Chapter 1

Welcome to the World of Neurobiology

In This Chapter

- Getting to know the neuron
- Finding out how the nervous system is organized
- Feeling cerebral with thoughts, learning, and memory
- Seeing the effects of mental illness and developmental problems

What 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. Worms have brains with neurons. So do dogs and monkeys. 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?

Neurobiologists would like to answer all these questions, but they can't yet. Thousands of them at universities all over the world are working on these problems. They have many hypotheses and data sets. This book, in a way, is a progress report on their 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 neurons than any other animal, allowing for richer experience to produce a unique kind of intelligence.

This chapter gives an overview of the brain, its functions, and its parts. It also looks at why humans are like many other animals, such as primates, because of similarities in our brains, and what differences in the human brain may distinguish us from other species, and from each other.

Introducing Neurons

Neurobiology is the study of neurons and nervous systems, such as brains. *Neurons* are cells. Like other cells, neurons interact with the external world and other cells through specialized receptors in their membranes and through biochemical processes inside their cytoplasm and nucleus.

Neural capabilities evolved from those of single-celled organisms, like bacteria and paramecia, which use membrane sensors to detect food and toxins, and cilia to move toward food and away from toxins. Single-cell organisms may also change their internal metabolism upon ingesting particular substances from the environment.

REMEMBER

Multicellular organisms consist of different types of cells that are specialized to do things like secrete hormones or digestive enzymes. They depend on other cells for nutrients, waste removal, and the maintenance of a supportive environment. Neurons are specialized cells in multicellular organisms that, among other things, enable rapid communication across the large distances from one end of an animal to another. This allows the animals to perform coordinated movements and to act upon sensing the surrounding environment.

Evolving cells on early earth

According to astronomers and astrophysicists, the universe as we know it came into existence about 14 billion years ago. After several cycles of star formation, our solar system, including the earth, formed about 4.5 billion years ago. The earth was too hot for life for about a billion years, as it continued to be bombarded by the solar system debris from which it was formed.

Eventually most of the solar system debris stuck to one or another planet, or stabilized in relevantly permanent orbits such as the asteroid belt between Mars and Jupiter. Earth cooled for about 1 billion years, and life arose. No one knows how. Some scientists are suspicious that life arose almost as soon as the earth was cool enough, suggesting either that it must occur almost automatically given the right conditions, or it came from elsewhere and established a foothold as soon as it was possible.

Looking at the origin of single cells

The living things that arose at the 1-billion-year mark were single-celled *prokaryote* cells that lack a nucleus, such as bacteria we have today. Life stayed unicellular for a long time after that. This doesn't mean that no progress was made, though. Undoubtedly the single cells that existed at the time of evolution to multicellularity were more sophisticated and diverse than those that could be found when life originated.

Catalyzing reactions in the primordial soup

All life forms carry out metabolism, using energy to build proteins and other cell constituents. The proteins in all cells are coded for by the same DNA coding scheme (see Chapter 2), one piece of evidence that argues for a common origin of all life. A particularly important type of protein that all cells make is an enzyme. Enzymes cause specific reactions such as cleaving proteins at a particular place or joining proteins to other molecules.

TIP

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

Separating inside from out: Membranes

A fundamental property of cells is that they have membranes that separate their insides from the external environment. What makes a cell what it is and does relies significantly on the receptors it has in its membrane and how they respond to external substances and energy inputs.

Cellular responses to substances that bind membrane receptors include biochemical cascades inside the cell, and, in neurons particularly, electrical activity. A significant percentage of all animal genes code for proteins that compose hundreds of different types of membrane receptors.

Comparing eukaryotes to prokaryotes

About 1 to 2 billion years after single-cell life arose, some single-cell life forms developed nuclei and became what are called *eukaryotes* (cells that have a nucleus). Soon after eukaryotes appeared, multicellular organisms came on the scene.

Plant-like multicellular organisms probably arose from aggregations of single cells in shallow ocean areas. These multicellular organisms diversified over more than a billion years. About half a billion years ago, 4 billion years after the earth formed, land plants and animals that we would recognize as such appeared from these multicellular ancestors.

Multicellularity: Sensing and moving

Multicellularity has advantages and disadvantages. Multicellular organisms can be big, have specialized sensors, and move around and ingest single-celled organisms. But movement requires coordination, and the environment of the cells at the periphery of the organisms is quite different from that of those in the middle.

Multicellularity allowed organisms to have cells specialized not only for niches in the external environment, but also for the internal environment created by the structure of the organism itself. Neural cells evolved as sensors, movers (muscles), and communicators.

Detecting food, waste, and toxins

Neurons have some functions that are like all other cells, including those of many single-celled organisms. These include taking in energy through glucose, and oxygen to fuel metabolism. Neurons also excrete metabolic waste products and carbon dioxide. Many of these functions are carried out by membrane receptors and transporters, some of which are highly conserved across the evolution of life on earth. But neurons adapted many functions that single cells use to interact with the environment in order to interact with each other.

Detecting other cells: Hormones and neurotransmitters

Even primitive single-celled and small multicellular organisms respond to the effects of other organisms around them. This happens via their metabolic waste products that signal overcrowding or the depletion of food resources. Neurons evolved the ability to include some specific substances in their waste excretions to signal to other neurons about the state of some part of the organism.

These signaling substances evolved to be secreted specifically into the extracellular space around cells in multicellular organisms as hormones. The next step was the extension of a cellular process, such as an axon, from one cell to the vicinity of several distant specific cells where a specific signaling substance, called a *neurotransmitter,* was released. Now, instead of a multicellular signaling soup, there are circuits.

Detecting energy

Although single-celled organisms have membrane receptors that can detect light, heat, and pressure, multicellular organisms devote large, complex cell systems for detecting these and other forms of environmental energy. Cellular systems allow the production of lenses in the visual system for seeing and mechanical amplification in the auditory system for hearing, to name but two examples. Cellular systems in multicellular organisms allow energy detection to be amplified and differentiated, which supports nuanced, complex behavioral outcomes based on the detection.

Cellular motors

Single cells move via cilia, flagella, and other mechanisms such as amoeboid movement. Multicellular organisms use cilia to move substances within the body, but moving the entire body requires other mechanisms.

Cilia and flagella

Cilia are common in multicellular organisms. Motile cilia on cells in the lungs remove debris by carrying it up the windpipe. Immotile or primary cilia have evolved in many multicellular animals into sensory receptors, such as photoreceptor outer segments where the light-absorbing photopigment molecules are located. Auditory hair cells and some olfactory receptors may also be derived from cilia. Flagella are used by sperm cells to propel themselves. However, moving an entire large body via cilia or flagella is not very effective, particularly on land.

Contraction

Animals evolved specialized cells called muscle cells, for movement. Muscle cells work by contracting. In voluntary skeletal muscle, muscle cells contract by being driven by motor neurons. A large group of contracting muscle cells pulls on a tendon that is attached to a bone, moving the joint.

REMEMBER

Neurons are necessary for coordinated movement in multicellular animals. Different muscles must be contracted in an organized manner, and information from the senses must be sent to remote parts of the body neurons to coordinate movement.

Neurons accomplish their role of coordinating and communicating activity across the body though chemical communication and electricity. The electrical properties of neurons allow them to communicate information precisely across long distances to specific target cells. In the case of connections to muscles, motor neurons produce movement by inducing their target muscle cells to contract.

Coordinating responses in simple circuits

Nervous systems are complex and hard to study. The human brain has been estimated to contain about 100 billion cells (a recent estimate that used a novel method of counting neural nuclei in emulsified brains produced a figure of 86 billion). All these neurons likely have from 100 trillion to a quadrillion synapses between them. This presents the challenges that we don’t know how single cells work, really, and we don’t know or cannot even count all the connections between them. So, where do we start?

People often wonder why scientists study the nervous systems of flies, worms, and squids. The reason is that these systems often have advantages in that the cells are fewer, bigger, or more amenable to genetic manipulation. Hodgkin and Huxley won the Nobel Prize for deducing the ionic basis of the action potential in the squid giant axon, which is almost a millimeter in diameter and can be handled and impaled with microelectrodes. It is also possible to squeeze out its internal contents and replace them with a specified salt solution by which it could be determined which ions flow which way through the membrane during electrical activity.

Many invertebrates such as worms and insects have less than a few thousand neurons that are more or less the same from animal to animal. Individual neurons in specific places are even numbered and named in some species. This vastly simplifies the problem of working out a complete neural circuit, including which neurotransmitters are used by which neurons to activate other neurons, and how all the electrical activity is integrated.

Recent progress has been made in making model systems from mammals, using either brain slices or neural tissue cultures that can be mounted on a microscope and recorded and stimulated under well-controlled conditions.

Robotics and bionics

Many scientists feel that we only understand a system when we can simulate it. This involves creating an artificial nervous system that simulates some properties of real ones. In robotics, behavior is simulated. A robot may perform some task, like welding in a car factory, that is otherwise done by intelligent humans. The electronic controllers of such robots can involve the use of neuron-like elements called artificial neural nets (ANNs) that emulate biological control systems. However, most controllers are written in standard computer languages using mathematical algorithms that may function quite differently from biological organizations.

Bionics is the field of applying biological principles of operation to man-made devices. An airplane is a bionic derivative of bird flight, which, however, differs in using engines for thrust rather than flapping wings. A recent use of bionics in computation involves devices called *memristors* that are integrated circuit devices that act like modifiable synapses between neurons. At this point, it's unclear whether memristors devices will have advantages for computing compared to traditional electronic computation done with transistors. They may, however, become a useful tool for simulating complex nervous systems to understand them.

Organizing the Nervous System

The study of the nervous system intrinsically involves many fields. Neurobiology, our focus here, depends on 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 the system does, how it's built, and how it works. We try to do these things by considering first various subsystems of the brain and nervous system, and then looking carefully at function in the neural circuitry within those subsystems.

Movement basics: Muscles and motor systems

Chapter 5 deals with the main purpose of the nervous system, the production of movement. Generally, animals move and have nervous systems to control movement, whereas plants don't. Voluntary movement, controlled by the central nervous system, involves the contraction of striated muscle triggered by the receipt of *acetylcholine,* a neurotransmitter released by motor neurons.

Individual muscles are made of thousands of muscle cells innervated by several different types of motor neurons. The contraction of the muscle is produced by the coordinated activity of all these motor neurons that fire in a specified sequence and rate depending on the type of movement programmed, its speed, duration, and variation in load the limb experiences as it moves. Differences or errors between the central commands and actual limb position and acceleration are reported by sensory neurons in the muscles, tendons, and joints that relay this information to the spinal cord in a feedback loop that adjusts the motor neuron output to match the upper-level command goal.

REMEMBER

The entire frontal lobe of the brain exists primarily to program and organize goal-directed movement. An abstract goal, such as hitting a tennis ball back into your opponent's court, is translated into a sequence of leg, torso, and arm movements to accomplish this goal. These sequences are programmed into the motor cortex following practice. This practice involves learning sequence timing with the help of the cerebellum. The cerebellum is involved in learning and setting up predictive, feed-forward control for appropriate timing of sequences that transition more rapidly than feedback spinal sensory control could correct.

The spinal cord and autonomic nervous system

The spinal cord is like a subcontractor of the brain that executes the brain's instructions and reports on their progress. The spinal cord is part of the central nervous system, contiguous with it as it merges with the medulla of the brainstem. Chapter 6 discusses its basic organization.

REMEMBER

The spinal cord is the transition below the neck between the central and peripheral nervous systems. The peripheral nervous system includes the motor neuron axons that originate within the spinal cord gray area and project from the cord to synapse on muscle cells. Sensory neurons — whose cell bodies are located in dorsal root ganglia just outside the spinal cord — send one axon collateral to the periphery to elaborate into a sensory receptor, while the other collateral makes conventional synapses in the spinal cord gray area for both local circuit spinal feedback control and for relaying sensory information to the brain.

The autonomic and enteric nervous systems are involved in body *homeostasis* (keeping the body's major systems stable and functioning) through controlling glandular secretions, heart rate, respiration, and smooth muscle function. The autonomic nervous system has major subdivisions into sympathetic and parasympathetic branches that tend to oppose each other's actions. The sympathetic system prepares us for action in the fight-or-flight mode, while the parasympathetic system organizes resources for digestion, and the maintenance and conservation of energy.

The brainstem, limbic system, hypothalamus, and reticular formation

When we look at a human brain from above, almost all that we see is neocortex. Students beginning to study the brain often mistakenly think that the neocortex is the real, important part of the brain that has largely superseded phylogenetically older structures that are now almost vestigial and unnecessary (like the appendix).

This is an understandable mistake. However, non-mammalian vertebrates like lizards, frogs, and crocodiles execute complex behavior without any neocortex. Some mammals have very little neocortex as well. The relationship between the neocortex and "lower" brain areas is as much their servant as master, an idea Chapter 7 explores.

The brainstem is not only a transition region between the spinal cord and higher brain centers, but an essential integration and control center by itself. The brainstem includes the medulla at the intersection with the spinal cord, the pons just above the medulla, and the midbrain above that. The cerebellum hangs off the back of the brain behind the pons. The brainstem nuclei convey information between the senses and the spinal cord and higher brain centers. Brainstem nuclei also control essential aspects of homeostasis such as the regulation of heart rate, respiration, and temperature.

TIP

Limbic system is an archaic term for a diverse set of subcortical brain areas that are thought to control instinctive behaviors. Areas included in the limbic system's original formation include the hippocampus, amygdala, and cingulate cortex. Chapter 7 discusses how these areas interact with neocortex and other parts of the brain, not as a modular system, but as a set of crucial brain areas each with distinct functions.

The hypothalamus sits just above the pituitary gland and receives sensory input from the autonomic nervous system. It controls many homeostatic processes (such as circadian rhythms — the body's internal "clock") by secretions of hormones into the bloodstream and by projecting to the pituitary, which itself secretes hormones.

TIP

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

Basal ganglia, cerebellum, motor and premotor cortex, and thalamus

Chapter 8 takes up the basal ganglia, major controllers of behavior. The major basal ganglia nuclei include the caudate and putamen, which together make up the input region called the *striatum.* The globus pallidus is the major basal ganglia output to the motor portion of the thalamus, which projects and receives input from motor areas in the frontal lobe. The basal ganglia nuclei interact extensively with the substantia nigra in the midbrain, and the subthalamic nucleus.

The cerebellum is a motor learning and coordination center. It receives sensory input from spinal sensory neurons and cranial nerves of the vestibular and visual systems. Its major output is to motor thalamus that projects to frontal motor cortex. The cerebellum is necessary for learning coordinated, well-timed movements. It operates as a feed-forward controller that generates error signals used to reprogram motor areas such as premotor cortex to generate appropriate limb movements.

Two frontal areas just anterior to primary motor cortex, the supplementary motor area (SMA) and premotor cortex (PMC), contain motor programs that command and coordinate multi-limb movements to accomplish goals. One main difference between these two areas is that motor programs in SMA tend to be those that we can learn to do with little sensory feedback, such as typing. PMC control tends to occur when sequences are being learned, and depends more on peripheral feedback and cerebellar error signals.

The thalamus is often called the gateway to the neocortex, since all senses — except for some of *olfaction* (the sense of smell) — relay through it. But the neocortex projects back extensively to the thalamus. These back projections come from "higher" cortical areas, as well as from the primary areas that receive inputs from that area of the thalamus.

TIP

The gateway metaphor for the thalamus implicitly makes the neocortex the real seat of neural control and computation. The thalamus is the modulator of transmission to the cortex, emphasizing some pathways at the expense of others as a mediator of attention. A different metaphor for thalamic-cortical interactions is that the thalamus is running the "main" program, which makes "subroutine" calls to the neocortex for some detailed neural computations. This makes processing in the thalamus the primary controller of brain activity, including consciousness (see Chapter 14). Activity in the neocortex becomes the content of that consciousness. It's too early to say whether this subroutine metaphor will be as useful as the gateway metaphor has been.

The neocortex

The neocortex is one of the most important "inventions" of mammals. It dominates the mammalian brain in volume, particularly in primates. One of the most remarkable properties of the neocortex is that it has the same six-layered structure virtually everywhere, with the same cell types in what appears to be the same general minicolumn circuit. This is in stark contrast to the rest of the brain, where each area tends to have its own distinct set of cell types and neural circuits.

TIP

Mammals became the dominant land animals on earth after the demise of the dinosaurs about 65 million years ago. Some neurobiologists conjecture that mammals were able to rapidly diversify into all the niches abandoned by the extinction of the dinosaurs, as well as many new ones, by expanding the standard neocortex circuit for processing whatever visual, auditory, or fine motor acuity that niche demanded.

Neocortical processing power is primarily a function of area. Increased area in neocortex has two main uses:

- Increasing "acuity," whereby, for example, a larger area can support a higher density of peripheral receptors, such as retinal ganglion cells in the fovea or mechanoreceptors in the fingertips.
- Increasing the number of processing stages in a hierarchy of "association" areas that are increasingly specific and powerful with respect to particular features. Examples are the fusiform face area that allows you to instantly identify thousands of faces that all have the same major features (eyes, nose, mouth) in the same relative positions.

TIP

The neocortex goes digital

The expansion of the neocortex is reminiscent of the transition in the 1960s from analog to digital computers. When vacuum tubes and then transistors were made and handled individually, the most efficient control circuits were those in which a small number of devices modeled the control environment and generated a continuous control output from continuous inputs via the model.

But when integrated digital circuits arose using thousands and millions of transistors, it became more efficient to represent the control environment on standard microprocessors using software. This provided the advantages of *acuity* (insensitivity to transistor parameter values) and *adaptability* (software can be changed and augmented easily). The commonality of the representation and transformation of information in the cortical minicolumn appear to be an essential basis of its success in taking over the brain, and in mammals, including humans, taking over the earth.

Perceiving the World, Thinking, Learning, and Remembering

Different parts of the brain do different things. The front of the brain in the frontal lobe controls movement, the back and sides of the brain process sensory information. Specialized memory areas perform certain memory functions — the hippocampus and amygdala, for example. Chapters 10 through 14 deal with pathways and brain areas that process sensory information and memory, and produce motor output and thought.

Looking at vision and audition

The standard list of five major senses consists of vision, hearing, skin sensation, taste, and smell. The senses of limb position (called *proprioception*) and limb movement and acceleration (called *kinesthesis*) are built along similar lines and pathways with skin sensation.

Chapter 10 deals with vision and audition, starting with the peripheral receptors in the eye and ear, and marching up the projection pathways through the thalamus and onto primary, secondary, and higher-order cortical processing areas. In many mammals, particularly primates, visual processing dominates the brain — so much so that just less than 50 percent of the neurons in the brain have their activity modulated by visual input. 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.

Feeling, smelling, and tasting

Skin sensation is composed of a group of different types of sensory capabilities controlled by different receptors in the skin and a few other places, such as the mouth and trachea. Mechanoreceptors detect shallow and deep pressure, applied constantly or intermittently. Cold and warm temperature receptors respond to skin temperatures below or above body temperature. Pain receptors respond to mechanical or chemical inputs likely to cause injury.

The sense of smell is mediated by several thousand different receptor types in the olfactory organ in the roof of the nasal cavity. Evolutionary evidence suggests that some of the earliest neocortex in mammals may have been devoted to sorting out and identifying what produced the smells detected by the olfactory receptors.

A dog has about one billion olfactory receptors, a number comparable to the total number of neurons in its entire brain. I'm sure my dogs sniffing around the yard every morning know what was there last night, and probably when, and probably what each critter did, from the smells left over.

The olfactory system is unique in being divided between a pathway that projects (although indirectly) through the thalamus, of which we are aware, and a pathway that is non-thalamic, which influences our behavior, but of which we are not directly aware.

The sense of taste is mediated by salt, sweet, sour, and bitter receptors located mostly on the tongue. Some taste researchers also include the MSG taste, umami, as a fundamental taste.

Learning and memory: Circuits and plasticity

A behavioral hallmark of mammals is they can change their behavior through learning. High-level learning involves a neural representation of both an event and its context. Much of this representation occurs in the lateral prefrontal cortex as what is called *working memory.* This area of cortex has extensive connections with the hippocampus, where modifiable synapses containing NMDA receptors abound. Reciprocal connections between the hippocampus and the neocortical areas that originally represented that which is to be remembered instantiate the memory "trace" back in those areas of the neocortex.

The finding that the neocortex represents both original sensory input and its memory has profound implications for understanding what memory is. Many neuroscientists now believe that memory is intrinsically reconstructive — a hallucination, if you will. This is a very different metaphor from the token look up and address model taken from computer science. One important aspect of the reconstructive aspect of memory is that the act of reconstruction can distort the memory. Suggestions, guesses, and events after the memory can affect the reconstruction such that they become part of, and indistinguishable from, subsequent reconstructions.

The neurobiology of memory depends both on modifiable synaptic weights, such as with NMDA receptors in hippocampus and cortex, and the creation of new neurons in memory areas such as the hippocampus. The discovery of the birth of neurons in the adult hippocampus overturns the old idea of zero neurogenesis in the adult brain. Some senile dementia and even depression appear to be associated with failure of this mechanism.

The frontal lobes and executive brain

The frontal lobes are responsible for planning and executing behavior. Generally speaking, the output of the frontal lobe is in its most posterior portion, the primary motor cortex. Neurons in primary motor cortex send their axons down the spinal cord (or out some cranial nerves) to drive motor neurons that cause muscles throughout the body to contract.

Anterior to the primary motor cortex are the supplementary motor area and premotor cortex that organize the firing of groups of muscles. Anterior to those areas are the frontal eye fields and other areas called prefrontal cortex (even though they are in the frontal lobe) that are involved in more abstract aspects of planning.

It is generally held that there is 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. Some exceptional non-primate mammals such as the echidna have large frontal lobes, however. This has led to debate among neuroscientists about whether these frontal areas are really homologous across mammalian species. Whatever the result of that debate, we know that damage to prefrontal cortex in humans produces distinctive cognitive deficits such as impulsive behavior and profound changes in affect.

Language, emotions, lateralization, and thought

True grammatically ordered language distinguishes humans from all other species on earth. Recent evidence has suggested an important role for a gene called FOXP2 in generating language capability, although how this gene changes the brain to allow language isn't clear.

The human brain does not contain any distinct anatomical structures or types of neurons associated with language. The human brain areas most crucial for language, Wernicke's and Broca's areas on the left side (in most humans), have homologous areas in other primates, but these areas do not support language. Yet all normal human infants learn, without any explicit instruction, whatever language to which they are exposed, but other animals do not learn grammatical, word-order based language despite extensive instruction.

The capacity for learning language is built in, but neuroscience does not now know how. One clue may be brain lateralization, however. Left- versus right-side specialization for some types of audio processing and production exists in other mammals, and even some birds, but is nowhere near as extensive as in humans.

TIP

A similar association exists with right-hand dominance, driven by the left side of the brain, which is more extensive in humans than any other animal. Chimpanzees, for example, may be relatively right- or left-hand preferring, but most have no overall tendency to be strongly right-handed or left-handed, the way humans do.

Neuroscience's view of emotions has changed markedly in the last decades. Earlier views regarded emotions as leftovers from our evolution from non-rational species. *Star Trek*'s Mr. Spock could be taken as a model of a superior, more evolved humanoid. However, we now know that emotions are a means of nonverbal communication within our brains. Hunches and anxiety in certain situations are signs of danger and the need to be cautious.

TIP

We see the usefulness of this nonverbal information in people with damage to the orbitofrontal cortex or amygdala. They may gamble recklessly or commit social faux pas because they lack internal feelings about the mistakes they're making.

Developmental, Neurological, and Mental Disorders and Treatments

One of the most important reasons to understand neurobiology is to understand mental disorders and treatments. The good news is that great progress is being made in this field now. We know the genetic bases of many developmental disorders, such as Fragile X and William's syndrome. The bad news is that many disorders remain that we do not know about, and, even among disorders with known genetics, how the gene alteration produces the disorder, and what to do about it, are not clear. Chapters 15 through 18 discuss the background and current treatment approaches (if any) of many common neurological disorders.

Developing the brain and nervous system

The set of genes that define an organism is not a blueprint that is executed by a builder, but a set of procedures that brings about the development of the organism.

TIP

A useful metaphor is an ant hill or termite mound. No master ant or termite knows how to build a hill or mound and directs the other insects. Instead, ants and termites respond to each other, and to the environment, by digging holes and gluing arches together. Some holes and arches reach a critical mass that causes nearby insects to concentrate on those structures and related structures, which triggers the completion of the insect home as though its builders were following a design.

Developing cells have genetically coded responses to substances they detect by their membranes or ingest, including cell identity and brain location marker molecules. Cell responses include movement, division, and secretion of other markers and agents. The interactions among cells that have these responses in the embryological environment builds the brain.

Much of the genome is only expressed extensively during development, a time when the organism is also particularly susceptible to toxins that mimic or interfere with these markers and agents. The result of this interference is the construction of an improperly set-up brain, which is typically much worse than inferring temporarily with a properly constructed brain later in life, which often can be reversed.

Movement disorders and symptoms

Movement disorders can originate with brain damage that compromises the control of movement, or neurons that drive muscles, or the muscles themselves. Chapter 16 discusses some of the most common movement disorders. Cerebral palsy and epilepsy typically involve brain damage. Multiple sclerosis is caused by demyelination of axons of motor and other neurons. *Myasthenia gravis* is an autoimmune disease involving the cholinergic receptors on muscle cells.

Some well-known movement disorders, such as Parkinson's and Huntington's diseases, occur only later in life. Neither of these diseases is curable, but a number of treatments can partially alleviate the symptoms of Parkinson's disease. Accidents involving brain or spinal trauma still produce many cases of paralysis every year. Extensive research efforts using stem cells, neural growth factors, and electrical stimulation continue to be made for these problems.

Neural dysfunctions and mental illness

The history of clinical thought on mental illness is a pendulum ride between organic and environmental causes. In the United States, particularly, the dominance of behaviorism in academic psychology and psychiatry was associated with behavioral and cognitive therapeutic strategies based on "undoing" some sort of bad environmental influence or improper response to a relatively normal environment.

Knowledge of genetics, neurotransmitter systems, and the development of neurotransmitter-analog drugs led to pharmacological treatments that were at least partially effective in many psychiatric patients for whom traditional therapy had provided no relief. Schizophrenia and autism are cases in point. In the mid 20th century, the detection of schizophrenia or autism often was treated by family therapy sessions around behavioral theories such as withdrawn, uncaring so-called "refrigerator mothers" being the cause of these disorders.

It is now clear that both schizophrenia and autism have high heritability, although environmental factors are undoubtedly important in the expression and outcome of the disorder. Pharmacological agents deal well with many of the positive symptoms of schizophrenia such as hallucinations. But both schizophrenia and autism have multiple genetic causes, and the relation between the genetic anomaly and the neural dysfunction leading to the phenotype are poorly known. This situation is unfortunately also the case with many other mental disorders, including depression.

Repair and enhancement with artificial brains

Humans increasingly are electronically connected to each other through computers, cellphones, and soon, wearable devices like watches and electronic eyeglasses. It may be a short time before some of this technology is implantable. Brain implants may allow people who are paralyzed to operate computers or control their own or prosthetic limbs.

Deep brain stimulation, originally used widely to relieve Parkinson's disease symptoms, may also be effective in treating some types of depression. Transcranial magnetic stimulation may also mitigate depression without many of the side effects of electroconvulsive therapy (ECT, commonly referred to as "shock treatment"). Transcranial electrical stimulation has been shown in numerous studies to increase learning rates. A new term *electroceuticals* has been introduced for the field of electrical brain stimulation for therapeutic effect. Brain scientists live in exciting times!