Chapter 49

Nervous Systems

Lecture Outline

Overview: Command and Control System

- The human brain contains an estimated 10^{11} (100 billion) neurons**.**
  - Enormously complex circuits interconnect these brain cells.
- A recent technology expresses random combinations of colored proteins in brain cells.
  - The result is a "brainbow" in which each neuron expresses one of more than 90 different color combinations of four fluorescent proteins.
  - Using this technology, neuroscientists hope to develop detailed maps of the connections that transfer information between particular regions of the brain.
- Powerful imaging techniques reveal activity in the working brain.
  - Researchers monitor areas of the human brain while a subject is performing various tasks and look for a correlation between a particular task and activity in specific brain areas.

Concept 49.1 Nervous systems consist of circuits of neurons and supporting cells

- The ability to sense and react originated billions of years ago with prokaryotes that could detect changes in their environment and respond in ways that enhanced their survival and reproductive success.
- Bacteria continue moving in a particular direction as long as they encounter increasing concentrations of a food source.
  - Modification of simple recognition and response processes provided multicellular organisms with a mechanism for communication between cells of the body.
  - By the time of the Cambrian explosion, systems of neurons that allowed animals to sense and move rapidly were present in essentially their current forms.
- In most animals with nervous systems, clusters of neurons perform specialized functions.
- Such clustering is absent in the cnidarians, the simplest animals with nervous systems.
  - In cnidarians, a series of interconnected nerve cells form a diffuse **nerve net** that controls the contraction and expansion of the gastrovascular cavity.
- In more complex animals, the axons of multiple nerve cells may be bundled to form **nerves**.
  - Nerves channel and organize information that flows along specific routes through the nervous system.
- Sea stars have a set of radial nerves connecting to a central nerve ring**.**
  - Within each arm, the radial nerve is linked to a nerve net from which it receives input and to which it sends signals controlling motor activity.
- Animals with bilaterally symmetrical bodies have more specialized nervous systems.

- Such animals exhibit cephalization, the clustering of sensory neurons and interneurons at the anterior end.
- Anterior neurons communicate with cells elsewhere in the body including neurons in one or more nerve cords extending toward the posterior.

- In nonsegmented worms like the planarian, a small brain and longitudinal nerve cords make up the simplest clearly defined *central nervous system (CNS)*.
- The entire nervous system of such animals can be constructed from a small number of cells.
    - In the nematode *Caenorhabditis elegans*, an adult worm contains exactly 302 neurons.
- More complex invertebrates, such as annelids and arthropods, have many more neurons.
    - Behavior is regulated by complicated brains and ventral nerve cords containing ganglia, segmentally arranged clusters of neurons.
- Within an animal group, nervous system organization often correlates with lifestyle.
    - Sessile and slow-moving molluscs, such as clams and chitons, have relatively simple sense organs and little or no cephalization.
    - Active predatory molluscs, such as octopuses and squids, have the most sophisticated nervous systems of any invertebrate.
- In vertebrates, the brain and the spinal cord form the CNS; the nerves and ganglia make up the *peripheral nervous system (PNS)*.
    - Regional specialization is a hallmark of both systems.

The brain and spinal cord of the vertebrate CNS are tightly coordinated.

- The brain integrates the complex behavior of vertebrates.
- The spinal cord conveys information to and from the brain and generates basic patterns of locomotion.
- The spinal cord acts independently as part of the simple nerve circuits that produce **reflexes**, the body's automatic responses to stimuli.
    - A reflex protects the body by triggering a rapid, involuntary response to a particular stimulus, such as pulling your hand away from a hot stove.
- In vertebrates, the spinal cord runs along the dorsal side of the body.
    - Segmental organization is apparent in the arrangement of neurons within the spinal cord and segmental ganglia just outside the spinal cord.
- The brain and spinal cord of vertebrates derive from the chordate characteristic of a hollow dorsal embryonic nerve cord.
- The cavity of the nerve cord forms the narrow **central canal** of the spinal cord and the **ventricles** of the brain.
- Both are filled with **cerebrospinal fluid**, formed in the brain by filtration of arterial blood.
    - Cerebrospinal fluid circulates slowly through the central canal and the ventricles and then drains into the veins, bringing nutrients and hormones to the brain and clearing wastes.
    - In mammals, the cerebrospinal fluid cushions the brain and spinal cord by circulating between layers of connective tissue that surround the CNS.
- As well as fluid-filled spaces, the brain and the spinal cord contain gray and white matter.
    - **Gray matter** consists of mainly neuron cell bodies, dendrites, and unmyelinated axons.
    - **White matter** contains bundled axons with myelin sheaths, making them whitish.

- White matter is on the outside of the spinal cord, linking the CNS to the sensory and motor neurons of the PNS.
- White matter in the brain is on the inside, signaling between neurons in learning, emotion, processing of sensory information, and generating commands.

A variety of glia are present throughout the vertebrate brain and spinal cord.

- The major types of glia nourish, support and regulate neurons.
  - Ependymal cells line the ventricles and have cilia that circulate cerebrospinal fluid.
  - Microglia protect the nervous system from invading microorganisms.
  - Oligodendrocytes and Schwann cells function in axon myelination, a critical activity in the vertebrate nervous system.
- **Astrocytes** have the most diverse set of functions: They provide structural support for neurons and regulate the extracellular concentrations of ions and neurotransmitters.
  - Astrocytes facilitate information transfer at synapses and, in some instances, releasing neurotransmitters.
  - Those adjacent to active neurons cause nearby blood vessels to dilate, increasing blood flow to the area and enabling the neurons to obtain oxygen and glucose more quickly.
- Glia play an essential role in development of the nervous system.
  - *Radial glia* form tracks along which newly formed neurons migrate from the neural tube, the structure that gives rise to the CNS.
  - Astrocytes induce cells that line the capillaries in the CNS to form tight junctions.
  - The result is the *blood-brain barrier*, which controls the extracellular enironment of the CNS by restricting the entry of substances from the blood.
- Radial glia and astrocytes can also act as stem cells, generating neurons and additional glia to replace neurons and glia that are lost to injury or disease.

The PNS transmits information to and from the CNS and regulates a vertebrate's movement and internal environment.

- Sensory information reaches the CNS along *afferent* PNS neurons.
- After information is processed within the CNS, instructions travel to muscles, glands, and endocrine cells along *efferent* PNS neurons.
  - Most nerves contain both afferent and efferent neurons.
  - One exception is the olfactory nerve, which conveys sensory information from the nose to the brain.
- The PNS has two efferent components: the motor system and the autonomic nervous system.
- The **motor system** consists of neurons that carry signals to skeletal muscles.
  - Control of skeletal muscles can be voluntary, as when you raise your hand to ask a question, or involuntary, as in the knee-jerk reflex controlled by the spinal cord.
- Regulation of smooth and cardiac muscles by the **autonomic nervous system** is involuntary.
  - The three divisions of the autonomic nervous system—sympathetic, parasympathetic, and enteric—control the organs of the digestive, cardiovascular, excretory, and endocrine systems.
- The sympathetic and parasympathetic divisions function antagonistically in regulating organ function.
- The **sympathetic division** is responsible for arousal and energy generation.

- In the fight-or-flight response, the heart beats faster, the liver converts glycogen to glucose, digestion is inhibited, and secretion of epinephrine from the adrenal medulla is stimulated.

- Activation of the **parasympathetic division** causes opposite responses that promote calming and a return to self-maintenance functions (“rest and digest”).
  - Increased activity in the parasympathetic division lowers heart rate, increases glycogen production, and enhances digestion.
- The **enteric division** consists of networks of neurons in the digestive tract, pancreas, and gallbladder that regulate secretion and peristalsis.
  - The sympathetic and parasympathetic divisions normally regulate the enteric division.
- The somatic and autonomic nervous systems cooperate to maintain homeostasis.
  - If body temperature drops, the hypothalamus signals the autonomic nervous system to constrict surface blood vessels, reducing heat loss.
  - At the same time, the hypothalamus signals the somatic nervous system to cause shivering, increasing heat production.

Concept 49.2 The vertebrate brain is regionally specialized

- The human cerebrum is responsible for many activities we commonly associate with the brain, such as calculation, contemplation, and memory.
  - Underneath the cerebrum are additional brain structures with important activities, including homeostasis, coordination, and information transfer.

The brainstem and cerebrum control arousal and sleep.

- Transitions between alertness, drowsiness, and sleep are regulated by the brainstem and cerebrum.
  - Arousal is a state of awareness of the external world.
  - Sleep is a state in which external stimuli are received but not consciously perceived.
- Sleep is an active state for the brain.
  - Electroencephalogram (EEG) recordings show that brain wave frequencies change as the brain progresses through distinct stages of sleep.
- Although sleep is essential for survival, we know very little about its function.
  - One hypothesis is that sleep and dreams are involved in consolidating learning and memory.
  - Experiments show that regions of the brain activated during a learning task can become active again during sleep.
- Arousal and sleep are controlled in part by the **reticular formation**, a diffuse network of neurons in the core of the brainstem.
  - Acting as a sensory filter, the reticular formation determines which incoming information reaches the cerebrum.
  - The more information the cerebrum receives, the more alert and aware a person is, although the brain ignores certain stimuli while actively processing other inputs.
- Besides the diffuse reticular formation, specific parts of the brainstem also regulate sleep and wakefulness: The pons and medulla contain centers that cause sleep when stimulated, and the midbrain has a center that causes arousal.
- All birds and mammals show characteristic sleep/wake cycles.

- Melatonin, a hormone produced by the pineal gland, plays an important role in these cycles.

- Some animals display evolutionary adaptations that allow for substantial activity during sleep.
  - Bottlenose dolphins swim while sleeping, rising to the surface to breathe air on a regular basis.
  - In fact, dolphins do sleep with one brain hemisphere at a time.

Circadian rhythms rely on a biological clock.

- Circadian rhythms are daily cycles of biological activity that occur in organisms ranging from bacteria to fungi, plants, insects, birds, and humans.
- Circadian rhythms rely on a **biological clock**, a molecular mechanism that directs periodic gene expression and cellular activity.
  - Although biological clocks are typically synchronized to the cycles of light and dark in the environment, they can maintain a roughly 24-hour cycle even in the absence of environmental cues.
- In mammals, circadian rhythms are coordinated by a group of neurons in the hypothalamus called the **suprachiasmatic nucleus** or **SCN**.
  - The SCN acts as a pacemaker, synchronizing the biological clock in cells throughout the body to the natural cycles of day length.
  - By surgically removing the SCN from laboratory animals, scientists demonstrated that the SCN is required for circadian rhythms: Animals without an SCN lack rhythmicity in behaviors and in electrical activity of the brain.

Emotions depend on many brain structures.

- The generation and experience of emotions depend on many brain structures, including the amygdala, hippocampus, and parts of the thalamus.
  - These structures border the brainstem in mammals and are grouped as the *limbic system.*
  - The limbic system also functions in motivation, olfaction, behavior, and memory.
- Other parts of the brain are involved in generating emotion and experiencing emotion.
  - Emotions expressed by behaviors such as laughing and crying involve an interaction of parts of the limbic system with sensory areas of the cerebrum.
  - Structures in the forebrain attach emotions to basic functions controlled by the brainstem, including aggression, feeding, and sexuality.
- Emotional memory related to fear is stored separately from the memory system that supports explicit recall of events.
  - The brain structure with the most important role in storage of emotional memory is the **amygdala**, an almond-shaped mass of nuclei located near the base of the cerebrum.
- To study the function of the human amygdala, researchers present adult subjects with an image followed by an unpleasant experience, such as a mild electrical shock.
  - After several trials, study participants experience autonomic arousal—as measured by increased heart rate or sweating—if they see the image again.
  - Subjects with damage to the amygdala can recall the image, because their explicit memory is intact.
  - They lack autonomic arousal, because damage to the amygdala has reduced their capacity for emotional memory.

Concept 49.3 The cerebral cortex controls voluntary movement and cognitive functions

- The cerebrum is essential for awareness of our surroundings, language, cognition, memory, and consciousness.
- The cerebrum is the largest structure in the human brain and exhibits regional specialization.
- Cognitive functions reside in the cortex, the outer layer of the cerebrum.
    - Within the cortex, sensory areas receive and process sensory information, association areas integrate the information, and motor areas transmit instructions to other parts of the body.
- Each side of the cerebral cortex has a frontal, temporal, occipital, and parietal *lobe*, each named for a nearby bone of the skull.

Language and speech are localized in the cerebrum.

- Damage to particular regions of the cortex by injuries, strokes, or tumors produce distinctive changes in behavior.
- The French physician Pierre Broca conducted postmortem examinations of patients who could understand language but were unable to speak.
    - Many of these patients had defects in a small region of the left frontal lobe, *Broca's area*, that controls muscles in the face.
- German physician Karl Wernicke found damage to *Wernicke's area,* in a posterior portion of the left temporal lobe, abolished the ability to comprehend speech but not the ability to speak.
- Functional imaging studies show that Broca's area is active during speech generation and Wernicke's area is active when speech is heard.
- These areas belong to a much larger network of brain regions involved in language.
    - Reading a printed word without speaking activates the visual cortex, while reading a printed word out loud activates both the visual cortex and Broca's area.
    - Frontal and temporal areas become active when meaning must be attached to words, such as when a person generates verbs to go with nouns or groups related words or concepts.

Cortical function is lateralized.

- Both Broca's area and Wernicke's area are in the left cortical hemisphere, reflecting a greater role with regard to language for the left side of the cerebrum than for the right side.
- The left hemisphere is more adept at math and logical operations, while the right hemisphere is dominant in the recognition of faces and patterns, spatial relations, and nonverbal thinking.
- Such differences in hemisphere function in humans are **lateralization**.
- 90% of individuals are more skilled with their right hand than with their left hand.
- Studies using fMRI show that language processing differs in relation to handedness.
    - When subjects think but do not speak words, brain activity is localized to the left hemisphere in 96% of right-handed subjects but in only 76% of left-handed subjects.
- The two hemispheres trade information through the fibers of the corpus callosum.
    - Individuals with a severed corpus callosum exhibit a "split-brain" effect.
    - When they see a familiar word in their left field of vision, they cannot read the word: The sensory information that travels from the left field of vision to the right hemisphere cannot reach the language centers in the left hemisphere.

Information is processed in the cerebral cortex.

- Some of the sensory input to the cerebral cortex comes from groups of receptors clustered in dedicated sensory organs, such as the eyes and nose.
  - Sensory input also originates in receptors in the hands, scalp, and elsewhere in the body.
  - Somatic sensory, or *somatosensory*, receptors provide information about touch, pain, pressure, temperature, and the position of muscles and limbs.
- Most sensory information coming into the cortex is directed via the thalamus to primary sensory areas within the brain lobes.
  - The thalamus directs different types of input to distinct locations: Visual information is sent to the occipital lobe, whereas auditory input is directed to the temporal lobe.
- Information received by primary sensory areas is passed to nearby association areas, which process particular features in the sensory input.
  - In the occipital lobe, groups of neurons in the primary visual area are sensitive to rays of light oriented in a particular direction.
  - In the visual association area, information related to such features is combined in a region dedicated to recognizing complex images, such as faces.
- Integrated sensory information passes to the prefrontal cortex, which helps plan actions and movement.
- The cerebral cortex generates motor commands that cause behaviors such as movement or speech.
  - These commands consist of action potentials produced by neurons in the motor cortex, which lies at the rear of the frontal lobe.
  - The action potentials travel along axons to the brainstem and spinal cord, where they excite motor neurons, which in turn excite skeletal muscle cells.
- In the somatosensory cortex and motor cortex, neurons are arranged according to the part of the body that generates the sensory input or receives the motor commands.
  - Neurons that process sensory information from the legs and feet lie in the region of the somatosensory cortex closest to the midline.
  - Neurons that control muscles in the legs and feet are located in the corresponding region of the motor cortex.
- The cortical surface area devoted to each body part correlates with the extent of neuronal control needed (for the motor cortex) or with the number of sensory neurons that extend axons to that part (for the somatosensory cortex).
  - The surface area of the motor cortex devoted to the face is much larger than that devoted to the trunk, reflecting the extensive involvement of facial muscles in communication.
- Frontal lobes influence what are often called "executive functions."
- Tumors or brain damage in the frontal lobe may leave intellect and memory intact, while decision making is flawed and emotional responses are diminished.
  - The same problems were observed as a result of frontal lobotomy, a now banned surgical procedure that severed the connection between the prefrontal cortex and limbic system.
- In humans, the cerebral cortex accounts for about 80% of total brain mass and is highly convoluted.
  - The convolutions allow the cerebral cortex to have a large surface area and still fit inside the skull: Less than 5 mm thick, it has a surface area of approximately 1,000 cm^2.

- The outermost part of the human cerebral cortex forms the *neocortex*, six parallel layers of neurons arranged tangential to the brain surface.
- It was long thought that a highly convoluted neocortex was required for advanced *cognition*, the perception and reasoning that constitute knowledge.
    - Primates and cetaceans (whales, dolphins, and porpoises) possess an extensively convoluted neocortex.
- Birds lack such a structure and were thought to have much lower intellectual capacity.
    - Experiments in recent years have proven this assertion to be false.
    - Western scrub jays can remember the relative period of time that has passed after they stored and hid specific food items.
    - New Caledonian crows are highly skilled at making and using tools.
    - African gray parrots understand numerical and abstract concepts, distinguishing between "same" and "different" and grasping the idea of "none."
- The anatomical basis for sophisticated information processing in birds appears to be the clustering of nuclei within the *pallium*, the top or outer portion of the brain.
    - This arrangement is distinct from that in the human pallium that contains flat sheets of cells in six layers, but both types of pallium support complex and flexible brain function.
- How did the differences between the bird pallium and human pallium arise during evolution?
    - The common ancestor of birds and mammals had a pallium in which neurons were organized into nuclei, as is still found in birds.
    - Early in mammalian evolution, this nuclear organization of neurons was transformed into a layered one.
- Connectivity was maintained during this transformation such that, for example, the thalamus relays sensory input relating to sights, sounds, and touch to the pallium in both birds and mammals.

Concept 49.4 Changes in synaptic connections underlie memory and learning

- During embryonic development, regulated gene expression and signal transduction establish the overall structure of the nervous system.
- Two processes dominate the remaining development and remodeling of the nervous system.
- The first is a competition among neurons for survival.
    - Neurons compete for growth-supporting factors produced in limited quantities by tissues that direct neuron growth.
    - Cells that fail to receive such factors undergo programmed cell death.
    - Half the neurons formed in the embryo are eliminated, with the net effect of preferential survival of neurons properly located within the nervous system.
- Synapse elimination is the second major process that shapes the nervous system.
    - A developing neuron forms many more synapses than are required for its proper function.
    - The activity of the neuron stabilizes some synapses and destabilizes others.
    - By the end of embryonic development, neurons on average have lost more than half of their initial synapses, leaving behind the connections that survive into adulthood.
- Neuron death and synapse elimination set up the basic network of cells and connections within the nervous system required throughout life.

The nervous system is plastic.

- The nervous system has a great capacity to be remodeled in response to its own activity,
  - This is called **neural plasticity**.
- Much of the reshaping of the nervous system occurs at synapses.
  - When the activity of a synapse correlates with that of other synapses, the synaptic connection is reinforced.
  - When the activity of a synapse fails to correlate with that of other synapses, the synaptic connection becomes weaker.
- Synapses belonging to circuits that link information in useful ways are maintained, while those that convey information without context may be lost.
- *Autism*, a developmental disorder that first appears early in childhood, involves a disruption of activity-dependent remodeling at synapses.
  - Children affected with autism display impaired communication and social interaction, as well stereotyped and repetitive behaviors.
- There is a strong genetic contribution to autism and related disorders.
  - Extensive research has ruled out an effect of vaccine preservatives, once proposed as a potential risk factor.
  - Further understanding of the autism-associated disruption in synaptic plasticity may help efforts to better understand and treat this disorder.
- Remodeling and refining of the nervous system occur in many contexts.
  - After birth, the visual cortex of the mammalian brain undergoes reorganization in response to input from the optic nerve related to visual stimuli.
  - This remodeling is a necessary step in the development of normal visual ability.
- The nervous system's capacity to recover from injury and disease depends on remodeling of brain circuitry.
  - In a condition called the phantom limb syndrome, a person feels pain or discomfort that seems to originate from an arm or leg that has been amputated.
  - Viewing a reflection of the remaining limb through a mirrored box can reorganize the brain and eliminate the unpleasant feelings from the lost limb.

Memory and learning rely on neural plasticity.

- The formation of memories is due to neural plasticity.
- We constantly check what is happening against what just happened a few moments ago, holding information in **short-term memory** and releasing it if it becomes irrelevant.
  - To retain knowledge of a name or phone number requires activation of mechanisms of **long-term memory**.
  - If we need to recall the name or number, we fetch it from long-term memory and return it to short-term memory.
- Where in the brain are short-term and long-term memories located?
  - Both types of memory involve the storage of information in the cerebral cortex.
  - Short-term memory information is accessed via temporary links or associations formed in the hippocampus.
- When memories are made long-term, the links in the hippocampus are replaced by more permanent connections within the cerebral cortex.
  - Some of this consolidation of memory is thought to occur during sleep.

- The reactivation of the hippocampus that is required likely forms the basis for at least some of our dreams.

- The hippocampus is essential for acquiring new long-term memories but not for maintaining them.
  - Individuals who suffer damage to the hippocampus cannot form any new lasting memories but can freely recall events from before their injury.
  - In effect, their lack of normal hippocampal function traps them in their past.
- What evolutionary advantage is offered by organizing short-term and long-term memories differently?
  - Delays in forming connections in the cerebral cortex allows long-term memories to be integrated into existing knowledge and experience, allowing for meaningful associations.
  - Transfer of information from short-term to long-term memory is enhanced by the association of new data with data previously learned and stored in long-term memory.
- Motor skills are usually learned by repetition.
- Learning skills and procedures, such as those required to ride a bicycle, involves cellular mechanisms similar to those responsible for brain growth and development.
  - In such cases, neurons actually make new connections.
- Memorizing phone numbers, facts, and places relies mainly on changes in the strength of existing neuronal connections.
- In searching for the physiological basis of memory, researchers focus on processes that alter synaptic connections, making the flow of communication either more efficient or less efficient.
- **Long-term potentiation (LTP)**, a lasting increase in the strength of synaptic transmission, involves a presynaptic neuron that releases the excitatory neurotransmitter glutamate.
  - For LTP to occur, there must be a brief high-frequency series of action potentials in the presynaptic neuron.
  - These action potentials must arrive at the synaptic terminal at the same time that the postsynaptic cell receives a depolarizing stimulus.
- LTP involves two types of glutamate receptors, each named for a molecule—NMDA or AMPA—that artificially activates that particular receptor.
  - The set of receptors present on the postsynaptic membrane changes in response to an active synapse and a depolarizing stimulus.
  - The result is LTP—a stable increase in the size of the postsynaptic potentials at the synapse.
  - LTP can last for days or weeks in dissected tissue and is thought to represent one of the fundamental processes by which memories are stored and learning takes place.

Stem cells are found in the brain.

- The adult human brain contains neural stem cells, which retain the ability to divide indefinitely.
  - While some of their progeny remain undifferentiated, others differentiate into specialized cells.
- Stem cells in the brain give rise to neurons that mature, migrate to particular locations in the hippocampus, and become incorporated into the circuitry of the adult nervous system.
  - Such neurons play an essential role in learning and memory and contribute to the plasticity that enables remodeling of brain circuitry in response to experience.

- Researchers are now looking for ways to use neural stem cells as a means of replacing brain tissue that has ceased to function properly.
    - Unlike the PNS, the mammalian CNS cannot fully repair itself when damaged or diseased.
    - Surviving neurons in the brain can make new connections and sometimes compensate for damage, as occurs in the remarkable recoveries of some stroke victims.
    - Brain and spinal cord injuries, strokes, and disorders that destroy CNS neurons, such as Alzheimer's disease and Parkinson's disease, have devastating and irreversible effects.
- Expression of four genes converts differentiated adult cells into stem cells.

Concept 49.5 Many nervous system disorders can be understood in molecular terms

- Disorders of the nervous system are a major public health problem, resulting in more hospitalizations in the United States than do heart disease or cancer.
    - Many disorders that alter mood or behavior can now be treated with medication, reducing average hospital stays for these disorders to only a few weeks.
    - Societal attitudes are changing as awareness grows that nervous system disorders often result from chemical or anatomical changes in the brain.
- Major research efforts are under way to identify genes that cause or contribute to disorders of the nervous system.
    - Identifying such genes offers hope for identifying causes, predicting outcomes, and developing effective treatments.
- For most nervous system disorders, genetic contributions only partially account for which individuals are affected.
    - The other significant contribution to disease comes from environmental factors, which may be difficult to identify.
- Family studies may help scientists distinguish between genetic and environmental variables.
    - In such studies, researchers track how family members are related genetically, which individuals are affected, and which family members grew up in the same household.
    - These studies are especially informative when one of the affected individuals has either an identical twin or an adopted sibling who is genetically unrelated.
    - These studies indicate that certain nervous system disorders, such as schizophrenia, have a very strong genetic component.

Schizophrenia is a severe mental disturbance characterized by psychotic episodes.

- About 1% of the world's population suffers from **schizophrenia**, a severe mental disturbance characterized by psychotic episodes in which patients have a distorted perception of reality.
- People with schizophrenia typically experience hallucinations and delusions.
- Two lines of evidence suggest that schizophrenia affects neuronal pathways that use dopamine as a neurotransmitter.
    - The drug amphetamine, which stimulates dopamine release, can produce the same set of symptoms as schizophrenia.
    - Many drugs that alleviate the symptoms of schizophrenia block dopamine receptors.
- Schizophrenia may also alter glutamate signaling, since the street drug "angel dust," or PCP, blocks glutamate receptors and induces strong schizophrenia-like symptoms.

- Medications are available that alleviate the major symptoms of schizophrenia..

Depression is a disorder characterized by depressed mood plus abnormalities in sleep, appetite, and energy level.

- Two broad forms of depressive illness are known: major depressive disorder and bipolar disorder.
- Individuals affected by **major depressive disorder** have periods in which once enjoyable activities provide no pleasure and provoke no interest.
    - Major depression affects about one in every seven adults at some point, and twice as many women as men.
- **Bipolar disorder** involves swings of mood from high to low and affects about 1% of the world's population.
    - The manic phase is characterized by high self-esteem, increased energy, a flow of ideas, overtalkativeness, and increased risk taking. This phase may be associated with great creativity.
    - The depressive phase comes with lowered ability to feel pleasure, loss of motivation, sleep disturbances, and feelings of worthlessness that may lead to suicide.
- Many drugs used to treat depressive illness, including fluoxetine (Prozac), increase the activity of biogenic amines in the brain.

Drug addiction is linked to the brain's reward system.

- Drug addiction is a disorder characterized by compulsive consumption of a drug and loss of control in limiting intake.
- Addictive drugs include stimulants, such as cocaine and amphetamine, and sedatives, such as heroin.
- All of these drugs, as well as alcohol and nicotine, are addictive for the same reason: Each increases activity of the brain's reward system, neural circuitry that normally functions in pleasure, motivation, and learning.
    - The reward system of the brain provides motivation for activities that enhance survival and reproduction.
    - In addicted individuals, "wanting" is instead directed toward further drug consumption.
- Inputs to the reward system are received by neurons in a region near the base of the brain called the *ventral tegmental area (VTA)*.
    - When activated, these neurons release dopamine from their synaptic terminals in specific regions of the cerebrum, including the *nucleus accumbens*.
- Addictive drugs affect the reward system in several ways.
    - Each drug has an immediate and direct effect that enhances the activity of the dopamine pathway.
    - As addiction develops, there are also long-lasting changes in the reward circuitry.
    - The result is a craving for the drug, independent of any pleasure associated with consumption.
- As scientists expand their knowledge about both the reward system and the various forms of addiction, there is hope that the insights will lead to more effective prevention measures and treatments.

Alzheimer's disease is dementia characterized by confusion and memory loss.

- The incidence of **Alzheimer's disease** is age related, rising from about 10% at age 65 to about 35% at age 85.
- The disease is progressive, with patients gradually becoming less able to function and eventually needing to be dressed, bathed, and fed by others.
  - Patients also lose their ability to recognize people, including their immediate family, and may treat them with suspicion and hostility.
- Alzheimer's disease leads to the death of neurons in many areas of the brain, including the hippocampus and cerebral cortex, leading to massive shrinkage of brain tissue.
- Postmortem examination of the remaining brain tissue reveals two characteristic features—amyloid plaques and neurofibrillary tangles.
- The plaques are aggregates of β-amyloid, an insoluble peptide that is cleaved from a membrane protein found in neurons.
  - Membrane enzymes, called secretases, catalyze the cleavage, causing β-amyloid to accumulate in plaques outside the neurons.
  - The plaques trigger the death of surrounding neurons.
- The neurofibrillary tangles observed in Alzheimer's disease are primarily made up of the tau protein.
  - The normal function of tau in neurons is to help regulate the movement of nutrients along microtubules.
  - In Alzheimer's disease, tau undergoes changes that cause it to bind to itself, resulting in neurofibrillary tangles.
- Recently developed drugs are partially effective in relieving some of the symptoms of Alzheimer's disease.

Parkinson's disease is a motor disorder including muscle tremors, poor balance, a flexed posture, and a shuffling gait.

- Like Alzheimer's disease, Parkinson's disease is a progressive brain illness and is more common with advancing age.
  - The incidence of Parkinson's disease is about 1% at age 65 and about 5% at age 85. In the U.S. population, approximately 1 million people are afflicted.
- The symptoms of Parkinson's disease result from the death of neurons in the midbrain that normally release dopamine at synapses in the basal nuclei.
  - As with Alzheimer's disease, protein aggregates accumulate.
- A rare form of the disease that appears in relatively young adults has a clear genetic basis.
  - Molecular studies of mutations linked to early-onset Parkinson's disease reveal disruption of genes required for certain mitochondrial functions.
- At present, there is no cure for Parkinson's disease.
  - Approaches used to manage the symptoms include brain surgery, deep-brain stimulation, and drugs such as l-dopa, a molecule that can cross the blood-brain barrier and be converted to dopamine in the CNS.
  - One potential cure is to implant dopamine-secreting neurons, either in the midbrain or in the basal nuclei.
- In rats with an experimentally induced condition that mimics Parkinson's disease, implanting dopamine-secreting neurons can lead to a recovery of motor control.