

## IN THIS CHAPTER

- » Getting to know how neurons evolved
- » Seeing how the nervous system is organized
- » Meeting neurons and glial cells
- » Taking a tour around the brain

# Chapter 1

# Welcome to the World of Neurobiology

**W**hat makes you *you*? Your brain, most people would answer. Then what is it about your brain that makes you *you*? The brain is made of neurons and glial cells. Worms and bees have brains with neurons and glia. So do dogs and chimpanzees. What about the brain distinguishes these animals from each other, and for that matter, one human from another? Is it more neurons, different neurons, special neural circuits? And what happens when these neurons, glia, and circuits are disrupted or dysfunctional?

Neurobiologists like the two of us want to answer these questions. Thousands of us at universities, research institutes, and pharmaceutical companies all over the world are working on these questions. We have many hypotheses and data sets. This book, in a way, is a progress report on the efforts.

Virtually all neurobiologists believe that intelligence comes from nervous systems that are broadly programmed by genes and fine-tuned by experience. Generally, the human genetic program creates a brain with more cortical neurons than other animals have, allowing for richer experience to produce a unique kind of cognition and intelligence.

Here we introduce you to the basics of neurobiology and give you a jumping-off point to use this book in understanding the human nervous system.

# Starting with Neurobiology — Just the Basics

*Neurobiology* is the study of neurons, glia, and the nervous system. It involves many fields of study including physiology, anatomy, biochemistry, molecular biology, cognitive and behavioral psychology, and artificial intelligence. The basic goals of neurobiology are to describe how the nervous system operates in terms of what neurons and glial cells do, how they're built, how they work, and what happens when their functions are disrupted.

*Neurons* are the detecting and signaling cells of the nervous system that use electrical and chemical signaling to communicate. *Glial* cells are the supporting cells that provide metabolic, structural, and functional support.

## EVOLVING THE NERVOUS SYSTEM

Many of the DNA sequences, proteins, and reactions that exist in neurons and glia are similar to those in single-celled organisms. This apparent conservation of genes and biochemistry is an important argument for life having a common origin.

Cells have membranes that separate their insides from the external environment. Receptors embedded in the membrane enable cells to respond to external signals. Receptor responses include biochemical cascades inside the cell, and, in neurons particularly, electrical activity.

Animals are multicellular eukaryotic organisms that evolved around 600 million years ago. Early animals evolved different types of cells that are specialized to do things like secrete hormones or digestive enzymes and undergo contraction. As animals increased cells and got bigger, their sensor cells became separated from other cells and movement required coordination.

Neurons evolved between about 600 to 550 million years ago, most likely from epithelial cells. This probably occurred when animals needed to send sensory information over longer distances and control contraction of muscles for movement. Neurons developed as electrical signaling cells that formed nerve nets in cnidarian and/or ctenophore evolution.

Later, the evolution of special sense organs and nerve ganglia occurred several times in *bilaterans* (the clade that gave rise to crustaceans, insects, and vertebrates). There's still much debate over the origin of neurons and nervous systems in the tree of life.

Neurons evolved extensions called *axons* and *dendrites* that allow them to communicate rapidly, specifically, and over long distances. Action potentials are electrical signals transmitted along the axon. The axon forms connections called synapses with its targets (the majority on dendrites) where chemical communication occurs and typically produces electrical responses. The following sections discuss when and how neurons most likely evolved during animal evolution.

## Arriving at a nervous system

Electrical signaling in the form of action potentials and cell-to-cell communication evolved in single-celled organisms before multicellularity evolved. Some nonmetazoan single-celled organisms express genes for secreted molecules and synaptic-related proteins. Evolving neurons adapted functions that single cells use to interact with the environment and other cells.

The next step was the extension of an axon, from one cell to distant cells where a specific signaling substance, called a *neurotransmitter*, is released. Now, instead of a multicellular signaling soup, there are circuits. Electrical and chemical signaling allowed for rapid communication across the distances from one end of an animal to another for sensing the surrounding environment and performing coordinated movements.

## Coordinating responses in simple circuits

Nervous systems are complex and hard to study. The human brain is estimated to contain about 86 billion neurons and about the same number of glial cells. An average neuron receives a thousand or more synapses, meaning there are more than a hundred trillion synapses in the human brain. Neurobiologists don't really know yet how single neurons work and don't know, and can't count, all of the connections between neurons.

## Studying invertebrates

People often wonder why scientists study the nervous systems of flies, worms, squids, and slugs. The reason is they have advantages in that the cells are fewer, bigger, and/or more amenable to genetic manipulation. Alan Hodgkin and Andrew Huxley won the Nobel Prize for deducing the ionic basis of the action potential in the squid giant axon. Eric Kandel won the Nobel Prize for identifying memory mechanisms in the sea slug *Aplysia*.

Many invertebrates such as worms and insects have several hundred to a few thousand neurons. This vastly simplifies the problem of working out a complete

neural circuit, including which neurotransmitters are used by which neurons, what responses are produced and how activity is integrated.



Recent progress has been made in making model systems from mammals, studying intact brains and behavior, and using brain slices, neural tissue cultures, and brain organoids and that can be investigated using molecular biology, microscopy, and electrical techniques.

## Introducing Neurons and Glia

When neurobiologists talk about the nervous system, we often use the term *neural*. *Neural* refers to any part of the nervous system that involves neurons or glia. Part 1 of this book gives you more detailed information about neurons and glia. Here we describe how neurons and glia are functionally organized in the nervous system.

### Beginning with functional anatomy

The nervous system has two main components that are connected and communicate with each other:

- » **Central nervous system (CNS):** The CNS is composed of the brain and spinal cord.
- » **Peripheral nervous system (PNS):** The PNS includes the spinal nerves, cranial nerves, ganglia, and the enteric nervous system.

Neurons in the PNS are responsible for detecting and relaying sensory signals in the external world (somatic sensory system) and in the internal body (visceral sensory system). The PNS then relays that information to the CNS.

The CNS receives sensory information and uses it for perception and homeostasis. These are crucial for the other main functions of the CNS: to control the body's movements and produce survival responses and behaviors. To help control and regulate this output, the mammalian CNS also provides emotion and cognitive functions.

The CNS sends output signals from motor neurons that extend axons in the nerves (the PNS) to your muscles, organs, and glands that control their contraction, relaxation, or secretion. The output in the PNS has two main divisions:

- » The somatic system controls skeletal muscles to control our movements.
- » The autonomic system controls organs and glands to regulate internal functions.

## Establishing the cells

Both neurons and glial cells have a *cell body* where the nucleus and cellular organelles are located. Cellular organelles include mitochondria, the endoplasmic reticulum, Golgi complex, and lysosomes. The nucleus contains the chromosomes and is where RNA is produced. Organelles carry out biochemical activities including energy metabolism and protein synthesis. Figure 1-1 gives you a snapshot of typical neurons and glial cells that we discuss in the following sections. We describe the biochemistry and cell biology of neurons and glia in Chapter 2.

Neurons and glia are derived from parts of ectoderm that form the neural tube and neural crest. Prenatal development involves hard-wired genetic programs. Postnatal development involves the sculpting of synaptic connections and depends on experience and activity. Chapter 3 focuses on the development of the nervous system.

## Specializing the functions

Neurons, also referred to as *nerve cells* or *neuronal cells*, are the main signaling cells of the nervous system. Functionally, neurons can be classified as the following:

- » **Sensory neurons:** Sensory neurons detect external and internal stimuli. The majority are located in the PNS and they transmit information to the CNS.
- » **Motor neurons:** Motor neurons send signals out to control muscle contraction. They're found in both the CNS and PNS.
- » **Interneurons:** Interneurons include projection (or principal neurons) and local circuit neurons. They're located in the CNS where they integrate information for perception, cognition, and/or the control of movement and behaviors for survival and homeostasis.

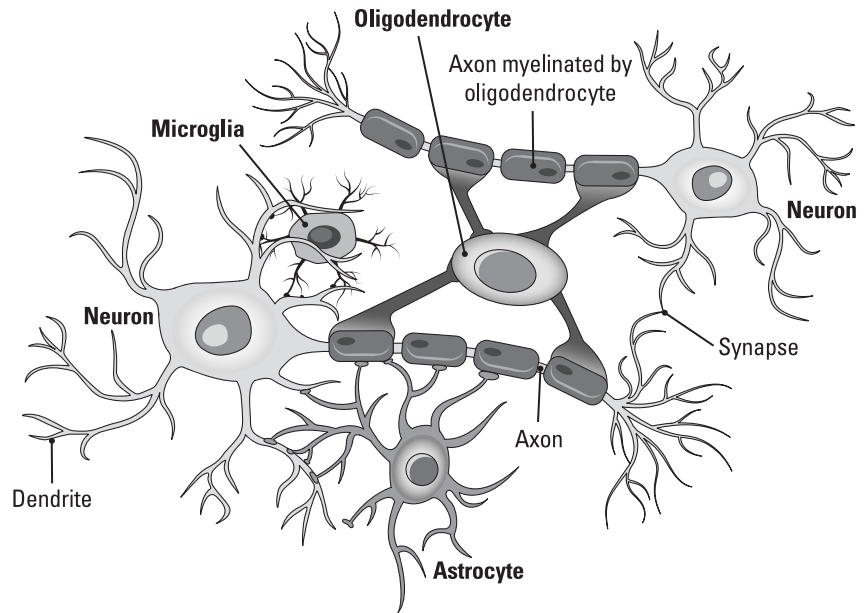


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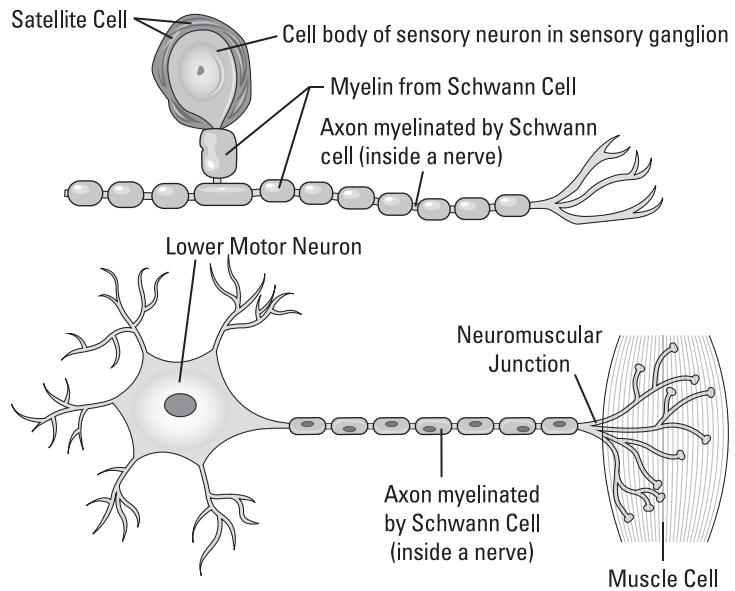
Neurons can also be classified based on the neurotransmitter they make and release, the effect they produce, and their morphology.

Glial cells are also referred to as *neuroglia* or *glia*. Microglia are the resident immune cells in the CNS. Astrocytes are located in the CNS where they provide metabolic support for neurons and other glia. Some astrocytes surround synapses where they regulate ion and neurotransmitter levels. Other astrocytes extend processes called *end feet* to surround brain capillaries where they transport nutrients into the CNS.

**Interneurons and Glia in CNS**



**Sensory and Motor Neuron and Glia in PNS**



**FIGURE 1-1:** Typical neurons and supporting glial cells.

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## Forming the barriers

Brain capillaries are formed by vascular endothelial cells that make tight junctions. These junctions prevent the direct diffusion of water soluble nutrients from the blood into the CNS and forms the blood–brain barrier. It’s the reason the CNS requires astrocytes to transport nutrients between capillaries and neurons. Another type of glial cell called *pericytes* surround the capillaries and help regulate the capillary diameter or vasodilation. Microglia are the resident immune cells in the CNS that help with the detection and removal of pathogens and damaged cells.



REMEMBER

In the CNS, about half of the axons are myelinated by oligodendrocytes. *Myelination* involves the wrapping of an axon by many layers of the oligodendrocyte cell membrane. In the PNS, the majority of axons are myelinated within the nerve where the Schwann cells provide the myelin membrane. Myelination of axons increases the speed and efficiency of action potentials traveling along the axon.

The brain contains fluid–filled tubes inside called the *ventricles*, which are continuous with the central canal in the spinal cord. The ventricles are lined by ependymal cells and contain a region called the *choroid plexus* formed by specialized ependymal cells and capillaries. The ependymal cells synthesize and transport cerebrospinal fluid (CSF) inside the ventricles.

## Electrifying the membrane

All cells have a *membrane potential*, a difference in electrical charge across the membrane. Neurons use changes in the membrane potential for communication. The axon is where an action potential is produced and conducted to the presynaptic region. We describe the basis of electrical signaling and action potentials in Chapter 4.

## Communicating with targets

The dendrites are typically branched and are the main receiving processes in neurons. Many dendrites contain small bumps or protrusions called dendritic spines. Dendrites and dendritic spines receive incoming signals from other neurons at synapses. These electrical signals are also described in Chapter 4.

At the synapse, action potentials are converted into release of chemicals called neurotransmitters. Neurotransmitters activate receptors on the target cell. We describe the mechanism of synaptic transmission in Chapter 5 and neurotransmitter systems in Chapter 6.

# Protecting and Nourishing the Parts

Here we explain how the nervous system is protected by non-neural structures, how it receives its blood supply, and what nerves contain.

## Safeguarding the CNS

The brain is encased in the skull bone and the spinal cord is surrounded by the bones of the vertebral column. Underneath the bones are the *meninges*, three layers of membranes that cover the brain and spinal cord. We describe the meninges in Chapter 3.

## Providing the supplies

The brain and spinal cord are highly *vascularized*, containing many arteries, veins, arterioles, venules, and capillaries. The main blood supply to the front and middle regions of the brain is from the internal carotid arteries. The blood supply to the posterior brain and spinal cord is from the vertebral arteries.

The CNS capillaries are different from the rest of the body's general capillaries in that they, together with astrocytes and pericytes, form a *blood-brain barrier*. The brain contains many venous plexuses that receive the blood and drain it into the jugular veins. A lymphatic system in the meninges mediates the movement of waste and immune cells.



The ventricles inside the brain synthesize and circulate CSF. Some CSF is diverted around the brain where the meninges transfers the CSF to the blood. The rest of the CSF flows in the central canal inside the spinal cord.

## Supporting the PNS

In the PNS, the nerves are bundles of axons that are covered with layers of connective tissue. Nerves also contain the myelinating Schwann cells and blood vessels. The axons in nerves originate or terminate in the spinal cord or brainstem.

In the PNS, ganglia are groups neuron cell bodies clustered in regions outside the spinal cord or brainstem (refer to Chapter 7). The PNS is divided into the somatic, autonomic (visceral), and enteric nervous systems. The two types of ganglia are sensory ganglia and autonomic ganglia. The enteric nervous system contains both sensory and motor neurons in the gastrointestinal tracts.

# Navigating Around the Nervous System

The brain and spinal cord are formed by groups of neurons that work together to connect to other neurons through tracts. Examining the CNS in fixed sections, you see regions the following regions:

- » *Gray matter* contains neuronal cell bodies, dendrites, synapses, and astrocytes.
- » *White matter* contains myelinated axons, oligodendrocytes, and astrocytes.

These sections explain the gray and white matter regions in the CNS.

## Organizing gray matter

Gray matter in the CNS is organized in several ways:

- » In the brain the cortical gray matter is layered and found in the cerebral cortex and cerebellar cortex.
- » The other groups of neurons in the brain are called nuclei (a single nucleus). Subcortical brain structures, including the basal ganglia, thalamus, hypothalamus, amygdala, and brainstem, are formed by many separate nuclei.
- » In the spinal cord, the gray matter is located in the horns. The ventral horns contain motor neurons while the dorsal horn contains sensory relay neurons. Both regions contain spinal interneurons.

## Tracking along white matter

Within the CNS, axon tracts form the white matter. There are different types of tracts in the brain that connect neurons in one cortical region to another cortical region or to subcortical areas. In the spinal cord, the white matter is located in the regions around the white matter and contains the axons of all the ascending sensory and descending motor tracts.

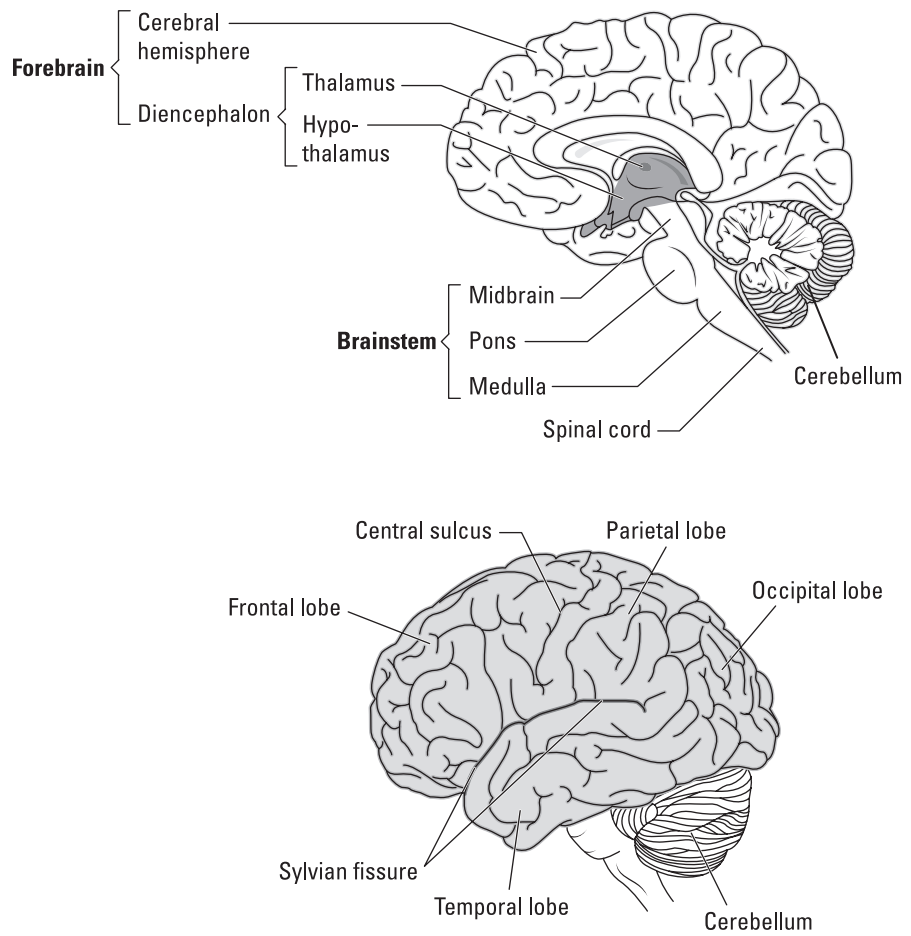
## Dissecting functions of the CNS

Looking at the mammalian brain from the outside, shown in Figure 1-2, you can see three major parts:

- » **Forebrain:** The largest part of the brain, it contains the cerebrum and subcortical nuclei. The cerebrum is composed of the cerebral cortices and

cerebral white matter. Subcortical structures including the basal ganglia, amygdala, thalamus, hypothalamus, and pituitary gland.

- » **Brain stem:** The midbrain is located underneath the thalamus. Below that is the pons, and below that the medulla that ends at the top of the spinal cord. The brain stem is the oldest part of the brain that's essential for survival responses and homeostasis.
- » **Cerebellum:** It sticks out from the back of the pons in the brainstem. It contains as many neurons as the rest of the brain combined. Though it evolved first in vertebrates, the cerebellum continued to evolve as mammals added the larger neocortex. It functions in motor control.



**FIGURE 1-2:**  
Views of the  
human brain.

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## Looking at the cerebrum

The cerebrum contains the cerebral cortex and the underlying cerebral white matter. Figure 1-2 shows that from the outside you see many *gyri* (singular: gyrus), which are ridges, and many *sulci* (singular: sulcus), which are grooves that give the human and some mammalian brains their folded appearance. Folding allowed more cortical areas to fit inside the skull during evolution.

The longitudinal fissure separates the left and right cerebral hemispheres. Deep sulci separate the cerebrum into four lobes on each side, called the frontal, parietal, temporal, and occipital lobe, named for the cranial bones that overlies each (see the next section for more about these lobes). The central sulcus separates the frontal and parietal lobes while the lateral sulcus separates the temporal lobe from the other three lobes.

## Figuring out the lobes' functions

Figure 1-2 also illustrates the lobes of the cerebrum. Here is a brief overview (Chapter 11 examines the functional anatomy of the lobes in greater detail):

- » **Frontal lobe:** It contains the motor cortex, prefrontal cortex, frontal eye fields, and Broca's area. The frontal lobe operates primarily to program and organize goal-directed movements, speech, and executive functions.
- » **Parietal lobe:** It contains the somatosensory cortex and posterior parietal cortex, a sensory association area that integrates somatosensory, visual, and auditory inputs.
- » **Temporal lobe:** It contains the auditory cortex, hippocampus, and amygdala. The temporal lobe functions in processing emotion, deciphering auditory information, understanding language, and encoding memory.
- » **Occipital lobe:** It contains the visual cortex composed of multiple visual processing areas.

## Situating underneath the cortex

Underneath and within the cerebral white matter are the subcortical areas. They include the thalamus, hypothalamus, basal ganglia, cerebellum, and brainstem. We introduce the functions of these areas in the next section and in Part 2 of this book.

# Moving the Correct Way

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An important function of the brain is the control of motor systems. Motor systems involve somatic control of skeletal muscles. They also control contraction of the heart and smooth muscles in organs and tissues by the autonomic motor system. Part 2 of this book focuses on mechanisms and control of movements and behaviors. Here we introduce the basics.

## Making the movements

Upper motor neurons from the motor cortex send axons to the lower motor neurons and nearby interneurons. The lower motor neurons provide the output to skeletal muscles to control their contraction (see Chapter 7).

## Controlling the output

The motor cortex contains areas involved in control of motor output. The primary motor cortex provides direct motor commands to produce movements. The supplementary motor area and premotor cortex receive inputs from cortical and subcortical areas and control the output from the primary motor cortex.

The basal ganglia provide action selection and inhibit unwanted movements. The cerebellum is necessary for learning movement sequences and detecting and correcting errors to coordinate movements. Chapter 8 discusses these brain regions in motor control.

## Focusing on older parts

Both the spinal cord and brainstem function like subcontractors of the brain to execute the brain's instructions and report on their progress. They contain lower motor neurons whose axons control muscle cell contraction. They receive sensory inputs for both local circuit reflexes and for relaying sensory information to the thalamus, which then transmits to the sensory cortices.

The brainstem and spinal cord are also essential in survival and homeostasis. Both control the autonomic nervous system involved in regulation of heart rate, blood pressure, and respiration. The sympathetic system prepares us for action in the fight-or-flight mode, while the parasympathetic system organizes resources for digestion and the conservation of energy. Chapter 9 describes the basic organization and functions of these regions.

## Ensuring homeostasis

The hypothalamus receives input from many brain areas and controls homeostatic processes including regulation of temperature and feeding. It provides control of the autonomic nervous system and circadian rhythms, the body's internal clock. It also links the brain with the endocrine system by controlling the secretion of hormones from the pituitary gland.

The cingulate cortex is involved in processing pain, error, and conflict detection, processing and regulating emotions, regulating autonomic functions, social behavior, and empathy. Regions involved in memory provide key inputs for our survival responses and cognition (see Chapter 15).

The amygdala is an emotion processing center for emotions like fear and motivation. It's where fear memories are encoded. Its outputs contribute to regulation of autonomic and endocrine functions, as well as executive functions such as decision making and emotional control.

The reticular formation is a diffuse network of neurons and axon tracts that runs through the brainstem up into portions of the thalamus. It controls body state through processes such as controlling wakefulness versus sleep, alertness, and homeostatic mechanisms such as heart rate.

Chapter 10 describes survival and homeostatic functions of the brainstem and *limbic system*. We discuss the specific functions of these brain areas and how they interact with other parts of the brain.

## Completing the circuit

The neocortex dominates the mammalian brain in volume, particularly in primates. It has the same six-layered structure virtually everywhere, with the similar cell types and cortical minicolumn circuits. It's responsible for producing sensory perception and controlling voluntary movement and cognitive functions. Chapter 11 describes the neocortex and its functions.

Chapter 12 focuses on the types of injury, degeneration, and dysfunction that can compromise the control or production of movement. We describe the most common developmental disorders and movement disorders that involve motor systems.

# Perceiving the World, Thinking, and Remembering

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Part 3 describes how sensory systems generate perception and how brain areas cooperate to provide cognitive functions, including executive functions, language, and memory. Chapter 18 discusses neurodevelopmental and mental disorders that impact cognitive functions. Here we give a brief overview.

## Seeing and hearing is believing

In many mammals, visual processing dominates the brain. In both vision and audition, high-order brain areas process complex inputs, such as face-specific neurons in inferotemporal cortex in vision, and language specific areas in audition such as Wernicke's area. Chapter 13 focuses on the visual and auditory sensory systems.

## Sensing touch, smell, and taste

In the somatosensory system, sensation is composed of sensory receptors including mechanoreceptors, thermoreceptors, and nociceptors in the skin, muscles, and joints. These allow you to perceive touch, temperature, and painful stimuli.

The sense of smell is mediated by olfactory receptor cells in the nose while the sense of taste is mediated by receptors mostly in taste buds on the tongue. Your perception of flavor is formed by a combination of taste and smell. Chapter 14 examines somatosensory, smell, and taste systems in more detail.

## Focusing on learning, memory, and plasticity

A hallmark of mammals is they can change their behavior through learning and memory (see Chapter 15). The short-term representation of an event and its context occurs in the prefrontal cortex as *working memory*. The hippocampus encodes long-term declarative memory for facts and events and spatial memory. The amygdala encodes fear memory. The basal ganglia and cerebellum encode procedural memory for habits and motor skills.

The encoding of memory involves synaptic plasticity in each of the brain areas identified. Research suggests that long-term memory is stored in cortical circuits in the cerebral cortex. This means that the neocortex is involved in not only the integration and processing of sensory, motor, and cognitive information, but also in its storage as well.

## Controlling with the executive brain

The frontal lobes are responsible for planning and executing behavior (refer to Chapter 16). During evolution there was a relative expansion of the frontal lobe compared to the rest of the brain in humans compared to other primates, and primates compared to other mammals.

The motor cortex controls motor neurons for regulation of contraction of skeletal muscles. The frontal eye fields control eye movements, and Broca's area mediates language production. The prefrontal cortex produces executive functions for performing goal-directed movements and controlling behavior.

## Thinking about cognition

Several cognitive functions, including language, are lateralized in humans. The capacity for learning language is innate in humans and involves Wernicke's and Broca's areas. Neurobiology research is working to understand how human language systems operate. Chapter 17 examines the components of the human brain areas most important for cognitive functions.



REMEMBER

*Intelligence* is the ability to acquire and apply knowledge and skills. The prefrontal cortex is involved in higher-order cognitive processes such as working memory, planning, decision-making, reasoning, problem-solving, and goal setting. The prefrontal cortex also acts in behavioral self-control and emotional control. These cognitive functions, together with your long-term declarative memory, form the components of intelligence.

*Consciousness* is subjective and includes being aware of your sensations, thoughts, experiences, and emotions. Researchers have studied brain mechanisms that may underlie consciousness and have proposed many hypotheses about the basis of consciousness.

