at which genes produce proteins. The expression rate of different genes in the same genome may vary from 0 to approximately 100,000 proteins per second. Thus, not only do genes produce proteins, but they also do so at different rates. The crucial question becomes what causes a gene to turn on or off.

Genome is the name given to the complete set of genes in a given cell. The Human Genome Project was started in 1990 by the United States with the goal of mapping all the genes of the human body. It was an international project that was declared complete in 2003. The estimation at that time was that there are approximately 20,500 genes in a human cell.

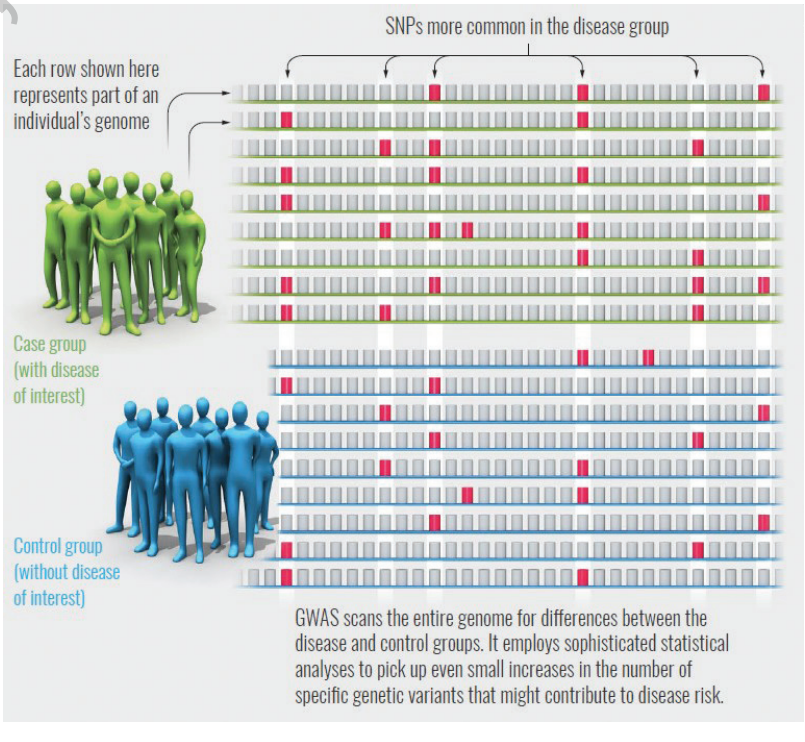
One current way to understand the relationship between genes and mental illness is to examine the effects of many genes on psychological processes. Current research suggests that the high heritability of mental disorders is related to many genetic differences, each having a small effect (Plomin, 2018). This approach has been referred to as genome-wide association (GWA) studies (Breen et al., 2016). Researchers go through hundreds or thousands of changes in DNA called single-nucleotide polymorphisms (SNPs, pronounced "snips"). Each of us has about 4 million SNPs, but we all do not have the same 4 million. As shown in *Figure 2.26,* the task is to find similar SNPs in those with a particular disorder as compared to a control group. These studies have been applied to psychological disorders and involve researchers from over 40 countries (Breen et al., 2016; Sullivan et al., 2018). A catalog of these studies is available at www.ebi.ac.uk/gwas/.

How Do Genes Influence Behavior?

In terms of behavior and experience, the production of proteins can be transitory. For example, touching a cat's whiskers causes changes in gene expression in the cells of the sensory cortex of the brain (Mack & Mack, 1992). This is just a momentary change. Changes can also be long term. Turning on one set of genes may have lasting influence on the ability of other

FIGURE 2.26 SNPs in those with a disorder as compared to a control group in a genome-wide association study.

Source: Balter, M. (2017, May). Schizophrenia's Unyielding Mysteries. *Scientific American.*



When a songbird first hears the specific song of its species, a particular set of genes comes into play, which, once set, determines the song produced by that bird for its entire life.

genes to produce specific proteins. For example, when a songbird first hears the specific song of its species, a particular set of genes comes into play, which, once set, determines the song produced by that bird for its entire life. This process has been mapped by a number of researchers (see, for example, Mello, Vicario, & Clayton, 1992; Ribeiro & Mello, 2000). Likewise, raising mice in an enriched environment—that is, one with lots of toys and stimulation—will cause increased gene expression in genes that are associated with learning and memory (Rampon et al., 2000).

How do we know which genes are involved? In the Rampon et al. (2000) study, the genes of mice in enriched environments were compared with those of control mice who did not have this experience. Another way to know which genes are involved in a process is to actually change the genes in a particular organism. So-called knockout mice are genetically engineered to have particular genes turned off by breeding them in specific ways. Research shows that simple genetic changes made experimentally in animals can result in protein changes that influence social behavior. Some examples of such behaviors are increased fear and anxiety, increased grooming, hyperactivity, and even increased alcohol consumption when stressed.

EPIGENETIC PROCESSES

One basic idea from Mendelian genetics was that genes are not changed by experience. What is passed on, except in the case of damage to the gene, is exactly the same gene that was received by the organism from its parents. This came to be called the central dogma of molecular biology as described by Francis Crick. He basically stated that information flow was one-directional. That is, it went from the gene to the protein. What came to be called reverse translation was seen as impossible. Thus, the gene could not be influenced or changed by changes in proteins. This was the basic view from the 1950s until very recently.

As researchers became interested in how genes turn on and off and what factors influence this, it became apparent that the story was more complicated. It was discovered that the processes that determine which genes turn on and off could themselves be passed on to the next generation. Of course, which factors turn the genes on and off are largely influenced by the environment of the organism. Thus, although DNA itself could not be influenced by the environment, it was possible for the environment to influence future generations through its changes to those processes that turn genes on and off.

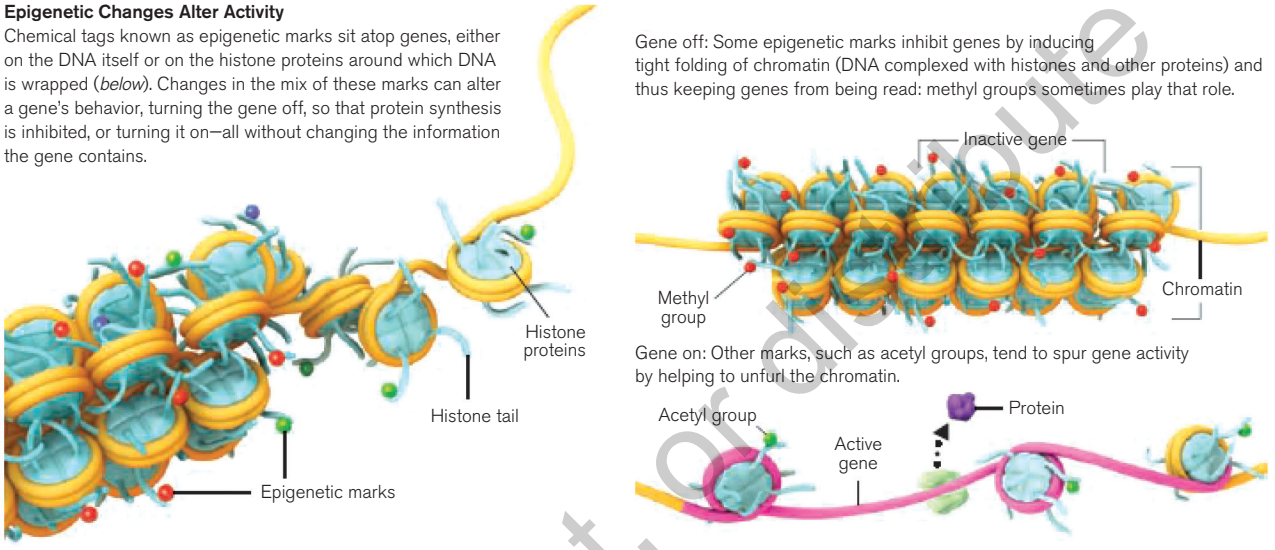
This possibility of another form of inheritance came to be called **epigenetic inheritance** (Hallgrímsson & Hall, 2011; Nestler, 2011). Instead of actually changing the gene itself, epigenetic modifications *mark* a gene. This alters how it is turned on and off. Briefly, DNA is wrapped around clusters of proteins called histones. These are further bundled into structures called chromosomes. Being tightly packed keeps genes in an inactive state by preventing access to processes that turn genes on. When action is needed, a section of DNA unfurls and the gene turns on. Whether a segment is relaxed and able to be activated or condensed resulting in no action is influenced by **epigenetic marks or tags** (see *Figure 2.27*). As a tag, histone acetylation tends to promote gene activity and is called a *writer*. Histone methylation and DNA methylation tend to inhibit it and are called *erasers*.

The environment can influence these writer and eraser tags. Tags help an organism respond to a changing environment. Some tags last a short time, whereas others can last a lifetime. In a now classic study, researchers observed that some rat mothers displayed high levels of nurturing behavior, licking and grooming their pups, while others were less diligent (Weaver et al., 2004). Behaviorally, the offspring of the more active mothers were less anxious

FIGURE 2.27 Epigenetic Changes Alter Gene Activity

Genes can be turned on or turned off. Being tightly packed keeps genes in an inactive state by preventing access to processes that turn genes on. When action is needed, a section of DNA unfurls and the gene turns on. Whether a segment is relaxed and able to be activated or condensed resulting in no action is influenced by epigenetic marks or tags.

Source: Nestler (2011).



and produced less stress hormone when disturbed than pups cared for by more passive mothers. Further, the females raised by nurturing mothers became nurturing mothers themselves.

The intriguing part of this study was that the offspring of the rat mothers who showed more licking and grooming differed in epigenetic factors. Pups raised by passive mothers showed more DNA methylation than aggressively groomed pups in the regulatory sequences of a gene encoding the glucocorticoid receptor, which is a protein present in most cells in the body that mediates an animal's response to the stress hormone cortisol. This excessive methylation was detected in the hippocampus, a brain region involved in learning and memory, and this causes nerve cells to make less of the receptor. Activation of the glucocorticoid receptor in the hippocampus actually signals the body to slow production of cortisol. The epigenetic reduction in receptor number exacerbated the stress response in the animals. This made the animals more anxious and fearful. Further, these traits persisted throughout their lifetime. Overall, attentive mothers cause the methyl marks to be removed. Inattentive mothers, on the other hand, cause methyl marks to be added. Thus, rats inherit certain behaviors based on experience. The genes had not changed, but the tags had.

In a classic study, rat pups raised by actively nurturing mothers versus more passive mothers differed in epigenetic factors.

Photo by Seweryn Olkowicz, Wikipedia

At this point, a variety of studies have shown other examples of epigenetic mechanisms at work. For example, the diet of a mouse mother before conception can influence the hair color of her infants and even her infants' infants (e.g., Cropley, Suter, Beckman, & Martin, 2006). One interesting aspect of this research

is the suggestion that a mother's diet can influence future generations, independent of later changes in diet.

Fathers can also influence their offspring. It has been shown that a mouse will develop a diabetes-like disease if her father's diet before her conception was high in fat (M. Skinner, 2010). Also, if a mouse father is overweight, then gene activity in the pancreas of his offspring will be abnormal (Ng et al., 2010). Since the pancreas makes insulin, which regulates blood sugar, this may set up the possibility of future diabetes. The opposite is also the case. If the father's diet results in an underweight condition, then genes in the liver associated with fat and cholesterol synthesis were shown to be more active in his offspring (Carone et al., 2010). Another study suggested that whether a human father smoked early in life was associated with his sons being heavier in weight at age 9 (Pembrey et al., 2006).

Overall, this type of research implies that behavior and environmental experiences at critical periods could later influence characteristics for future generations. Current health research related to such disorders as diabetes and cancer, as well as types of psychopathology, is suggestive of such a relationship (see Katsnelson, 2010; van Os, 2010, for overviews). Both addiction and depression have been shown to have an epigenetic component (Nestler, 2011). Thus, epigenetic inheritance, which involves tags or marks that determine when genes are turned off or on, offers a parallel track to traditional Mendelian inheritance for influencing phenotypes. Further, a new area of research uses identical twins to study specific epigenetic mechanisms with the goal of determining how genetic and environmental factors influence epigenetics (e.g., J. T. Bell & Spector, 2011). This approach may offer better insight into the expression of complex traits as seen in both normal and psychopathological processes.

MITOCHONDRIA AND MITOCHONDRIAL INHERITANCE

Mitochondria are structures within a cell that are involved in the production of energy. It is assumed that mitochondria descended from bacteria that began to live inside single-celled organisms more than a billion years ago. As such, mitochondria have their own DNA (see next paragraph), which contains 13 coding genes with about 16,000 base pairs. Thus, a given cell in your body contains both the nuclear DNA and mitochondria and their DNA.

What is interesting is that generally **mitochondrial DNA (mtDNA)** is inherited only from the mother, clearly a violation of Mendelian inheritance. Because mtDNA does not recombine sections of DNA from the mother and father, it is very stable and mutates slowly. This gives mtDNA a special application in the study of evolution. It has helped researchers to discover the genetic link in certain disorders that show maternal or **mitochondrial inheritance** patterns, such as Leber's hereditary optic neuropathy, a disorder that results in rapid loss of vision beginning in adolescence.

Evidence is also accumulating that mitochondrial dysfunction is involved in specific mental disorders (Regenold et al., 2009; Rossignol & Frye, 2012). This is referred to as the *mitochondrial dysfunction hypothesis*. Mitochondrial dysfunction has been identified using a number of different techniques. One technique is to identify structural changes in mitochondria. A second is to examine the manner in which the mitochondrially related genes produce proteins. A third is the use of metabolic studies. Since mitochondria are involved with energy production, it is possible to measure glucose concentration in cerebrospinal fluid. These studies have shown differences in mitochondrial functioning in individuals with bipolar disorder, schizophrenia, and autism spectrum disorders as compared to healthy controls.

What Are Endophenotypes?

In a move to go beyond using only the signs and symptoms of psychopathology, there has been a search for stable internal physiological or psychological markers that underlie a disorder (Gottesman & Hanson, 2005; Gottesman & Shields, 1972; Insel & Cuthbert, 2009; G. Miller & Rockstroh, 2013). Such markers have been called *endophenotypes*. **Endophenotypes** are patterns of processes that lie between the gene (the genotype) and the

manifestations of the gene in the external environment (the phenotype). Unlike symptoms that can be observed, endophenotypes cannot be seen except with special equipment and computational analysis such as brain imaging procedures or patterns of performance on neuropsychological tests. For example, individuals with a given disorder may show certain types of electroencephalogram (EEG) responses to particular stimuli or a certain pattern of brain activity that is different from that seen in healthy individuals. Those with autism have been shown to have fewer connections between brain areas than siblings or controls, and this is seen as an endophenotype (Moseley et al., 2015).

Like genes, the presence of the endophenotype does not necessarily mean that the disorder itself will be present. For example, a specific endophenotype may be seen in both a person with schizophrenia and his or her first-degree relatives, although the relatives themselves do not have schizophrenia. As such, an endophenotype can help to identify the systems involved in a particular disorder as well as note which genes are influenced by environmental and other internal factors related to a disorder. The potential of endophenotypes is their ability to better articulate the relationship between genetic and environmental factors in the development of psychopathology and to clarify which processes are influenced. In Chapter 4, you will learn about a National Institute of Mental Health (NIMH)–supported diagnostic approach based on endophenotypes, the Research Domain Criteria (RDoC).

CONCEPT CHECK

- What are the two important principles of Mendelian genetics? What evidence led Mendel to their discovery?
- What do genes do, and how and where do they do it? What are the roles of DNA and RNA in that process?
- How do we know that genes change behavior? What kinds of research have been done with animals to identify the specific genes involved?
- What is epigenetic inheritance? How does it work?
- What is an endophenotype, and how does it relate to psychopathology?

Evolution and Psychopathology

Thus far, we have considered brain changes and genes turning off and on. These events are typically short term and can change quickly. Moving to the evolutionary perspective, we will look at a longer time frame in which environmental factors influence the genes that are passed on to the next generation. Let's begin with the major themes of evolution and then consider psychopathology from an evolutionary perspective.

The Themes of Evolution

One of the main themes of evolution is the manner in which organisms are in close connection with their environment. It is this close connection that allows for change to take place, including the turning on and off of genetic processes. In humans, there is another layer of complexity involved in the process. Part of this complexity comes from the fact that humans are born less fully developed at birth than many other species and thus are sensitive to changes in their environment as they continue to develop. This includes our relationships with our family and others with whom we initially come in contact. As humans, we also develop societal and cultural perspectives. These perspectives become the backdrop of our environment. Unlike animals that live within nature, we as humans largely live within the backdrop of our culture. Thus, we are influenced by our culture and pay close attention to it.

Human infants are helpless at birth.
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Many species are able to function on their own shortly after birth.
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Another part of our complexity as humans is our ability to reflect on ourselves and our world. In this way, a layer of thought can be injected between the person and the environment. This allows for expectation and imagination to play a role in human behavior and experience. Some have even suggested that humans may be the only species to imagine the world and themselves differently from how they appear. In this sense, our inner world of thoughts and feelings becomes another environment in which we live. For example, you can tell yourself you are wonderful or you are stupid, and there is no one inside you to dispute this. One positive aspect of this is that your inner world allows you to plan future actions and reflect on past ones, but it can also be experienced as distress when your internal thoughts reflect such states as anxiety or hopelessness. Our internal thoughts at times may lead to interpretations of the environment or ourselves that may not be productive. This adaptive human ability to reflect, which should lead to successful survival, sexuality, and social relations, sometimes leads instead to interactions that reduce the close connection between the individual and his or her internal and external environment. As we will see, this lack of connectedness lies at the heart of psychopathology.

As noted in Chapter 1, humans not only consider themselves but also consider others. A positive side of this is the ability to understand the internal experiences of another. This allows us to experience empathy. We can also consider how we appear to others and other questions of self-image. One aspect of this is related to sexual processes. That is, we can say or do things that make us more attractive to a potential mate. In terms of self-preservation, humans also have a personal history that allows each individual to learn from the past and develop strategies for living. These strategies tend to protect us and may even have saved our lives in exceptional cases. However, it is also possible for the strategies that work in one environmental situation not to work in another. When a person loses contact with the current environment and applies strategies that worked perhaps in an earlier time, then unsuccessful adaptation is the result.

This lack of connectedness to our environment may take place on both an external and an internal level. On an external level, the person finds herself different from the group or even seeks to be separate from others. This is not our historical experience, since individual

humans have never lived in isolation. As a species, we have always lived in close contact with other humans, which has led to the development of societies and cultures. In fact, many of the specific abilities of humans are geared to social interactions on a variety of levels. When they no longer have the connection with the group, many individuals experience a sense of loss. This loss typically carries with it the experience of negative affect and depression and often a need to withdraw from contact with others and even themselves. On an internal level, humans frequently have the need to explain to themselves the events that have just occurred, which may include anger, distorted perceptions, or a genuine plan for recovery. The extreme cases we refer to as psychopathology.

Psychopathology From an Evolutionary Perspective

Psychopathology from an evolutionary perspective goes beyond the traditional psychological and physiological considerations. Considering the evolutionary perspective, we ask additional questions. One question might be, how long in terms of our human history has a particular psychopathological disorder existed? As noted in Chapter 1, a WHO study examined the presence of schizophrenia in a number of countries with very different racial and cultural backgrounds (Sartorius et al., 1986). What these authors found was that despite the different cultural and racial backgrounds surveyed, the experience of schizophrenia was remarkably similar across countries. Likewise, the risk of developing schizophrenia was similar in terms of total population presence (about 1%). Further, the disorder had a similar time course in its occurrence, with its characteristics first being seen in young adults.

If you put these facts together, it suggests that schizophrenia is a disorder that has always been part of the human experience. Because it is found throughout the world in strikingly similar ways, this suggests that it existed before humans migrated out of Africa. The genes related to schizophrenia were carried by early humans who migrated from Africa, and thus, its presence is equally likely throughout the world. Given these estimates as to the history of the disorder, one might ask why schizophrenia continues to exist. We know, for example, that individuals with schizophrenia tend to have fewer children than individuals without the disorder. Fewer children with these genes would over time lead to even fewer children with the genes. Thus, we might assume that schizophrenia would have disappeared over evolutionary time in that it reduces reproductive success and has a genetic component. However, this is not the case.

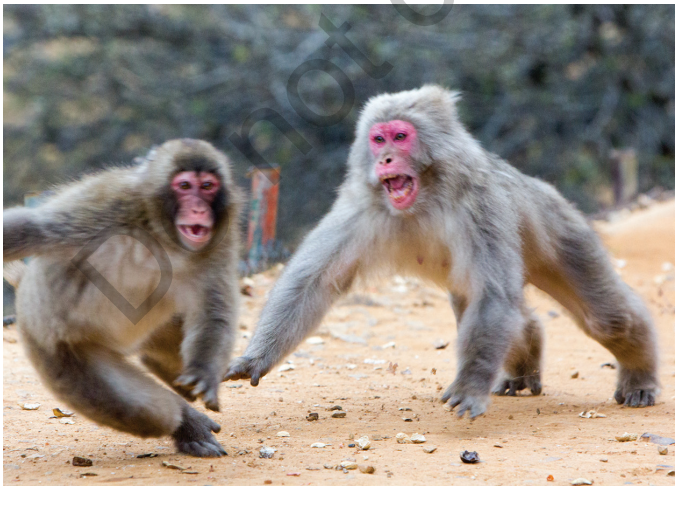
This creates a mystery for evolutionary psychologists to solve. To answer this question, we can draw on many considerations. Perhaps, in the same way that sickle-cell anemia is associated with a protection against malaria, schizophrenia protects the person from another disorder. Or perhaps, like the reaction of rats to stress, which results in depression-like symptoms, the symptoms seen in schizophrenia are the result of a long chain of stressful events in which the organism breaks down in its ability to function. Psychopathology could even go in a more positive direction and be associated with creative and nontraditional views of the world. For example, there are a number of accounts that have noted greater creativity in families of individuals with schizophrenia, which may have a genetic connection (Power et al., 2015).

The evolutionary perspective helps us ask such questions as what function a disorder might serve as well as how it came about. In the same way that pain can be seen as a warning system to the body to protect it from tissue damage, anxiety may have evolved to protect the person from other types of potential threats. For example, many of the outward expressions of social anxiety parallel what is seen in dominance interactions in primates. Submissive monkeys avoid contact with most dominant ones in much the way that human individuals experiencing social anxiety avoid dominant members of their group. This suggests the possibility that anxiety may have its evolutionary origins in dominance structures. If this were the case, then we might expect to see some relationship to sexual instinctual processes—as is the case with dominance. The evolutionary perspective also helps us think about what might be solutions to how psychopathology should be treated. As touched on in Chapter 1, these are some of the questions that will be discussed in this book.

One perspective of the evolutionary approach has been to redirect psychology back to the basic processes of human existence such as survival, sexual processes, and social behavior. We can then ask what types of disorders are found within each broad category. We can also consider the developmental and social processes and ask how these processes may be involved in psychopathology. Thinking in these terms, we may come to discover that disorders that have very similar end states may have developed from distinct beginning conditions. Depression, for example, can result from extreme stress that brings forth self-preservation instincts. Depression can also result from the loss of significant people in one's life. Further, loss of social status is also associated with depression. Thus, what appear to be similar symptoms may have been produced by separate and distinct trajectories.

Another psychopathology that has been approached from an evolutionary perspective is the category of personality disorders. Personality disorders reflect a rigid approach to dealing with social relationships. Two commonly discussed personality disorders are antisocial personal disorder (also known as psychopathic personality) and histrionic personality disorder. Psychopaths are described as manipulative, callous, dishonest, and self-centered. They are antisocial in the sense that they display no need to follow the traditional rules of a society and little remorse or guilt for their actions. For example, they would contract and collect money for a job they had no intention of doing. They would clearly qualify as those whom evolutionary psychologists refer to as cheaters. On the other hand, individuals with a histrionic personality disorder overly seek the attention of others and are very emotional in their reactions. They can be manipulative in their interpersonal relationships.

Harpending and Sobus (1987) suggested that the psychopathic and the histrionic personality styles represent different adaptive strategies in relation to sexuality. Both of these personality types were viewed by Harpending and Sobus as cheaters. Given that it is more common to see male psychopaths and female hysterics, these researchers suggest that this results from different reproductive strategies. A male cheater in a sexual relationship should be able to persuade a female to copulate with him while deceiving her about his commitment to her and his willingness to offer resources for the offspring. A female cheater, on the other hand, would exaggerate her need for the male and make herself appear helpless and in need so that he would give her additional attention and resources. She would also be willing to put her own needs ahead of those of her offspring, even to the extent of abandoning them. The work of Harpending and Sobus shows how evolutionary thinking can help to explain possible motivational factors of a particular disorder as well as the demonstrated gender differences.



Submissive monkeys avoid contact with dominant ones, just as humans experiencing social anxiety avoid dominant members of their group.

Let's look at another well-studied process—sleep—as a model for thinking about psychopathology. Since sleep disturbance is often associated with a variety of psychopathological disorders, this will let us consider how normal processes may be influenced to appear pathological. Most people would like to go to sleep when they want to and not be awakened during the night. However, evolution is not always about what makes us feel good. The critical question from an evolutionary perspective is what function sleep plays. In considering this question, we can look at sleep as a model for how we might approach other basic psychological processes.

One initial question to ask is this: Has sleep been shaped by natural selection? Some researchers answer yes to this question (Nesse & Williams, 1994). They offer at least five reasons for why this is so. First, sleep is found in a variety of organisms and is perhaps universal among vertebrates. However, not all animals sleep in the same way. Elephants and cows spend

most of their sleep time standing up. Dolphins sleep with one half of their brain, while the other half remains awake. Second, all vertebrates share similar mechanisms that control sleep and dreaming. These mechanisms are found in the more primitive areas of the brain. Third, the pattern of sleep seen in mammals with periods of rapid eye movement and faster EEG activity within the sleep period is also seen in birds. Since the evolution of birds went down a different pathway before the time of dinosaurs, this suggests that sleep is a very primitive and basic mechanism. Fourth, in examining the sleep patterns across species, there appears to be support for the idea that these patterns adapted to match the ecological niche of that particular animal. Fifth and finally, all animals show deficits in response to a lack of sleep. Currently, a variety of researchers are seeking to determine the function of sleep. The best evidence suggests that it allows for restoration of certain physiological processes. There is also evidence that sleep consolidates information learned during waking hours. One conceptual idea is that, given the light–dark cycle produced by the earth's rotation around the sun, sleep developed as a protective mechanism, since it is more dangerous to be out alone at night.

In summary, we can ask critical questions concerning psychopathology that relate to other evolutionary processes:

1. We can ask if the experience of mental illness is universal. If it were not universal, then it would be difficult to argue that we should study psychopathology from an evolutionary perspective. If it is a universal process such as emotionality or language, then we can begin to ask about the nature of mental illness and how its existence fits into our history as humans.
2. We can ask if there is an adaptive value to the behaviors and experiences displayed in psychopathology. It is easy to see that there is a value in not trusting what someone tells you some of the time, but is there any adaptive value in not trusting what anyone tells you all of the time or to think that everyone is always out to get you?
3. We can look for evidence of psychopathology across human history. This includes the question of whether we see signs of psychopathology in nonhuman species.
4. We can seek to understand the nature of psychopathology. That is to say, should we consider psychopathology to be qualitatively different from normal functioning, or is it the situation in which normal processes have been taken to the extreme? We know, for example, that allergic reactions are situations in which our immune system is overreactive. We also know that fever is the process by which body temperature is raised to fight infection. However, the fever uses energy and can damage the body.
5. We can ask if it is protective in some manner. Like carrying the trait for sickle-cell anemia, does having schizophrenia or depression, for example, make you less likely to experience another disorder?
6. We can ask if psychopathology is a recent process. That is, should we consider psychopathology as the result of a mental system that evolved in the Stone Age and is interacting with a high-paced modern environment? For example, aggression in teenage gangs may reflect behaviors that were adaptive in previous times but are no longer adaptive for society today.

These questions are not mutually exclusive. As you will see, they also represent some of the ways scientists and others have sought to understand psychopathology. From an evolutionary perspective, the study of psychopathology begins with the three instincts of survival, sexuality, and socialness. From this perspective, psychopathology becomes a disturbance of these instinctual processes. Throughout this text, considerations of how certain evolutionary processes might contribute to psychological disorders will be discussed.

CONCEPT CHECK

- One of the main themes of evolution is the manner in which organisms are in close connection with their environment. Animals live in nature, but for humans there is another layer of complexity. Describe three uniquely human characteristics that impact our connectedness to our environment. What role do they play in psychopathology?
- What are the six critical questions an evolutionary perspective asks concerning psychopathology?

SUMMARY

The basic element of the brain is the neuron that is connected to other neurons. Since the human brain has been estimated to contain 86 billion neurons and more than 100,000 kilometers of interconnections, scientists have analyzed them in the context of networks. Three specific networks have been examined relating to psychopathology: the default network (also called the intrinsic network), the central executive network, and the salience network. Psychopathological disorders have been shown to have problems in turning networks on or off as well as problems in the connections within the network itself.

Scientists have been able to use the manner in which neurons work as a window into their function. A variety of techniques for observing activity in the brain have been developed. Currently, the major types of brain imaging techniques are EEG, MEG, PET, and fMRI. There are a number of trade-offs that researchers and clinicians must consider when choosing a brain imaging technique. It begins with the research or clinical question one is asking, which determines whether the appropriate measure is one of structure (spatial resolution) or how fast a process can be measured (temporal resolution). With the opening of this window into individuals' internal processes, the new field of neuroethics has started asking questions concerning who should have access to that information.

Genes form the blueprint that determines what an organism is to become. They are found on chromosomes in every cell of the body. Within each gene, DNA (the information storage molecule) transfers information to RNA (the information transfer molecule) to produce a particular protein. The location of the genes in the body makes a difference in that cells in the brain produce different proteins from those in the muscles, liver, or heart. A gene is turned on (produces the protein) or turned off (does not produce the protein) relative to specific events.

The basis of evolution is genetic variations that occur in response to the environment and that can be inherited and passed on to future generations. The study of genetics began in the 1800s with the work of Gregor Mendel, who established the initial principles of genetic inheritance. Subsequent research has added complexity to that initial conceptualization. Mitochondrial inheritance, for example, has been found to involve the mtDNA that generally is inherited only from the mother. Epigenetic inheritance is based on the fact that the processes that determine which genes turn on and off can be passed on to the next generation. Thus, although DNA itself could not be influenced by the environment, it is possible for the environment to influence future generations through its changes to those processes that turn genes on and off. Given this complexity, it is no wonder the original hope of finding a few genes that were involved in particular mental disorders has not panned out. Currently, one promising focus of research has been to identify endophenotypes—patterns of processes lying between the gene (the genotype) and the manifestations of the gene in the external environment (the phenotype)—for particular psychological disorders.

One of the main themes of evolution is the manner in which organisms are in close connection with their environment. It is this close connection that allows for change to take place, including the turning on and off of genetic processes. In humans, there is another layer of complexity involved in the process. Part of this complexity comes from the fact that humans are born less fully developed at birth than many other species and thus are sensitive to changes in their environment as they continue to develop. Unlike animals that live within nature, we as humans largely live within the backdrop of our culture. Another part of our complexity as humans is our ability to reflect on ourselves and our world. In this way, a layer of thought can be injected between the person and the environment. This allows for expectation and imagination to play a role in human behavior and experience. This lack of connectedness to our environment may take place on both an external and an internal level.

From an evolutionary perspective, the study of psychopathology begins with the three instincts of survival, sexuality, and socialness. From this perspective, psychopathology

becomes a disturbance of these instinctual processes. The evolutionary perspective goes beyond the traditional psychological and physiological considerations and asks some critical questions concerning psychopathology. First, is the experience of mental illness universal? Second, is there an adaptive value to the behaviors and experiences displayed in psychopathology? Third, can we see evidence of psychopathology across human history as well as in nonhuman species? Fourth, what is the nature of psychopathology—is it qualitatively different from normal functioning, or have normal processes been taken to the extreme? Fifth, is psychopathology protective in some manner? Sixth, is psychopathology a recent process—a result of a mental system designed in prehistory interacting with a thoroughly modern environment?

STUDY RESOURCES

REVIEW QUESTIONS

1. What are genotypes, phenotypes, and endophenotypes? How are these three concepts used in understanding the development of psychopathology?
2. This chapter states that there is a complicated relationship between genetic conditions and environmental factors. How are these two concepts involved in the development and maintenance of psychopathology? How is it made even more complex by epigenetic processes?
3. How have the discoveries of epigenetic inheritance and mitochondrial inheritance enriched our understanding and added to the complexity of Mendel's initial theory of genetic inheritance?
4. How does the small world framework from social science help us understand how neurons are connected in a network? What implications does this have for the transmission of information within a network and across networks?
5. Historically, those interested in neuroscience research have focused more on the universality of human processing rather than the diversity found in different cultures. What evidence can you present to show that culture creates diversity in human psychological processing?

FOR FURTHER READING

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