

10 Principles of Neocortical Function

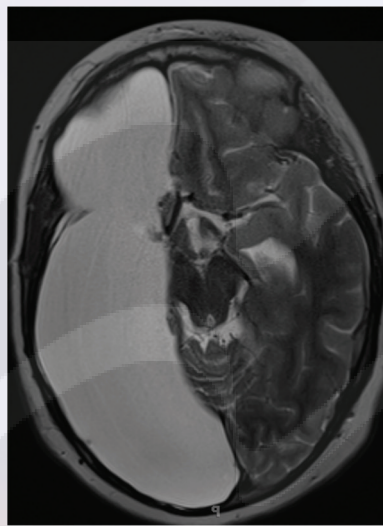


PORTRAIT

Hemispherectomy

A.R. was a strictly average boy until the age of 11, when he developed seizures on only the right side of his body. In time, persistent right-side weakness emerged, along with increasing difficulty talking, or **dysphasia**, impairment of speech caused by damage to the CNS. Although A.R. was admitted to the hospital many times over the next 6 years, the cause of his seizures and language and motor problems remained undetermined. He was initially right-handed but became unable to use that hand and began to write and draw with his left hand.

By age 15, A.R.'s IQ score had dropped by 30 points, and by age 17, his language and emotional problems were severe enough to render psychological testing impossible. At 17, his condition was diagnosed as Rasmussen encephalitis, a chronic brain infection that slowly leads to a virtual loss of function in one cerebral



hemisphere. Because the only successful treatment is removal of the diseased tissue, most of A.R.'s left cerebral hemisphere was surgically removed, a procedure called **hemispherectomy**. (The adjoining postoperative MRI scan shows a patient's brain in dorsal view after a left hemispherectomy.)

When A.R. was reassessed 10 years later, at age 27, he showed remarkable improvement. His oral language skills appeared to be average. He communicated freely and could both initiate and respond to conversation. He was, however, functionally illiterate, unable to read or write except at a most basic level.

His motor skills also had improved. He could move about on his own, although he still had a significant limp and could lift his right arm only to shoulder level. He could also open and close his right hand to grasp objects.

People can lose enormous amounts of cerebral tissue and still retain remarkable cognitive and motor abilities. The achievements of hemispherectomy patients such as A.R., even those with severe neuron loss in both hemispheres, prompt the question: What roles do the cerebral hemispheres and subcortical regions play in controlling behavior? To search for answers, in this chapter we focus on the CNS's hierarchical organization from spinal cord to cortex, the structure of the cortex, functional theories of brain organization, and the principles of the organization of neuronal networks in the cortex. We conclude by considering another question: Do human brains possess unique properties?

10.1 A Hierarchy of Function from Spinal Cord to Cortex

Within the brain's functional hierarchy, higher levels provide an animal with more precision and flexibility in behavior. A.R.'s intelligence test score was 70 (borderline intellectually disabled) after his surgery, much below his childhood IQ score of about

100 (average). Although severely impaired, A.R. nonetheless functioned rather well given that so much of his brain was gone, for two reasons:

1. **Brain plasticity.** The brain's considerable capacity for change in response to experience, drugs, hormones, or injury is due to its plasticity, as is its ability to compensate for loss of function caused by damage. Rats or people with hemispherectomy, like A.R., have a unique organization of the intact hemisphere that is characterized by increased *intrahemispheric connections* (Kliemann et al., 2019).
2. **Levels of function.** Subcortical structures can mediate complex behaviors. The relationship of the cortex to subcortical structures is analogous to the relationship of a piano player to a piano. The cortex represents the piano player, producing behavior by playing on subcortical keys. This idea dates to Herbert Spencer's mid-nineteenth-century speculation that successive steps in evolution have added new levels of brain and behavioral complexity. John Hughlings-Jackson adopted Spencer's idea, and it became a central focus of neurological theories in the twentieth and twenty-first centuries (see Section 1.3).

Indeed, we can trace the focus on functional levels of nervous system organization in part to early findings that the brain has remarkable plasticity. In the past 50 years, it has become clear that both laboratory animals and humans can function surprisingly well with considerable amounts of the brain removed. At the time of his surgery, A.R. had no language ability at all, partly because the dysfunctional left hemisphere, where language functions are concentrated in most of us, was interfering with the right hemisphere's ability to engage in language functions. Shortly after the left hemisphere was removed, at least some of A.R.'s language functions reemerged, as though the left hemisphere had been suppressing functioning in the right.

We must hasten to point out that the mere fact that people can lead fairly normal lives with large amounts of brain tissue missing does not imply that those brain parts are unnecessary. People can compensate for lost brain tissue just as they can compensate for lost limbs. But this ability does not mean that such people would not be better off with their limbs — or brain — intact.

Throughout the twentieth century, the capacities of animals with extensive regions of the nervous system removed were recorded in many neurologic studies. One study, conducted by Kent Berridge and Ian Whishaw (1992), examined grooming in the rat. Recall from Section 9.2 that rats (like other animals, including ourselves) begin by grooming the head and then work their way down the body. As illustrated in **Figure 10.1**, a rat begins to groom by using its paws, rubbing its nose with symmetrical circular movements. Then it sweeps its paws across its face and behind its ears before turning to lick its body. This series of actions can be divided into as many as 50 linked movements.

In examining this movement complex, Berridge and Whishaw found that many levels of the nervous system participate in producing the elements and the syntax (the organization) of grooming behavior: it is produced not by one locus in the brain but rather by many brain areas and levels, from the spinal cord to the cortex. These successive nervous system layers do not simply replicate function; rather, each region adds a different dimension to the behavior.

This hierarchical organization holds not only for grooming but also for virtually every behavior in which we (as well as rats) engage. Understanding the principle of hierarchical organization is critical to understanding how cortical control contributes to behavior. **Figure 10.2** diagrams some functions mediated at different anatomical levels in the nervous system. In the following sections, we note parallel functions that may exist in humans, as appropriate. We begin next with the “lowest” CNS level, the spinal cord, and then add structures to see how the corresponding behaviors increase in complexity.

The Spinal Cord: Reflexes

Section 3.4 explains the effects of spinal-cord injury, including paraplegia and quadriplegia, and describes how the late actor Christopher Reeve's spinal cord was severed just below the brain in an equestrian accident. Reeve, who portrayed Superman in a

Figure 10.1 ▼

Grooming Sequences in the Rat

Rats have a fixed grooming sequence, which starts with ellipical strokes to the head,...



...followed by grooming of each side of the face.



They move to the ears, using bilateral strokes,...

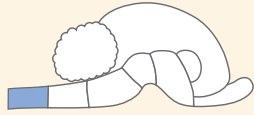
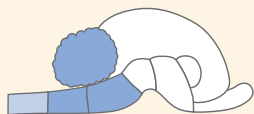


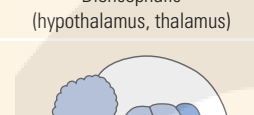



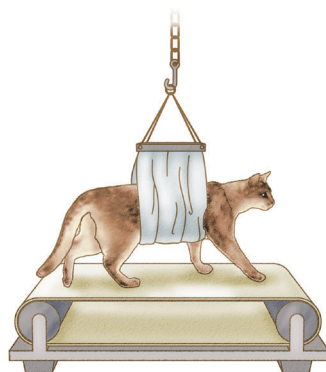
...and then continue moving toward the rear of the body.



Figure 10.2 ►**Central Nervous System**

Hierarchy Anatomical and behavioral levels in the CNS, shown here in an inverted hierarchy from spinal cord to cortex, highlighting the highest remaining functional area at each level.

Highest remaining functional area	Behaviors
 Spinal (spinal cord)	Reflexes: Responds to appropriate sensory stimulation by stretching, withdrawal, support, scratching, paw shaking, etc.
 Low decerebrate (hindbrain)	Postural support: Performs units of movement (e.g., hissing, biting, growling, chewing, lapping, licking) when stimulated; shows exaggerated standing, postural reflexes, and elements of sleepwalking behavior.
 High decerebrate (midbrain)	Spontaneous movement: Responds to simple visual and auditory stimulation; performs automatic behaviors such as grooming; and when stimulated performs subsets of voluntary movements (e.g., standing, walking turning, jumping, climbing).
 Diencephalic (hypothalamus, thalamus)	Affect and motivation: Voluntary movements occur spontaneously and excessively but are aimless; shows well-integrated but poorly directed affective behavior; thermoregulates effectively.
 Decorticate (basal ganglia)	Self-maintenance: Links voluntary movements and automatic movements sufficiently well for self-maintenance (eating, drinking) in a simple environment.
 Typical (cortex)	Control and intention: Performs sequences of voluntary movements in organized patterns; responds to patterns of sensory stimulation. Contains circuits for forming cognitive maps and for responding to the relationships between objects, events, and things. Adds emotional value.

**Figure 10.3 ▲****Spinal Animal Walking on Treadmill**

series of movies beginning in 1978, survived for nearly a decade after his injury but was unable to move and unable to breathe without the aid of a respirator. What behaviors could his spinal cord initiate without any descending influence from the brain?

Like Christopher Reeve, an animal whose spinal cord is disconnected from the brain (spinal-cord transection) is unable to move voluntarily because the brain cannot communicate with the spinal neurons. Nonetheless, the intact spinal cord can mediate many reflexes, such as limb approach to a tactile stimulus and limb withdrawal from a noxious stimulus (Grillner, 1973).

The spinal cord also contains the neural circuitry to produce stepping responses and walking, provided that body weight is supported. For example, if **spinal animals** (in which an injury has severed the connection between the spinal cord and the CNS) are suspended in a hammock and placed such that their limbs are in light contact with a moving treadmill, their legs will begin to make stepping movements automatically, as illustrated in **Figure 10.3**. This behavior tells us that circuitry in the spinal cord, not the brain, produces the stepping movements. The brain's role is control: to make those movements at the right time and place.

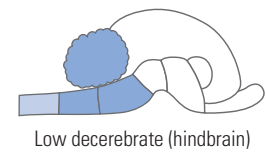
The Hindbrain: Postural Support

If the hindbrain and spinal cord remain connected after an injury but both are disconnected from the rest of the brain, the subject is called a **low decerebrate**. This type of injury produces a far different syndrome from that produced in an animal with a

spinal-cord transection. A spinal animal is alert; a person who has sustained such an injury can still talk, express emotion, and so on. However, a low-decerebrate animal has difficulty maintaining consciousness because many essential inputs to the brain regions above the injury are disconnected, presumably leaving the forebrain “in the dark.”

Sensory input into the hindbrain comes predominantly from the head and is carried over cranial nerves 4 to 12 (see Figure 3.14). Most cranial nerves also have motor nuclei in the hindbrain, whose efferent (outgoing) fibers control muscles in the head and neck. Sensory input to the hindbrain is not limited to the cranial nerves: the spinal somatosensory system has access to hindbrain motor systems, just as the hindbrain has access to spinal motor systems. But sensory input into the hindbrain of a low decerebrate can no longer reach the upper parts of the brain, resulting in a serious disturbance of consciousness.

The behavioral changes seen in low-decerebrate animals—including decerebrate rigidity (body stiffness due to excessive muscle tone) and narcolepsy (sudden loss of all body tone)—are paralleled in people who enter a persistent vegetative state (PVS) after the type of brainstem damage that essentially separates the lower brainstem from the rest of the brain. R. Barrett and his colleagues (1967) documented numerous cases. People in a PVS—such as Terri Schiavo (see Chapter 1 Snapshot)—may alternate between states of consciousness resembling sleeping and waking, make eye movements to follow moving stimuli, cough, smile, swallow food, and display decerebrate rigidity and postural adjustments when moved. With extraordinary care, PVS patients may live, little changed, for months or years.



The Midbrain: Spontaneous Movement

The next level in the brain organization hierarchy can be seen in an animal with an intact midbrain (mesencephalon) but lacking higher-center functioning. **High decerebration** results from damage that separates the diencephalon from the midbrain regions containing, in the tectum, the coordinating centers for vision (superior colliculus) and hearing (inferior colliculus) and, in the tegmentum, a number of motor nuclei. Visual and auditory inputs allow the animal to perceive events at a distance, and a high-decerebrate animal can respond to distant objects by moving toward them.

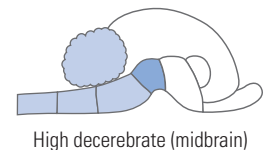
Bard and Macht (1958) reported that high-decerebrate cats can walk, stand, resume upright posture when turned on their backs, and even run and climb when stimulated. Bignall and Schramm (1974) found that kittens decerebrated in infancy could orient themselves toward visual and auditory stimuli. The animals could even execute an attack response and pounce on objects at the source of a sound.

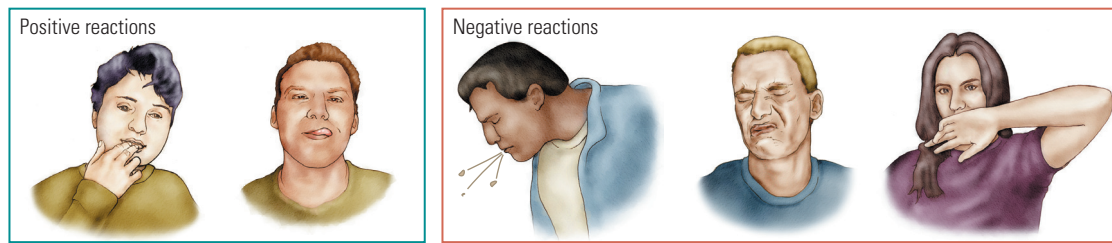
In fact, Bignall and Schramm fed the cats by exploiting this behavior: they placed food near the source of the sound. Attacking the sound source, the cats then consumed the food. Although the cats attacked moving objects, they gave no evidence of being able to see because they bumped into things when they walked.

These experiments demonstrate that all of the subsets of **voluntary movements**—movements that take an animal from one place to another, such as turning, walking, climbing, swimming, and flying—are present at the subcortical level of the midbrain. Animals typically use voluntary movements to satisfy a variety of needs—to find food, water, or a new home territory or to escape a predator, for example. Voluntary movements also are called *appetitive*, *instrumental*, *purposive*, or *operant*.

High-decerebrate animals can also effectively perform **automatic movements**, units of stereotyped behavior linked in a sequence. Grooming, chewing food, lapping water, and rejecting food are representative automatic behaviors of the rat. Also variously called *reflexive*, *consummatory*, or *respondent*, automatic behaviors generally are directed toward completing an act and are not directed specifically toward moving an animal from one place to another.

Grooming provides an excellent example of automatic behavior because it consists of many movements executed sequentially in an organized and stereotyped fashion (as described in Figure 10.1). Food rejection comprises a similarly complex behavioral series. If high-decerebrate rats are given food when they are not hungry, they perform a



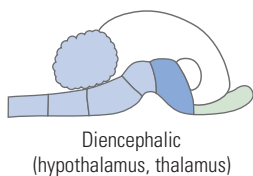
**Figure 10.4** ▲**Human Reactions to Taste**

Positive (hedonic) reactions, such as licking the fingers or lips, are elicited by sweet and other palatable tastes. Negative (aversive) reactions, elicited by bitter tastes (such as quinine) and by other unpalatable flavors, include spitting, making a face of distaste, and wiping the mouth with the back of the hand. (Information from Berridge, 1996.)

series of movements consisting of tongue flicks, chin rubbing, and paw shaking to reject the food. These behaviors are similar to the rejection behaviors of typical rats—as well as of people, as illustrated in **Figure 10.4**—in response to food they find noxious. If the animals are not sated, they will lap water and chew food brought to their mouths.

Among the accounts of infants born with large parts of the forebrain missing, one child studied by E. Gamper (Jung & Hassler, 1960) nearly a century ago had no brain above the diencephalon and only a few traces of the diencephalon intact. This mesencephalic child was, therefore, anatomically and behaviorally equivalent to a high-decerebrate animal. A mesencephalic child shows many behaviors of newborn infants, periodically sleeping and waking, sucking, yawning, stretching, crying, and following visual stimuli with the eyes. However, even though these children can sit up, they show little spontaneous activity and, if left alone, remain mostly in a drowsy state.

Yvonne Brackbill (1971) studied a similar child and found that in response to moderately loud sounds (60–90 decibels), this infant oriented to stimuli in much the same way as typical infants do. Unlike typical babies, however, this child's responses did not change in magnitude and did not habituate (gradually decrease in intensity) to repeated presentations. Brackbill concluded that the forebrain is not important in producing movements but is important in attenuating and inhibiting them. Babies born with such extensive brain abnormalities usually do not live long, and among those who live for several months—or even for years—the complex behaviors typically seen in infants do not develop.

**The Diencephalon: Affect and Motivation**

A **diencephalic animal**, although lacking the basal ganglia and cerebral hemispheres, has an intact olfactory system, enabling it to smell odors at a distance. The hypothalamus and pituitary also are intact, and their control over hormonal systems and homeostasis no doubt integrates the body's physiology with the brain's activity. Diencephalic animals thermoregulate, for example, but they do not eat or drink well enough to sustain themselves.

The diencephalon adds affective and motivational dimensions to behavior in the sense that it becomes “energized” and sustained. As mentioned earlier, high-decerebrate animals show many component behaviors of rage, but their behaviors are not energetic, well integrated, or sustained. Walter Cannon and S. W. Britton (1924) studied diencephalic cats and described what they called “quasi-emotional phenomena,” or sham rage, such as that usually seen in an infuriated animal. This affective behavior is inappropriately displayed and is thus called sham rage to distinguish it from the directed rage typical of a cat.

Bard removed varying amounts of forebrain and brainstem from cats and found that, for sham rage to occur, at least the posterior part of the hypothalamus must be intact. Clinical reports indicate that similar sham emotional attacks can occur in people who have hypothalamic lesions. These people show unchecked rage or literally die laughing. In addition to sham rage, another pronounced feature of a diencephalic animal's behavior is constant activity. For example, when placed in an open field, it wanders aimlessly.

Sham rage and hyperactivity suggest that the diencephalon energizes an animal's behavior, which may have led some researchers to consider the behaviors affective or

motivated. Perhaps a diencephalic animal's hyperactivity should be called *sham motivation* to distinguish it from a typical animal's goal-oriented behavior. Under appropriate forebrain control, the behavior can be released for functional purposes, but in the absence of that control, the behavior of a diencephalic animal is excessive and seems inappropriate (see Grill & Norgren, 1978).

The Basal Ganglia: Self-Maintenance

Decortication, removal of the neocortex, leaves the basal ganglia and brainstem intact. Decorticate animals have been studied more closely than any other neurologically impaired class because they are able to maintain themselves without special care in laboratory conditions.

The first careful experiments of decorticate animals were done by Friedrich Goltz (1960), who worked with dogs (see Section 1.3), but the most thorough studies have used rats as subjects (e.g., Whishaw, 1989). Within a day after surgery, rats eat and maintain body weight on a wet mash diet and eat dry food and drink water brought in contact with the mouth. With a little training in drinking (holding the water spout to the mouth), they find water and become able to maintain themselves on water and laboratory chow. They have typical sleep–wake cycles; run, climb, and swim; and even negotiate simple mazes. They can also sequence series of movements. For example, copulation consists of a number of movements that take place sequentially and last for hours, yet decorticate animals can perform these acts, as well as others including grooming, almost normally.

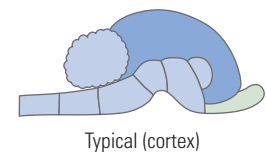
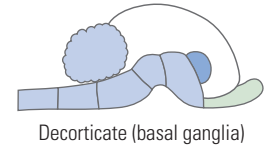
In sum, to a casual observer, a decorticate rat appears indistinguishable from normal animals. In fact, in laboratory exercises in which students are tasked to distinguish between normal and decorticate animals, not only do they find the job difficult, often they fail. A decorticate rat does indeed have a lot of behavioral difficulties, as we'll see in the next section, but seeing these problems requires a trained eye. All the elementary movements that animals might make seem to be part of their behavioral repertoire after decortication. They can walk, eat, drink, mate, and raise litters of pups in a seemingly adequate fashion, provided that they are housed in a small enclosed environment where they will not get lost.

What is observed in a decorticate rat, and what is presumably conferred by functions in the basal ganglia, is the ability to link automatic movements to voluntary movements so that the behaviors are biologically adaptive. A major part of this linking probably includes the inhibition or facilitation of voluntary movements. For example, the animal walks until it finds food or water and then inhibits walking to consume the food or water. Thus, the basal ganglia probably provide the circuitry required for the stimulus to inhibit movement so that ingestion can occur.

The Cortex: Intention

What the cortex does can be ascertained by studying what decorticate animals (with the neocortex alone removed or with the limbic system also removed) do not do. They do not build nests, although they engage in some nest-building behaviors. They do not hoard food, although they might carry food around. They also have difficulty making skilled movements with the tongue and limbs because they are unable to reach for food by protruding the tongue or by reaching with one forelimb.

Decorticate animals can perform pattern discriminations in different sensory modalities—but only if these tasks are relatively simple. For example, a decorticate animal could discriminate two pure tones but would be unable to distinguish complex sounds such as the noises from a lawnmower and from an automobile. The results of a series of experiments by David Oakley (1979) show that decorticate animals can perform well in tests of classical conditioning, operant conditioning, approach learning, cue learning, and pattern discrimination. These experiments confirm that the cortex is not essential for learning itself. However, decorticate animals fail at some



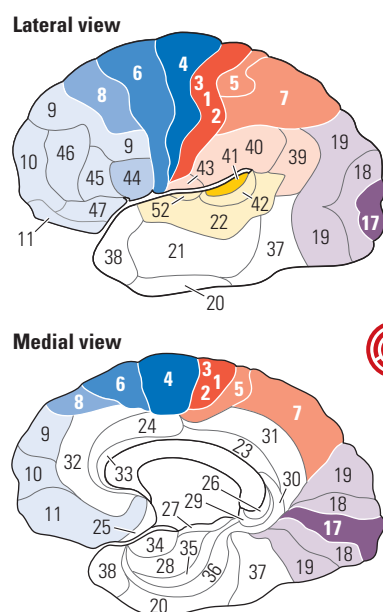


Figure 10.5 ▲

Brodmann's Map Lateral and medial views highlighted with primary, secondary, and tertiary (association) areas, as described by Paul Flechsig (1920) from his studies of myelin development in the cortex. The primary cortex is brightest (areas 4, 3-1-2, 41, 17), the secondary cortex is medium in tone, and the tertiary cortex is lightest.

types of learning, such as complex pattern discriminations and how to find their way around in a space.

The results of studies of decortication tell us that the cortex does not add much to an animal's behavioral repertoire in the way of new movements. Rather, the cortex appears to extend the usefulness of all behaviors or to make them adaptive in new situations. An animal without a cortex can see and hear and can use its limbs for many purposes, but a typical animal with a cortex can make plans and combine movement sequences to generate more complex behavioral patterns.

10.2 The Structure of the Cortex

As our summary of the behaviors of animals with only subcortical brain function makes clear, the cortex adds new dimensions to sensory analysis and new levels of movement control. What cortical structures permit these enhancements?

Section 1.4 explains the ideas behind topographic maps that divide up the cortex based on anatomical and functional criteria. Alfred Campbell published the first complete cortical map of the human brain in 1905, based on both cell structure and myelin distribution. Soon after, several alternative versions emerged, the most notable by Korbinian Brodmann, reproduced in **Figure 10.5**.

Based on his studies of myelin development in the cortex, Paul Flechsig (1920) divided cortical regions into (1) an early-myelinating primordial zone including the motor cortex and a region of visual, auditory, and somatosensory cortex; (2) a secondary field bordering the primordial zone that myelinates next; and (3) a late-myelinating (tertiary) zone that he called "association." The three zones are color-coded in Figure 10.5. Flechsig hypothesized psychological functions for his hierarchy: primary zones perform simple sensorimotor functions, whereas the secondary and tertiary zones conduct increasingly complex mental analyses.

Various cortical maps do not correspond exactly, and they use different criteria and nomenclature. As new staining techniques are devised, enabling a truly bewildering variety of subdivisions and redefinitions, estimates of the number of cortical areas in the human brain can range from the approximately 50 areas Brodmann mapped to more than 200! MRI analyses have allowed researchers to create brain atlases with a spatial resolution of about 1 mm. This voxel size (which refers to the resolution in a 3D scan, similar to pixel size in a 2D image) allows visualization of gross markers such as sulci, gyri, and subcortical nuclei. It does not allow fine-grained anatomical resolution of cortical regions at a cytoarchitectural level, however. Most recently, MRI has been combined with standard histological analysis to map the human brain objectively in a project known as BigBrain, described in the Snapshot.

Cortical Cells

Nerve cells are easily distinguished in the cortex as **spiny neurons** or **aspiny neurons** by the presence or absence, respectively, of dendritic spines. Much as thorns extend the surface area of rosebush branches, dendritic spines extend the dendrite's surface area. Spiny neurons are excitatory—about 95% of their excitatory synapses are found on the spines—and are likely to have receptors for the excitatory transmitter glutamate or aspartate. (For an extensive series of books on the structure of the cortex, see Peters & Jones, 1984–1999.)

Spiny neurons include **pyramidal cells**—so named for the shape of their substantial cell bodies, whose long axons generally send information from a cortical region to another area of the CNS (e.g., within the corticospinal [pyramidal] tracts described in Section 9.3). Spiny **stellate cells** are smaller star-shaped interneurons whose processes remain within the region of the brain where the cell body is located.

Pyramidal cells, which are the efferent projection neurons of the cortex, constitute the largest population of cortical neurons (70–85%). They are found in layers II, III, V, and VI.

SNAPSHOT

Mapping the Human Cortex



BigBrain, a high-resolution three-dimensional atlas compiled by researchers at the Montreal Neurological Institute and Germany's Forschungszentrum Jülich, was created by using a large-scale microtome to cut the brain of a 65-year-old female coronally into 7400 20-micrometer sections. The sections were stained for cell bodies (Nissl stain), digitized, and combined by a supercomputer. The freely available BigBrain atlas allows a microscopic view of the entire human brain.

BigBrain will enable testing of new hypotheses about brain connectivity and will redefine traditional neuroanatomy maps such as those created by Brodmann. Whereas these earlier neuroanatomical analyses were based on visual inspection of brain sections, the BigBrain project has used computer analysis to create a **gray level index (GLI)** that calculates brightness differences among the cell bodies and the **neuropil**. Neuropil is any area in the nervous system composed of mostly unmyelinated axons, dendrites, and glial cell processes that forms a synaptically dense region.

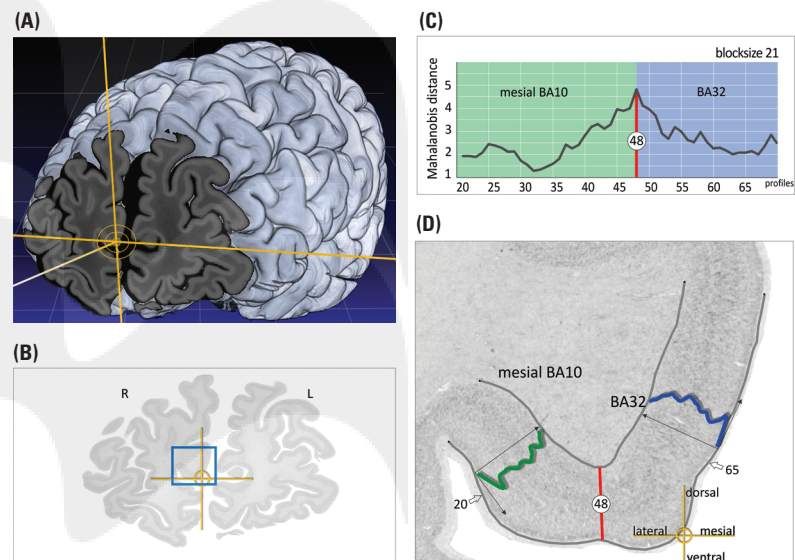
As shown in the accompanying illustrations, the shading pattern identified by the GLI differs significantly between areas. These differences allow the computer to identify objective borders between different regions. GLI analysis has allowed even more cortical regions to be identified than was possible with visual inspection alone.

One unexpected outcome of the BigBrain project is the finding that interbrain variability is much larger than anticipated, leading to the conclusion that neuroscientists cannot present a dogmatic map that represents “the” human brain. The borders of different regions in different people simply are not similar enough, and the total areal differences in a population are at least twofold different. By superimposing the maps of 10 to 20 brains, however, it is possible to create a single probability map that statistically estimates an “average” brain.

The BigBrain project now is expanding its analysis to generate a 3D map of cortical structure as way of bridging traditional 2D cytoarchitecture and modern 3D neuroimaging (see Wagstyl et al., 2018).

Amunts, K., Lepage, C., Boregeat, L., Mohlberg, H., Dickscheid, T., Rousseau, M.-E., Bludau, S., Bazin, P. L., Lewis, L. B., Oros-Peusquens, A. M., Shah, N. J., Lippert, T., Zilles, K., & Evans, A. C. (2013). Big-Brain: An ultrahigh-resolution 3D human brain model. *Science*, 340, 1472–1475.

Wagstyl, K., Lepage, C., Bludau, S., Zilles, K., Fletcher, P. C., Amunts, K., & Evans, A. C. (2018). Mapping cortical laminar structure in the 3D Big-Brain. *Cerebral Cortex*, 28, 2551–2562.



Defining cortical regions objectively. (A) Surface rendering of the three-dimensional reconstructed brain with the frontal pole (anterior part of the frontal lobe) removed. (B) Coronal section 6704 of 7400. (C) The GLI identifies a unique pattern for each cortical area, which allows (D) an objective distinction between cortical regions, in this case Brodmann's areas (BA) 10 and 32. (Republished with permission of American Association for the Advancement of Science, from Amunts, K., Cl. Lepage, L. Boregeat, H. Mohlberg, T. et al., “Big-Brain: An ultrahigh-resolution 3D human brain model.” *Science* 340 (6139) 1472–1475, June 2013, Figure 3. Permission conveyed through Copyright Clearance Center, Inc.)

In general, the largest cells send their axons the farthest. The pyramidal cells of layer V are the largest, projecting from the cortex to the brainstem and spinal cord. Those in layers II and III are smaller and project to other cortical regions, as diagrammed in **Figure 10.6**.

Aspiny neurons are interneurons with short axons and no dendritic spines. They are diverse in appearance, with different types named largely on the basis of the configurations of their axons and dendrites. One type of aspiny stellate cell shown in

Figure 10.6 ▶

Neocortical Cells The most important spiny neuron types, pyramidal cells and stellate cells, are elaborated here along with aspiny stellate and basket cells. The directions of the arrows indicate afferent (up, incoming) or efferent (down, outgoing) neuronal projections. (Research from Szentagothai, 1969.)

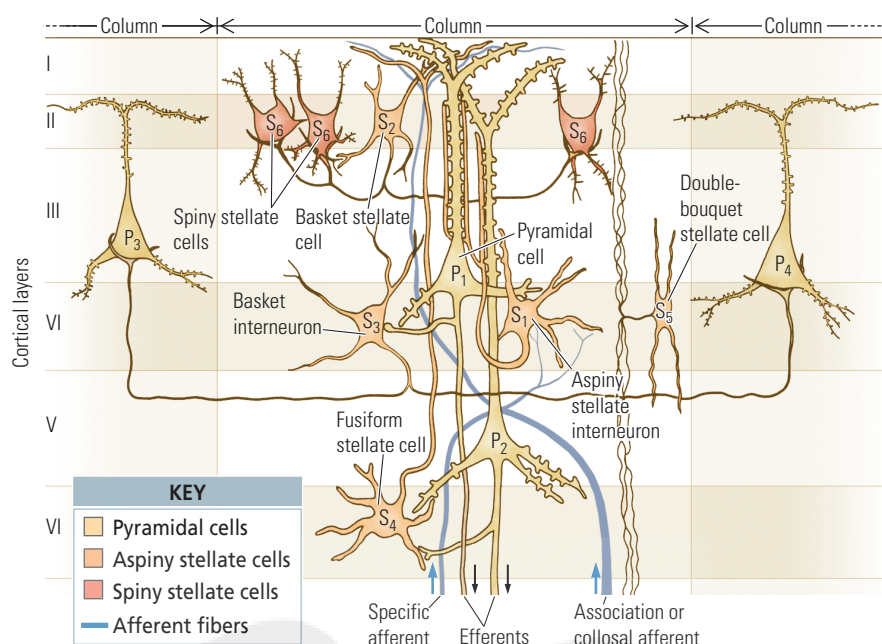


Figure 10.6 is called a *basket cell* because its axon projects horizontally, forming synapses that envelop the postsynaptic cell like a basket. Another, the *double-bouquet* type, has a proliferation of dendrites on either side of the cell body, much as if two bouquets of flowers were aligned stem to stem.

Despite differences in shape, all aspiny neurons are inhibitory and are likely to use gamma-aminobutyric acid (GABA) as a neurotransmitter. Aspiny neurons also use many other transmitters: virtually every classical transmitter and neuropeptide has been co-localized with GABA in aspiny cells. Thus, not only are aspiny cells morphologically diverse, they also show a remarkable chemical diversity.

The BigBrain project has mapped the distribution of excitatory (NMDA) and inhibitory (GABA) receptors, allowing identification of the “receptor fingerprints” for different cortical regions. The receptor maps can then be superimposed on GLI-based maps to yield an even finer identification of cortical regions. Not surprisingly, the receptor fingerprints highly correlate with the GLI profiles described in the Snapshot.

Cortical Layers, Efferents, and Afferents

Each of the four to six layers of the neocortex has different functions, different afferents, and different efferents. Cells of the middle cortical layers, especially in and around layer IV, constitute an input zone of sensory analysis: they receive projections from other cortical areas and from other areas of the brain. The cells of layers V and VI constitute an output zone, sending axons to other cortical areas or other brain areas.

Thus, the somatosensory cortex has a relatively large layer IV and a small layer V, whereas the motor cortex has a relatively large layer V and a small layer IV. **Figure 10.7** illustrates that the thickness of each layer corresponds to its function and shows that the various cortical layers can be distinguished by the neuronal elements they contain. The superficial layers (II and III) receive inputs from other cortical areas and can thus integrate information coming to layer IV as well as that from other cortical regions.

Another feature of cortical organization illustrated in Figure 10.7 is that afferents to the cortex are of two general types:

1. **Specific afferents** bring information (e.g., sensory information) to an area of the cortex and terminate in relatively discrete cortical regions, usually in only one or two layers. Specific afferents include projections from the thalamus as well as from the

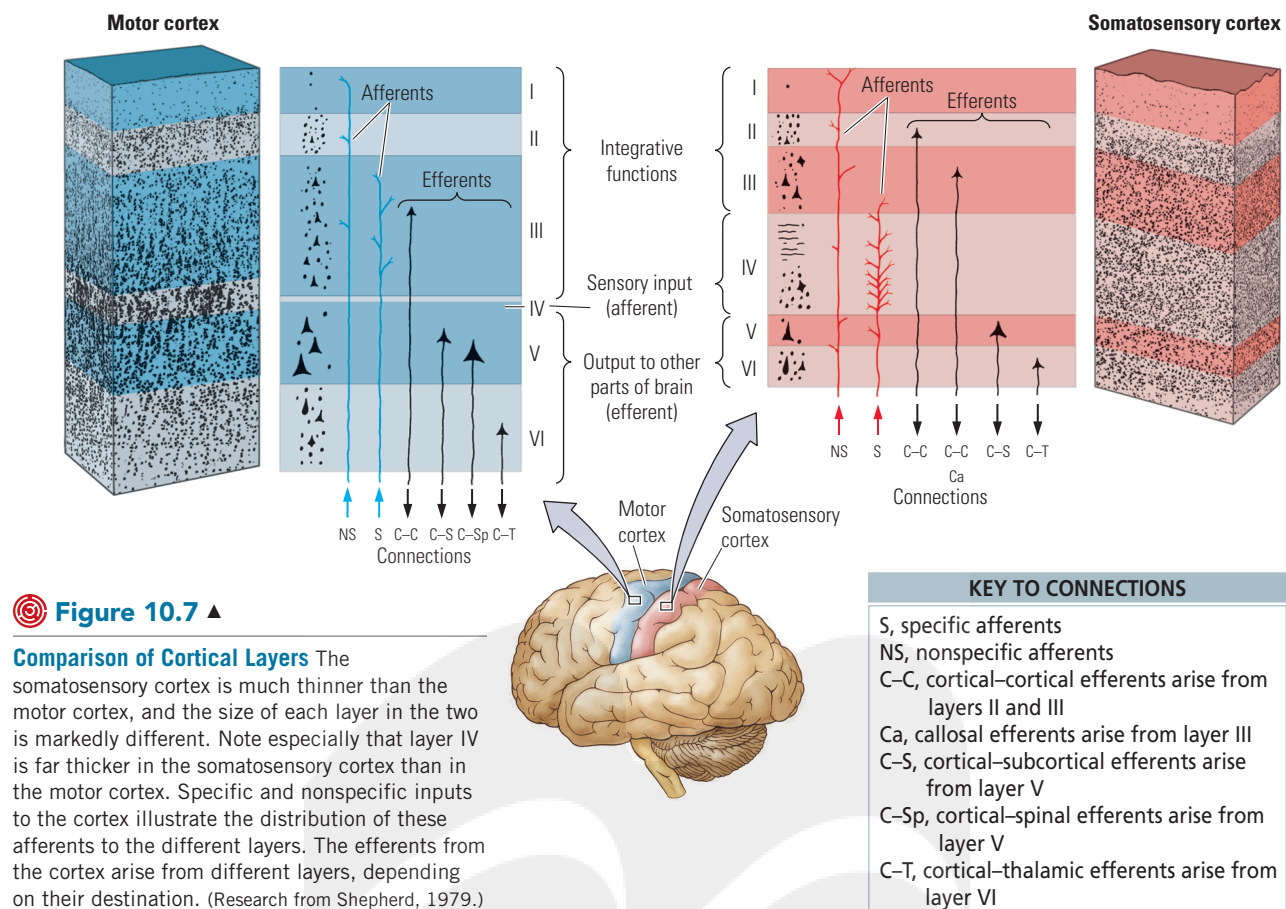


Figure 10.7 ▲

Comparison of Cortical Layers The somatosensory cortex is much thinner than the motor cortex, and the size of each layer in the two is markedly different. Note especially that layer IV is far thicker in the somatosensory cortex than in the motor cortex. Specific and nonspecific inputs to the cortex illustrate the distribution of these afferents to the different layers. The efferents from the cortex arise from different layers, depending on their destination. (Research from Shepherd, 1979.)

amygdala. Most of these projections terminate in layer IV, although projections from the amygdala and certain thalamic nuclei may terminate in the more superficial layers.

2. **Nonspecific afferents** presumably serve general functions, such as maintaining a level of activity or arousal so that the cortex can process information. They terminate diffusely over large regions of the cortex—in some cases, over all of it. Nonspecific afferents even release their transmitter substances into the extracellular space. Noradrenergic projections from the brainstem, cholinergic projections from the basal forebrain, and projections from certain thalamic nuclei are examples of nonspecific afferents. (Figure 5.19 diagrams the major neurotransmitter systems.)

Cortical Columns, Spots, and Stripes

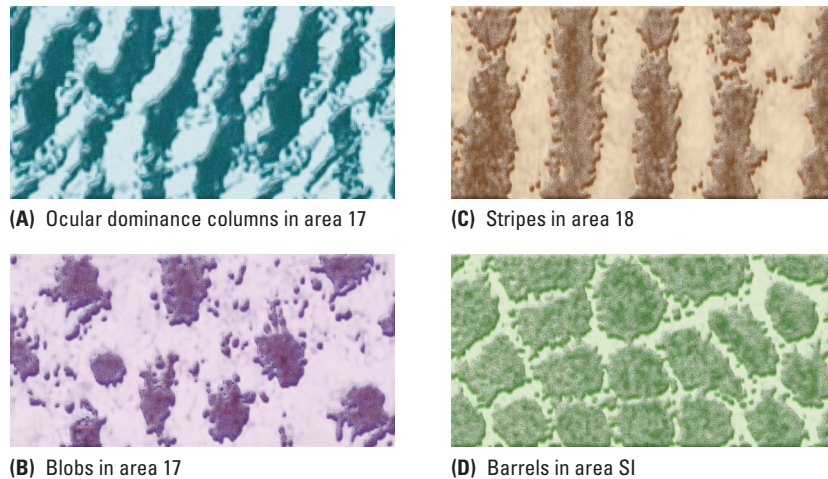
Most interactions between the cortical layers take place vertically, within the neurons directly above or below adjacent layers. Less interaction takes place with cells more than a couple of millimeters on either side. This vertical bias forms the basis for a second type of neocortical organization: **columns** or **modules** (see Figure 10.6).

Although these terms are not always interchangeable, the underlying idea is that groups of 150 to 300 neurons form minicircuits ranging from about 0.5 to 2.0 millimeters wide, depending on the cortical region. Evidence for some kind of modular unit comes principally from staining and probing. When the brain is cut horizontally and stained in special ways, patterns of spots or stripes in the cortex are visible (**Figure 10.8**). Some examples are as follows:

- If a radioactive amino acid is injected into one eye of a monkey, the radioactivity is transported across synapses to the primary visual cortex (region V1, or area 17). The radioactivity is not evenly distributed across the cortex, however; it travels

Figure 10.8 ▶**Cortical Spots and Stripes**

Staining reveals modular patterns.
(Research from Purves et al., 1992.)



only to places called *ocular dominance columns*, which connect with the affected eye (Figure 10.8A). The pattern of radioactivity seen in region V1 is a series of stripes, much like those on a zebra's coat.

- When a different technique is used, however, a different pattern emerges. If V1 is stained with cytochrome oxidase, which reveals areas of high metabolic activity by staining mitochondria, the area appears spotted. These spots, known as blobs, have a role in color perception (Figure 10.8B).
- Curiously, if the same stain is applied to area 18, a secondary visual region adjacent to V1, the pattern of staining looks more like stripes (Figure 10.8C) than like spots.
- If the primary somatosensory cortex (area S1) of a rat is stained with succinic dehydrogenase, the cortex shows a pattern of spots known as “barrels” (Figure 10.8D). Each barrel corresponds to a single vibrissa on the rat's face.

These examples illustrate that many types of cortical modules appear to exist and that the same stain shows a different modular organization in different regions.

A second way to demonstrate the modular organization of the cortex is physiological. If a microelectrode is placed in the somatosensory cortex and lowered vertically from layer I to layer VI, for example, all the neurons encountered appear functionally similar. Neurons in each layer are excited, say, by a particular tactile stimulus (e.g., a light touch) in a particular part of the body (e.g., the left thumb).

The cells of layer IV are activated earliest by an afferent input, not surprising considering the direct afferent connections to this layer. Cells of the other layers must have longer latencies: they would have at least one more synapse on an interneuron in layer IV before receiving the sensory input. The pyramidal neurons of layer V are the last to be activated—because, as we would expect, the efferents are there (see Figure 10.6).

The functional similarity of cells across all six layers at any point in the cortex suggests that its simplest functional unit is a vertical column of cells that constitutes a minicircuit. Groups of these columns may be organized in somewhat larger units as well. If an electrode samples the cells of area 17, all of the cells in a column will respond to a line of a given orientation (e.g., 45°). If the electrode is moved laterally across the cortex, adjacent columns will respond to successively different orientations (e.g., 60°, 90°, and so on) until all orientations covering 360° are sampled. The pattern will then repeat itself. Thus, in the visual cortex, columns are arranged into larger modules.

As interesting as cortical spots, stripes, and columns are, considerable controversy continues over defining a module and what its presence means functionally. One problem is that although modules are apparent in primary sensory regions, they are less apparent in the association or motor areas of the cortex. Another problem is that if we are looking for a common definition of a module's dimensions, then the stripes and spots are a problem because they differ greatly in size.

Furthermore, closely related species often have very different patterns of spots and stripes—an oddity if they are fundamental units of cortical function. For instance, although Old World monkeys, including baboons and macaques, have beautiful ocular dominance columns, these columns are not found in New World monkeys, such as spider monkeys and howler monkeys, even though the visual abilities of the two groups are similar.

Semir Zeki (1993) suggested that the search for the basic module of cortical organization is like the physicist's search for the basic unit of all matter. The underlying assumption is that the cortical module might be performing the same basic function throughout the cortex. In this view, the evolutionary expansion of the cortex corresponds to an increase in the number of basic units, much like the addition of chips to a computer to expand its memory or processing speed. This notion has some appeal, but we are left wondering what the basic function and operation of a given cortical module might be.

Dale Purves and his colleagues (1992) offered a provocative answer. Noting that the spots and stripes on the cortex resemble markings on the fur of many animals, they suggested that although these arresting patterns may provide camouflage or broadcast sexual signals, such functions are secondary to the fur's fundamental purpose of maintaining body temperature. By analogy, the researchers proposed that some modular patterns in the cortex may well correspond to secondary functions of cortical organization. One suggested possibility: cortical modules may be an incidental consequence of synaptic processing in the cortex. As the cortex forms its intrinsic connections to process information, that is, one efficient pattern of connectivity is the vertical column.

The module certainly conforms to an important aspect of cortical connectivity, but it does not *cause* cortical connectivity. There must be an alternative way (or ways) of organizing complex neural activity that does not require a constant module. Consider the bird's brain (**Figure 10.9**).

Birds clearly exhibit complex behavior, and some, such as crows, are extremely intelligent—more intelligent than many mammals (such as mice or even dogs). Despite its complex behavior, a bird lacks a cerebral cortex. In a bird's neural organization, different nuclei function rather like cortical layers. Thus we can see that although a cortical organization with columns is a useful arrangement, it is not the only possible brain organization.

Clearly, a vertical component to cortical organization exists, but the structure and function of a basic module are difficult to define at present. Furthermore, a single way of organizing cortical connectivity across all mammalian species and cortical regions seems unlikely.

Multiple Representations: Mapping Reality

Early ideas about visual, auditory, and somatic function in the cortex held that one or two representations of the external environment are responsible for our basic sensations. When Wilder Penfield and his colleagues stimulated their patients' motor and somatosensory strips at the Montreal Neurological Hospital in the 1950s, they identified two regions of the parietal cortex that appeared to represent localized body parts such as the leg, hand, and face (see Figure 9.4). These *homunculi* were seen as the cortical areas responsible for basic tactile sensations such as touch, pressure, temperature, and itch. Subsequent investigations of nonhuman subjects led to the identification of analogous maps of the visual and auditory worlds. Thus, half a century ago, most neuroscientists believed that the vast majority of the human cortex generally took part in complex mental analyses that we might loosely call **cognition** (knowledge and thought).

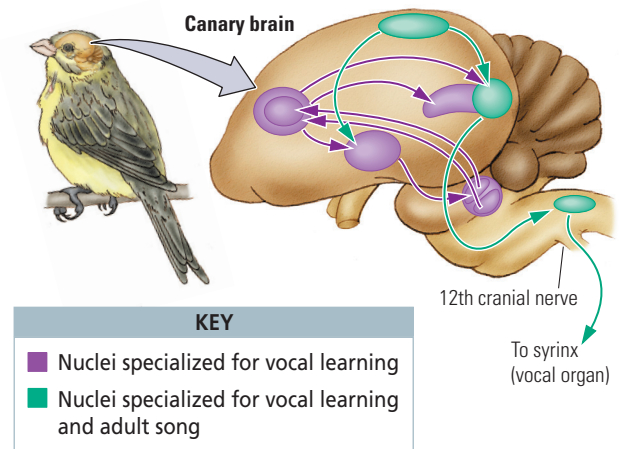
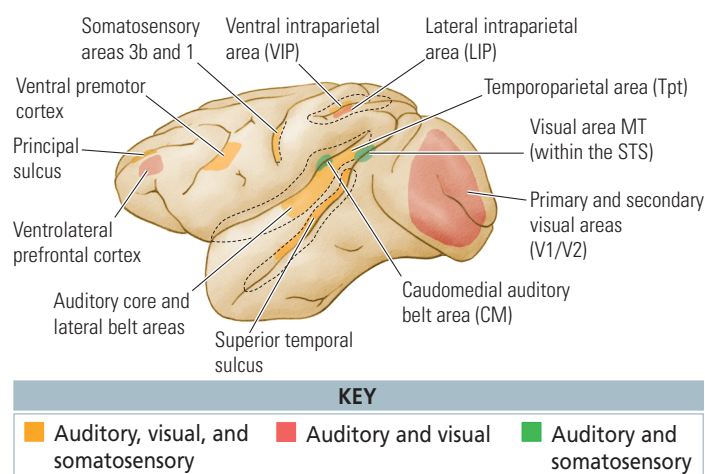


Figure 10.9 ▲

Avian Neuroanatomy Lateral view of the canary brain shows several nuclei that control vocal learning and their connections.

**Figure 10.10** ▲

Multisensory Areas in the Monkey Cortex Colored areas represent regions where anatomical and/or electrophysiological data demonstrate multisensory interactions. Dashed lines represent open sulci. (Research from Ghazanfar & Schroeder, 2006.)

Sensory Integration in the Cortex

In addition to the demonstration of multiple maps, areas were identified that function in more than one sensory modality (e.g., vision and touch). These areas, known as **multimodal cortex**, or **polymodal cortex**, presumably function to combine characteristics of stimuli across different sensory modalities. We can visually identify objects that we have only touched, for example. This implies some common perceptual system linking the visual and somatic systems.

Until recently, neuroscientists believed that several distinct regions of multimodal cortex exist, but it is becoming increasingly clear that multimodal processing is surprisingly pervasive. **Figure 10.10** summarizes the multisensory areas in the monkey brain and shows that multimodal cortex is found in both primary and secondary cortex. The integration of information from different sensory systems (described as *sensory synergies* in Section 8.3) thus appears to be a basic characteristic of cortical functioning. The convergence of qualitatively different sensory information clearly alters our perception of the world.

Asif Ghazanfar and his colleagues (2005) clearly illustrated this point in a study of neurons in the monkey auditory cortex. When monkeys listened to a recording of another monkey's voice (a coo), the auditory neurons' firing rate increased by about 25% if the voice was accompanied by a visual image of a monkey cooing—but only if the voice and facial movements were in synchrony; this is known as the McGurk effect (see Section 8.3). The Ghazanfar study is consistent with our own perception that speech is easier to hear and understand if we can see the speaker's face moving synchronously with the sound.

Multimodal cortex appears to be of two general types: one related to recognizing and processing information and the other to controlling movement related to the information in some manner. This important concept suggests that we have parallel cortical systems: one system functions to understand the world and the other to move us around in the world and allow us to manipulate our world. This distinction is counterintuitive because our impression is that our sensory and motor worlds are the same. We shall see that they are not.

Mapping Reality Through the Cortex

The emerging view is that the cortex is fundamentally an organ of sensory perception and related motor processes. This idea has an interesting implication: animals with more cortex must engage in more sensory processing than do animals with less or no cortex, and they must perceive the world differently as well. Harry Jerison (1991) pursued this

Doubt about this simple view of cortical organization arose in the late 1970s and the 1980s, however, as more refined physiological and anatomical research techniques began to reveal literally dozens of maps in each sensory modality rather than just one or two. For example, between 25 and 32 regions in the monkey cortex play roles in visual functioning, depending on the definition used.

Although the somatosensory and auditory maps are less numerous in the monkey, about 10 to 15 cortical maps in each of these modalities do not duplicate the original maps but rather process different aspects of sensory experience. For example, visual areas are specialized for analyzing basic features such as form, color, and movement. Furthermore, many psychological processes, such as visual object memory and visually guided movements, require visual information.

idea by suggesting that our knowledge of reality is related directly to the structure and number of our cortical maps.

As the number of maps in an animal's brain increases, more of the external world is known to the animal and more behavioral options are available to it. For instance, animals such as rats and dogs, whose brains lack a cortical region for analyzing color, perceive the world largely in black and white. It must limit their behavioral options, at least with respect to color. Similarly, although it is difficult for us to imagine, dogs are among those species more focused on smell than we are and may know their world through object-specific olfactory images that are as useful to them as our visual images are to us.

Jerison suggested that cortical maps determine reality for a given species and that the more maps a species has, the more complex its internal representation of the external world must be. Thus, if humans have more maps than dogs, then our representation of reality must be more complex than that of a dog. Similarly, if dogs have more maps than mice, then a dog's understanding of the world is more complex than that of a mouse.

This viewpoint implies that the relative intelligence of different mammalian species may be dependent on the number of maps used by the cortex to represent the world. Dogs would have more olfactory maps than people have and would thus be more intelligent about smells, but the total number of maps in all sensory regions taken together is far greater in humans than in dogs.

Cortical Systems: Frontal Lobe, Paralimbic Cortex, and Subcortical Loops

Connections among cortical areas in a sensory system constitute only a part of all cortical connections. The four other principal connections in the cortical hierarchy are with the frontal lobe, paralimbic cortex, multimodal cortex, and subcortical connections and loops (**Figure 10.11**).

The frontal lobe can be subdivided into (1) primary motor cortex, forming the motor homunculus; (2) premotor cortex lying just in front of the motor cortex; and (3) prefrontal cortex, which occupies the remainder of the frontal lobe (see Figure 9.2). The proprioceptive fibers of most sensory regions connect directly to the primary motor cortex and may project to either the premotor cortex or the prefrontal cortex. Premotor connections participate in ordering movements in time and controlling hand, limb, or eye movements with respect to specific sensory stimuli. Prefrontal projections take part in controlling movements in time and in forming short-term memories of sensory information (detailed in Section 18.5).

The **paralimbic cortex**, which is phylogenetically older than the neocortex, plays a role in forming long-term memories. It comprises roughly three layers adjacent and directly connected to the limbic structures (**Figure 10.12**). Paralimbic cortex can be seen in two places: (1) on the medial surface of the temporal lobe, where it is known as *perirhinal cortex*, *entorhinal cortex*, and *parahippocampal cortex*; and (2) just above the corpus callosum, where it is referred to as *cingulate cortex*.

The neocortex receives all of its sensory input from subcortical structures, either directly from the thalamus or indirectly through midbrain structures such as the tectum. These reciprocal cortical-subcortical connections, called **subcortical loops**, are feedback loops (**Figure 10.13**). Each level interacts and is integrated with higher and lower levels by ascending and descending connections. Subcortical loops connect the cortex, thalamus, amygdala, and hippocampus; an indirect loop with the striatum connects with the thalamus.

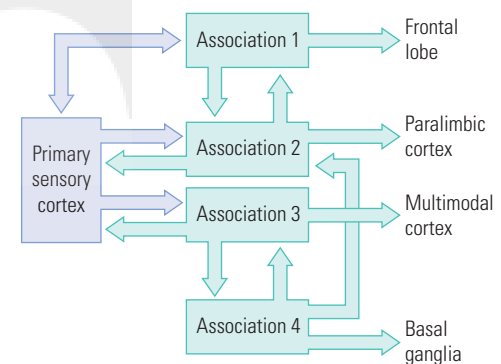


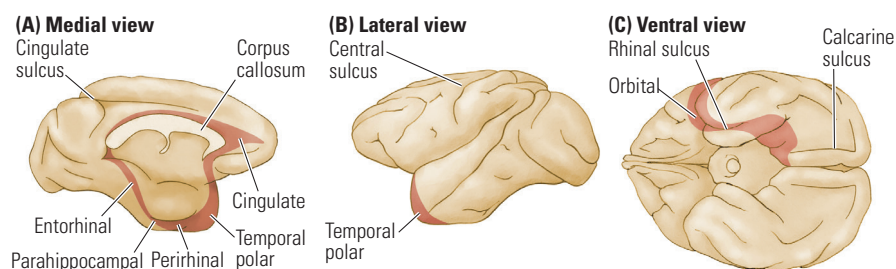
Figure 10.11 ▲

Levels of Cortical Organization

The primary sensory cortex projects to interconnected sensory association regions. These regions project to several cortical targets—including the frontal lobe, paralimbic cortex, and multimodal cortex—and to a subcortical target, the basal ganglia. For simplicity, only one of the several levels of association cortex is illustrated here.

Figure 10.12 ►

Paralimbic Cortex In these views of the rhesus monkey's cerebral cortex, the rusty color indicates the paralimbic areas in the frontal and temporal lobes and in the cingulate gyrus.



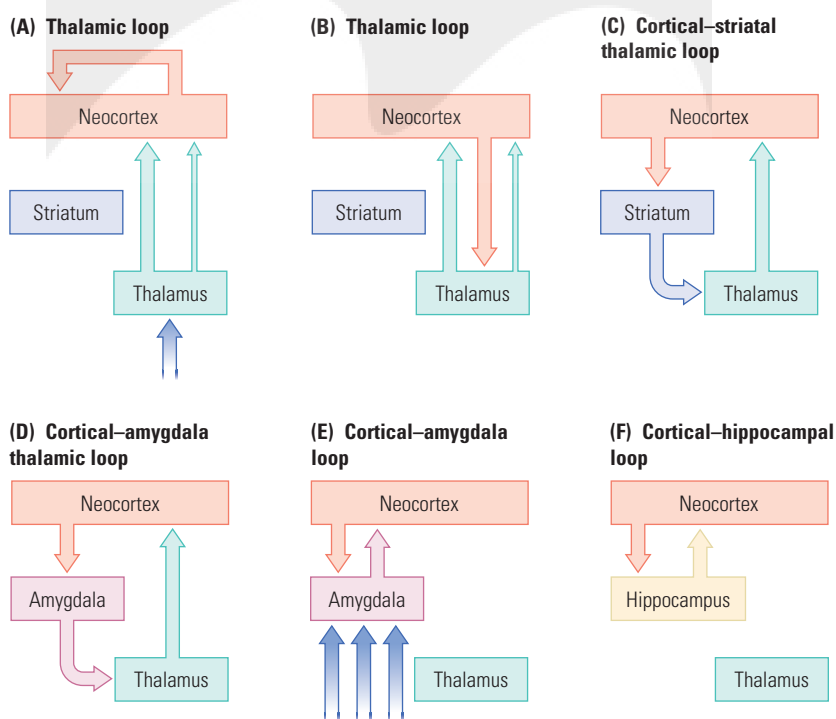
Subcortical loops presumably play some role in amplifying or modulating ongoing cortical activity. Consider, for example, how the amygdala adds affective tone to visual input. A ferocious dog may generate a strong affective response in us as it charges, in part because the amygdala adds affective tone to the visual threat of the dog. Indeed, in the absence of the amygdala, laboratory animals display absolutely no fear of threatening objects. Cats whose amygdala has been removed take leisurely strolls through rooms housing large monkeys, whereas no regular cat would even contemplate doing such a thing.

Cortical Connections, Reentry, and the Binding Problem

We have seen that the cortex has multiple anatomically segregated and functionally specialized areas. How does brain organization translate into our perception of the world as a **gestalt**—a unified and coherent whole? When you look at a person's face, for example, why do shape, color, and size combine into a coherent, unchanging image? This question defines the **binding problem**, which is focused on how the brain ties single and varied sensory and motor events together into a unified perception or behavior. How do sensations in specific channels (touch, vision, hearing, smell, and taste) combine into perceptions that translate as a unified experience that we call reality? Three possible solutions to the binding problem present themselves.

Figure 10.13 ►

Subcortical Loops Parts (A) and (B) show two thalamic loops. Each feedback loop through the midbrain (parts C–F) presumably functions to modify ongoing cortical activity. Thickness of the arrows represents the relative sizes of the connections. The arrows into the amygdala in part (E) indicate various subcortical inputs to it.



One is a high-order cortical center that receives input from all of the different cortical areas and integrates (binds) them into a single perception. Although this hierarchical idea makes sense, unfortunately no such area exists. A second solution is to interconnect all of the different cortical areas so that information is somehow shared. The problem here is that not all cortical areas connect with one another—not even within a single sensory modality. Various researchers have tried to determine the rules of connectivity, but these are beyond the scope of our discussion. (For details, see Felleman & van Essen, 1991; Pandya & Yeterian, 1985; and Zeki, 1993.)

Suffice it to say that only about 40% of the possible *intercortical* connections within a sensory modality are actually found, which leads us to the third solution: *intracortical* networks of connections among subsets of cortical regions. This idea has considerable appeal.

First, all cortical areas have internal connections among units with similar properties. These connections link neighboring neurons and synchronize their activity. Second, through a mechanism called **reentry**, any cortical area can influence the area from which it receives input (**Figure 10.14A**). This remarkable interactive aspect of cortical connectivity means that when area A sends information to area B, area B reciprocates and returns a message to area A (**Figure 10.14B**).

Zeki (1993) suggested that an area might actually modify its inputs from another area before it even receives them! An important point detailed in **Figure 10.14B** is that the connections from areas A and B do not originate from the same layers, suggesting that they play different roles in influencing each other's activity.

How can information flow through intra-areal and interareal connections and interaction through reentry solve the binding problem? Computer modeling suggests that the primary function of the neural connections is to coordinate activity within and between areas to produce a globally coherent pattern, or *integration*, over all areas of the perceptual systems.

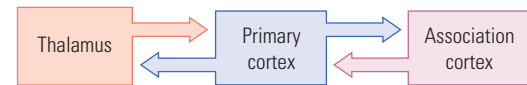
Integration requires a way of binding the areas together briefly to form a unified percept. The computer models show that perceptual integration can be almost immediate, on the order of 50 to 500 milliseconds.

Jerison (1991) related the binding problem to his analogy of multiple cortical maps. The evolutionary expansion, in area, of the cortex has implications for a brain with multiple neurosensory channels that are trying to integrate information into a single reality. Because so many different kinds of sensory information reach the cortex, it is necessary somehow to discriminate equivalent features in the external world. It would be useful to the brain to label these equivalencies and organize them.

Suppose that the brain creates labels to designate objects and a coordinate system to locate objects in the external world—that is, in space and time. Suppose also that some sensory information must be both tagged to persist through time (in memory) and categorized to be retrieved (remembered) when needed.

Labels, coordinates, and categories are products of cognition. Viewed in this way, Jerison's (1991) analogy of multiple cortical maps provides a basis for thinking about how the information that is arriving at the cortex is integrated into perception and organized as knowledge, thought, and memory. Indeed, injuries to discrete cortical areas alter the way people perceive the world, as well as the way they think about it. In Section 13.5 we shall see that one form of sensory deficit, **agnosia** (Greek for “not knowing”), renders a partial or complete inability to recognize sensory stimuli. Agnosias are unexplainable as subcortical deficits in elementary sensation or alertness.

(A) Information flow to and from the cortex



(B) Principles of reentry

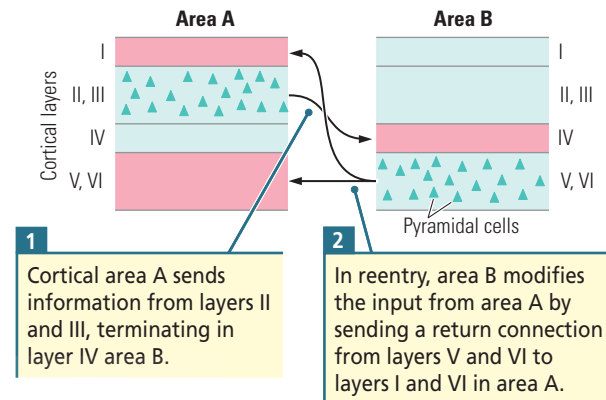


Figure 10.14 ▲

Interareal and Intra-areal Connections

(A) Information from the thalamus goes to the primary cortex, which then projects to the association cortex. The reciprocal connections at each level represent feedback loops. (B) A receiving cortical area can modify the inputs that it gets from another area. Reentry holds for all levels of cortical–cortical connectivity.

10.3 Functional Organization of the Cortex

To Jerison, “the mind” comprises an individual’s knowledge of the world constructed by the brain. As cortical maps develop, the brain must also develop the mind to organize those maps in a way that produces knowledge of the external world. It is a small jump to the idea that the next step in mental development is language. Language, after all, is a means of representing knowledge.

A Hierarchical Model of Cortical Function

Flechsigs was the first to suggest using anatomical criteria to delineate a hierarchy of cortical areas, but Alexander Luria fully developed the idea in the 1960s. Luria (1973) divided the cortex into two functional units:

- The posterior cortex (parietal, occipital, and temporal lobes) is the sensory unit that receives sensations, processes them, and stores them as information (**Figure 10.15A**).
- The anterior cortex (frontal lobe) is the motor unit that formulates intentions, organizes them into programs of action, and executes the programs (**Figure 10.15B**).

Both of Luria’s cortical units are hierarchically structured, with three cortical zones arranged functionally, one above the other. The first zone corresponds to Flechsigs’s primary cortex; the second zone corresponds to the more slowly developing cortex bordering the primary cortex, labeled *secondary cortex* by Luria; and the third is the most slowly developing cortex, which Luria labeled *tertiary cortex*.

Luria conceived of the cortical units as working in concert along zonal pathways. Sensory input enters the primary sensory zones, is elaborated in the secondary zones, and is integrated in the tertiary zones of the posterior unit. To execute an action, activation is sent from the posterior tertiary sensory zones to the tertiary frontal motor zone for formulation, to the secondary motor zone for elaboration, and then to the primary frontal zone for execution.

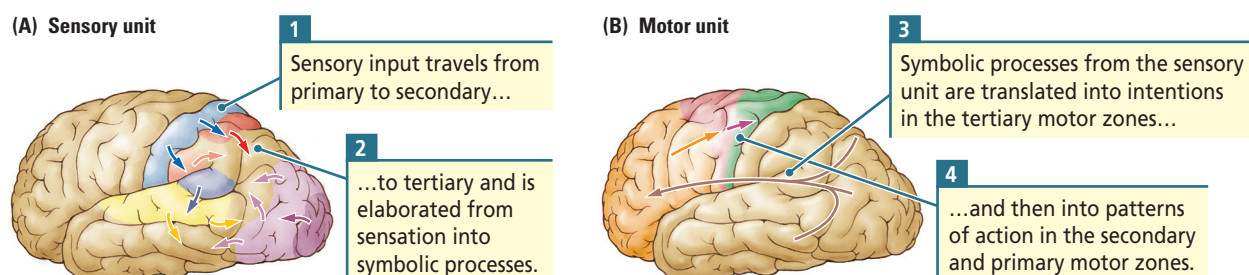
Consider a simplified example of Luria’s model: you are walking along and come upon a soccer game. The actual perception of the movements of players and the ball is in the primary visual area. The secondary visual sensory zone recognizes that those activities constitute a soccer game. In the tertiary zone, the sounds and movements of the game are synthesized into the realization that one team has scored and is ahead and that the game has significance for league standings. By the time the information is integrated in the tertiary sensory zone, it is considerably richer than what we would think of as “sensory.” Rather, it has become knowledge.

Information in the tertiary sensory zone activates the paralimbic cortex for memory processing and the amygdala for emotional assessment. These cortical events can then activate, in the tertiary zone of the frontal (motor) cortex, the intention to find a viewing spot and root for your team. The execution of this plan is formulated in the secondary

Figure 10.15 ▼

Functional Units of the Cortex

(A) In traveling from primary to secondary to tertiary zones, sensation is elaborated and integrated into information. (B) Information from the sensory unit travels forward to tertiary motor zones, where it is translated into intention and then into patterns of action in the secondary and primary motor zones. (Research from Luria, 1973.)



frontal zones. The actual movements required to join the crowd are initiated in the primary motor zone of the frontal cortex.

Using the soccer game example, we can also describe the effects of brain lesions on levels of processing. A lesion in the primary visual zone that produces a blind spot in some part of the visual field might require the spectator to move his or her head backward and forward to see the entire game. A lesion in the secondary visual zone might produce a perceptual deficit, making the person unable to recognize the activity as a soccer game. A lesion in the tertiary sensory zone might make it impossible to abstract the significance of the game—that one team wins.

Damage to the paralimbic cortex leaves no memory of the event, and damage to the amygdala renders the person unresponsive to the event's emotional significance. A lesion in the tertiary motor area might prevent formation of the intention to become a soccer player and join a club, buy a uniform, or get to practice on time. A lesion in the secondary motor zone might make it difficult to execute the sequences of movements required in play. A lesion in the primary zone might make it difficult to execute a discrete movement required in the game—for example, kicking the ball.

Evaluating the Hierarchical Model

Luria (1973) based his theory on three assumptions:

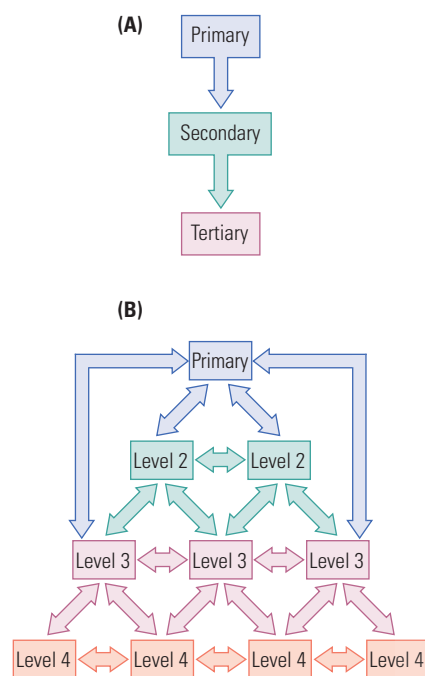
1. *The brain processes information serially*, one step at a time. Thus, information from sensory receptors goes to the thalamus, then to the primary cortex, then to the secondary cortex, and finally to the tertiary sensory cortex. Similarly, output goes from tertiary sensory to tertiary motor, then to secondary motor, and finally to primary motor.
2. *Serial processing is hierarchical*: each level adds complexity that is qualitatively different from the processing in the preceding levels. The tertiary cortex could be considered a terminal station insofar as it receives input from the sensorimotor and perceptual areas and performs higher cognitive processes on that input.
3. *Our perceptions of the world are unified and coherent*. Luria's formulation was in accord with the commonsense view that some active process produces each percept, and, naturally, the simplest way to do so is to form it in the tertiary cortex.

The beauty of Luria's theory is that it used the then-known anatomical organization of the cortex to craft a simple explanation for observations that Luria made daily in his clinic and published in 1973. The difficulty is that its basic assumptions have been questioned by newer anatomical and physiological findings. Consider the following problems.

First, a strictly hierarchical processing model requires that all cortical areas be linked serially, but there is no such serial linkage. We have seen that all cortical areas have reentrant (reciprocal) connections with the regions to which they connect; no simple “feed-forward” system exists. Furthermore, as noted in Section 10.2, only about 40% of the possible connections among different areas in a sensory modality are actually found. Thus no single area receives input from all other areas. This presents a difficulty in actively forming a single percept in one area.

Second, Zeki (1993) made an interesting point: because a zone of cortex has connections with many cortical areas, it follows that each cortical zone is probably undertaking more than one operation, which it relays to different cortical areas. Furthermore, the results of the same operation are likely to be of interest to more than one cortical area. This would account for multiple connections.

These principles can be seen in the primary visual cortex, which appears to make calculations related to color, motion, and form. These calculations are relayed to the specific cortical regions for these processes. And the same calculation may be sent to subcortical as well as to cortical regions.

**Figure 10.16** ▲**Two Hierarchical Models**

(A) Luria's simple serial hierarchical model of cortical processing. (B) Felleman and van Essen's distributed hierarchical model features multiple levels of association areas interconnected with one another at each level.

The fact that cortical operations are relayed directly to subcortical areas implies that cortical processing can bypass Luria's motor hierarchy and go directly to subcortical motor structures. In addition, the fact that cortical areas can perform multiple calculations that are sent to multiple areas raises a question about what is hierarchical in the processing: Can we assume that areas connected serially are actually undertaking more complicated operations? An area such as the primary visual cortex, which processes color, form, and movement, might be considered more complex than an area that processes only color.

Finally, Luria assumed that his introspection about perception being a unitary phenomenon was correct. It appears, however, that it is not. We can experience a single percept despite the fact that no single terminal area is producing it. This ability is the essence of the binding problem.

How can we put all of this knowledge together in a meaningful way to see organization in the cortex? Two logical possibilities exist. One is that there is no hierarchical organization but rather some sort of nonordered neural network. As individual organisms gain experiences, this network becomes ordered in some way and therefore produces perceptions, cognitions, and memories. Many neural-network models of brain function propose that this is exactly what happens. However, the results of a wealth of perceptual research suggest that the brain filters and orders sensory information in a species-typical fashion.

The other organizational possibility, suggested by Daniel Felleman and David van Essen (1991), is that cortical areas are hierarchically organized in some well-defined sense, with each area occupying a specific position relative to other areas but with more than one area occupying a given hierarchical level. Felleman and van Essen proposed using the pattern of forward and backward connections to determine hierarchical position.

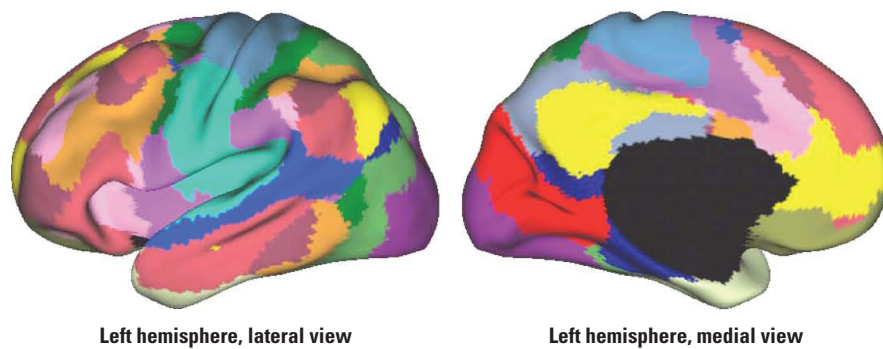
Thus, ascending (or forward) connections terminate in layer IV, whereas descending (or feedback) connections do not enter layer IV but usually terminate in the superficial and deep layers (see Figure 10.14B). Felleman and van Essen also recognized a third type of connection, columnar in its distribution and terminating in all cortical layers. This type of connection is uncommon but provides a basis for placing areas in the same location in the hierarchy.

By analyzing the patterns of connectivity among the visual, auditory, and somatosensory areas, Felleman and van Essen found evidence of what they called a *distributed hierarchical system*. **Figure 10.16** contrasts this model with Luria's model. Notice in Figure 10.16B the several levels of processing and, across the levels, interconnected processing streams that presumably represent different elements of the sensory experience. Note, too, that some connections skip levels and that the number of areas expands as the hierarchy unfolds.

A Contemporary Model of Cortical Function

The Felleman and van Essen model and the process of reentry illustrate that cortical connectivity is not a simple junction of one cortical module with another but rather a dynamic interplay between and among the operations of different regions. Thus, brain areas should be regarded not as independent processors of specific information but instead as areas that act conjointly, forming large-scale neural networks that underlie complex cognitive operations (see review by Meehan & Bressler, 2012).

A key principle in understanding cortical networks is the need to identify the anatomical connections that form networks as well as the functional correlations between cortical regions. The Human Connectome Project (www.humanconnectomeproject.org) is an ambitious venture aimed at charting human brain connectivity using noninvasive neuroimaging in a population of 1200 healthy adults (aged 22–35) and a population



Left hemisphere, lateral view

Left hemisphere, medial view

of more than 1300 children, adolescents, and young adults (ages 5–21). The goal is to produce a large multimodal and freely available set of consistently acquired data for use by the neuroscientific community.

The Connectome Project is based on the observation that a living brain is always active, and researchers have succeeded in inferring brain function and connectivity by studying fMRI signals when participants are resting—that is, not engaged in any specific task. This signal, *resting-state fMRI* (rs-fMRI, introduced in Section 7.4), is collected when participants are asked to look at a fixation cross and to keep their eyes open. The scanner collects brain activity, typically for at least 4-minute-long blocks.

Utilizing rs-fMRI data from 1000 participants, Thomas Yeo and colleagues (2011) parcellated the human cerebral cortex into 17 networks (**Figure 10.17**). The cerebral cortex is made up of primary sensory and motor networks as well as the multiple large-scale networks that form the association cortex. The sensory and motor networks are largely local: adjacent areas tend to show strong functional coupling with one another.

In **Figure 10.17**, the turquoise and blue–gray regions in the somatosensory and motor cortex and the purple region in the visual cortex illustrate these couplings. In contrast, the association networks include areas distributed throughout the prefrontal, parietal, anterior temporal, and midline regions. The distributed yellow regions in the figure show prefrontal–posterior parietal connectivity. Some distributed networks, shown in light red, include temporal, posterior parietal, and prefrontal regions. There are marked individual differences, as shown in the two brains illustrated in **Figure 10.18**. The individual maps are so distinct that they can be used to distinguish individual brains, much like fingerprints (see Finn et al., 2015). Furthermore, the key features of the connectome are present in the third trimester of pregnancy, which underlies the importance of the prenatal period in future brain function and dysfunction (Turk et al., 2019).

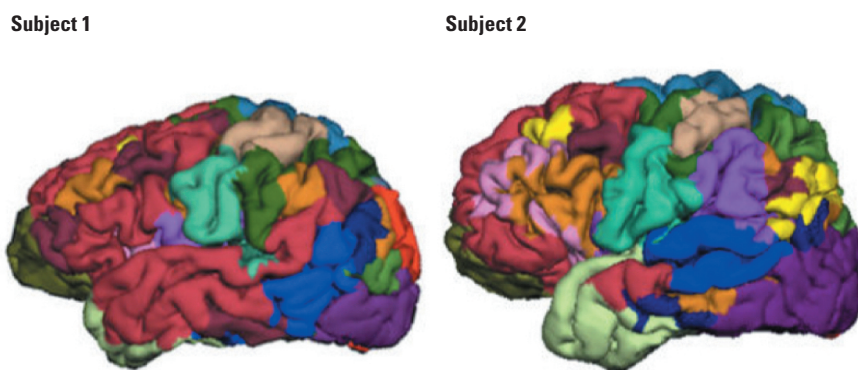
The Default Mode Network

Before the 1990s, it was generally believed that the brain is relatively inactive unless some type of focused activity is being performed. However, with the advent of positron

Figure 10.17 ◀

Parcellation of Cerebral Cortical Networks

An estimate of 17 cortical networks based on rs-fMRI data from 1000 participants. Each color represents a network. Some, such as the deep blue auditory areas in the temporal lobe, are localized; others are widely distributed, such as the yellow regions, which reveal prefrontal–posterior parietal connectivity. (Republished with permission of the American Physiological Society from B. T. T. Yeo, F. M. Krienen, J. Sepulcre, M. R. Sabuncu, D. Lashkari, et al., “The Organization of the Human Cerebral Cortex Estimated by Intrinsic Functional Connectivity,” 2011, September; *Journal of Neurophysiology*, 106 (3), pp. 1125–1165, Figure 7. Permission conveyed through Copyright Clearance Center, Inc.)



Subject 1

Subject 2

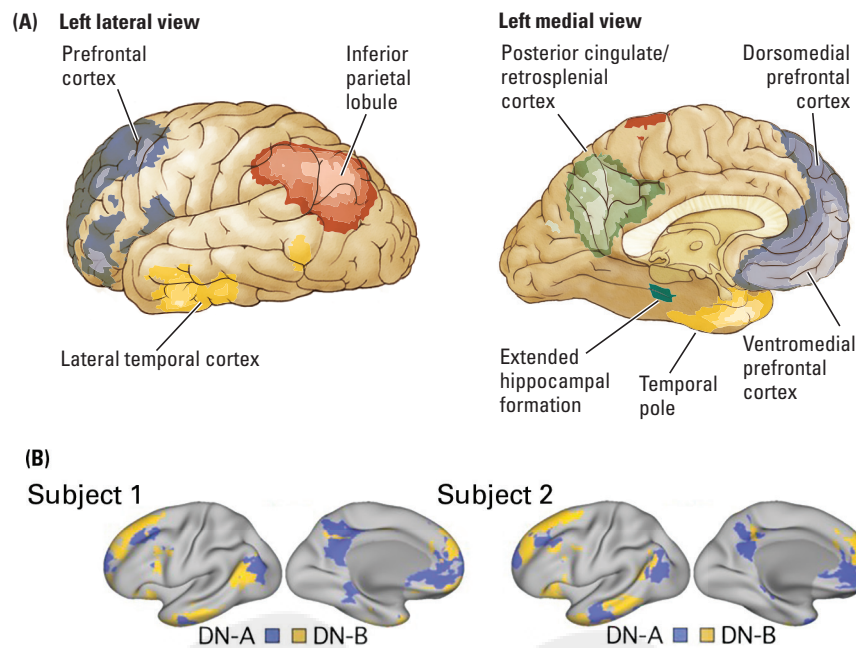
Figure 10.18 ◀

Individual Differences in Cerebral Networks

Brain networks in two healthy brains showing individual differences in details of both the gyrus patterns and networks. (Republished with permission of Nature Publishing Group, from Danhong Wang, Randy L. Buckner, Michael D. Fox, Daphne J. Holt, et al., “Parcellating cortical functional networks in individuals.” *Nature Neuroscience*, 2016, May; 18(12): 1853–1860, Figure 2. Permission conveyed through Copyright Clearance Center, Inc.)

Figure 10.19 ►**The Brain's Default Network**

(A) Brain regions that are more active when participants are resting—that is, in a passive condition—contrasted to brain activity during a wide range of simple active task conditions. Lighter color indicates greater activity. (B) Parallel networks can be resolved with high resolution in individual participants. Note the similarity to the group-averaged networks shown in (A). (B: American Physiological Society from Braga RM, Van Dijk KRA, Polimeni JR, Eldaief MC, Buckner RL, “Parallel distributed networks resolved at high resolution reveal close juxtaposition of distinct regions.” *Journal of Neurophysiology*, 2019 Apr 1;121(4):1513–1534, Figure 4. Creative Commons Attribution CC-BY 4.0.)



emission tomography (PET), it became clear that some connected areas of the brain are highly active when a person is not engaged in focused activities but rather appears to be resting in a passive condition. This network, which includes parts of the prefrontal cortex, posterior parietal cortex, posterior cingulate cortex, and medial temporal regions, came to be known as the **default mode network**, or **default network** (see **Figure 10.19A**). Similar networks have now been described in other species, including rats, cats, and monkeys.

The use of higher-resolution imaging has now revealed that there are at least two distinct parallel default networks in humans. Figure 10.19B shows the networks from two participants in a study by Braga and colleagues (2019), and although they are very similar, just as in the case of overall parcellation of cortical networks, individual default networks are not identical.

Because the default network was originally identified as a resting state, it was thought to reflect a mind-wandering state, such as daydreaming, but this is a misnomer. The default network is also active during such directed tasks as thinking about one's past (autobiographical memory), thinking about the future, or understanding a story.

10.4 Do Human Brains Possess Unique Properties?

Scholars who have looked for unique mental abilities in humans form a long tradition. Four allegedly unique abilities are grammatical language; phonological imagery—the ability to use language to make mental images; **theory of mind**, or social cognition—the capacity to understand another's mental state and to take it into account; and certain forms of intelligence, such as intuition. Although the nature and even the presence of such supposedly unmatched capacities remain debatable, we can consider whether the human brain has unique properties.

As discussed in Section 2.1, the human brain is relatively larger than the brains of other species, but all mammalian species have a common plan of cortical organization that evolution has modified to suit specific ecological niches (see review by Krubitzer & Kaas, 2005). Nonetheless, the basic architecture of the cortex is conserved across

mammals. For example, despite the 1000-fold difference in brain size and number of cells in the human and mouse cerebral cortices, the *transcriptomic organization* (i.e., the RNA transcripts of individual neurons) of cell classes and subclasses is remarkably similar. However, there are marked differences in gene expression and neuronal morphology among different mammal species, which are likely related to differences in microcircuit organization and function (Hodge et al., 2019).

The cerebral cortex can be subdivided into a mosaic of areas that can be identified based on differences in function, cytoarchitecture, connectivity, and topography (the FACT approach), and this approach reveals additional large interspecies differences. For example, the mouse cortex has about 41 distinct areas, the rhesus monkey about 140, and the human 180 (van Essen, Donahue, & Glasser, 2018). The increased parcellation reflects a disproportionate expansion of human frontal, temporal, and parietal association areas relative to those of other primates. These are also the regions that show the least myelin in the cortex and far less than is seen in other primates, including chimpanzees, and this cortex is also characterized by lower neuronal density and larger dendritic arbors in humans. The increasing size and parcellation of cortical regions as the human brain has evolved is presumably related to increased cognitive complexity in humans.

Overall, humans also have a higher density of cortical neurons than other mammals. The increased neuronal density means that the humans actually have more neurons in their brains than do animals with much larger brains, such as whales and elephants. As a result, the human brain possesses a relatively high processing capacity. But it comes at a metabolic cost. Suzana Herculano-Houzel (2012) suggested that our early ancestors solved the metabolic problem by cooking food: cooked food yields more energy per eating session than does raw food.

A final special characteristic of the human brain is a difference in some classes of cortical neurons. For example, one class of cortical neuron, *von Economo neurons*, is found only in humans; other great apes; and possibly in macaques, cetaceans, and elephants—but these neurons are most abundant in humans (Cauda et al., 2014). These large bipolar neurons are located in the dorsolateral prefrontal cortex and in deep layers of the insula (Figure 10.20A) and in a lateral cortical region of the anterior cingulate cortex (Figure 10.20B).

Von Economo neurons develop late in human ontogeny and only reach adult levels by about 4 years of age, possibly through the differentiation of some preexisting cell type or even through neurogenesis. John Allman and his colleagues (2005) proposed that von Economo neurons are associated with the emergence of theory of mind. Even more provocatively, Allman speculated that these cells fail to develop normally in people with *autism spectrum disorder* (ASD), leading to the faulty social intuition characteristic of the disorder (see Section 24.3). Thus, although human and nonhuman primate brains contain mirror neurons (see Section 9.1) that also have been related to ASD, humans have a disproportionate number of von Economo neurons. The broader distribution in humans and other great apes correlates with greater social cognitive abilities and self-awareness (see Section 20.6).

Another class of cortical neurons, known as *rosehip neurons* for their appearance, has been reported only in humans. These inhibitory GABA neurons are present in layer I of the human cerebral cortex (Boldog et al., 2018). The presence of specialized neuronal types in the human brain would be expected to modify the functional organization of cortical circuits.

In sum, although humans do not evince any obvious, gross difference in brain organization from that of other mammals, the intrinsic organization of the human neocortex, including the presence of specialized neurons and increased cortical parcellation, may allow the emergence of mental capacities that are qualitatively different from those found in other mammals.

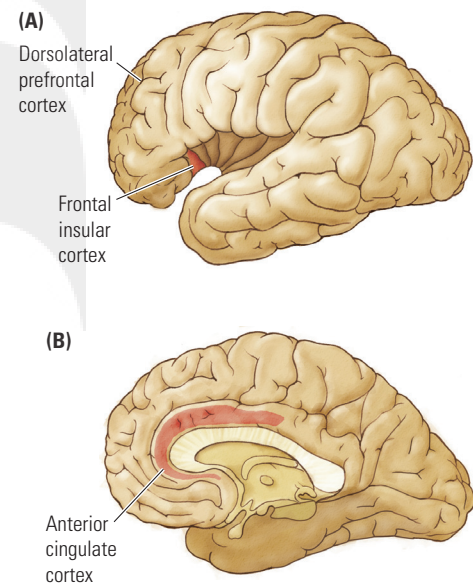


Figure 10.20 ▲

Locations of von Economo Neurons

(A) The frontal insula at the border of the temporal lobe, the dorsolateral prefrontal cortex, and (B) the anterior cingulate cortex are among the areas that contain von Economo neurons. They bear the name of anatomist Constantin von Economo, who first described them in the 1920s. (Research from Allman et al., 2005, and Cauda et al., 2014.)

SUMMARY

Human neocortical function is of primary interest to neuropsychologists—the hierarchical levels of function in the CNS and the structure, functional organization, and connectivity of the cortex.

10.1 There is a hierarchy of function from the spinal cord to the cortex

The functional levels in the CNS begin in the spinal cord and end in the neocortex, as demonstrated by study of animals that have undergone surgical removals of successively more brain tissue. See Figure 10.2 on page 240.

10.2 The structure of the cortex reflects its functions

The neocortex comprises two basic types of neurons—spiny and aspiny—organized into about six layers considered sensory, motor, and associational. Their vertical organization in columns, or modules, is revealed in the spots and stripes visible in specific histological preparations and in neuroimaging.

Multiple representations of sensory and motor functions exist in the cortex, and an evolutionary change in mammals has been an increase in their number. A characteristic of cortical connectivity is reentry: each cortical area is reciprocally connected with many other regions in a given sensory modality—but not all.

The cortex processes information about the world in multiple representations that are not formally connected, yet we

perceive the world as a unified whole. This conundrum is the binding problem.

10.3 The cortex is organized by distributed networks

Cortical activity is influenced by feedback loops not only from other cortical regions but also from subcortical forebrain regions such as the amygdala and hippocampus. Thus the cortex is functionally organized as a distributed hierarchical network. The Human Connectome Project is detailing the connectivity of the cortex, which is not a single network but rather multiple networks with different functions.

10.4 Human brains possess unique properties

Although the basic architecture of the cortex is conserved across all mammals, analysis using the FACT approach reveals some significant interspecies differences. The frontal, temporal, and parietal association areas in the human brain have expanded disproportionately relative to those of other primates, and this expansion has been accompanied by an increased parcellation of these regions. Together with unique cell types found in humans, including von Economo neurons and rosehip neurons, these differences may be clues to the neural basis of these qualitatively different cognitions, such as social intuition in humans.

Key Terms

agnosia, p. 253
aspiny neurons, p. 244
automatic movements, p. 241
binding problem, p. 252
cognition, p. 249
column p. 247
decortication, p. 243
default (mode) network, p. 258
diencephalic animal, p. 242
dysphasia, p. 238

gestalt, p. 252
gray level index (GLI), p. 245
hemispherectomy, p. 238
high decerebration, p. 241
low decerebrate, p. 240
module, p. 247
multimodal (polymodal) cortex,
p. 250
neuropil, p. 245
nonspecific afferent, p. 247

paralimbic cortex, p. 251
pyramidal cells, p. 244
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spinal animals, p. 240
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stellate cells, p. 244
subcortical loops, p. 251
theory of mind, p. 258
voluntary movements, p. 241

References

- Allman, J. M., Watson, K. K., Tetreault, N. A., & Hakeem, A. Y. (2005). Intuition and autism: A possible role for von Economo neurons. *Trends in Cognitive Science*, 9, 367–373.
- Bard, P., & Macht, M. B. (1958). The behavior of chronically decerebrate cats. In G. E. W. Wolstenholm & C. M. O'Connor (Eds.), *Ciba Foundation Symposium on Neurological Basis of Behavior*. Churchill.
- Barrett, R., Merritt, H. H., & Wolf, A. (1967). Depression of consciousness as a result of cerebral lesions. *Research Publications of the Association for Research in Nervous and Mental Disease*, 45, 241–276.
- Berridge, K. C. (1996). Food reward: Brain substrates of wanting and liking. *Neuroscience and Biobehavioral Reviews*, 20(6), 1–25.
- Berridge, K. C., & Whishaw, I. Q. (1992). Cortex, striatum, and cerebellum: Control of serial order in a grooming sequence. *Experimental Brain Research*, 90, 275–290.
- Bignall, K. E., & Schramm, L. (1974). Behavior of chronically decerebrate kittens. *Experimental Neurology*, 42, 519–531.
- Boldog, E., Bakken, T. E., Hodge, R. D., Novotny, M., Aevermann, B. D., Baka, J., Bordé, S., Close, J. L., Diez-Fuertes, F., Ding, S. L., Faragó, N., Kocsis, Á. K., Kovács, B., Maltzer, Z., McCarrison, J. M., Miller, J. A., Molnár, G., Oláh, G.,

- Ozsvár, A., Rózsa, M., et al. (2018). Transcriptomic and morphological evidence of a specialized human cortical GABAergic cell type. *Nature Neuroscience*, 21, 1185–1195.
- Brackbill, Y. (1971). The role of the cortex in orienting: Orienting reflex in an anencephalic human infant. *Developmental Psychology*, 5, 195–201.
- Braga, R. M., Van Dijk, R. A., Polimeni, J. R., Eldaief, M. C., & Buckner, R. L. (2019). Parallel distributed networks resolved at high resolution reveal close juxtaposition of distinct regions. *Journal of Neurophysiology*, 121, 1513–1534.
- Campbell, A. W. (1905). *Histological studies on the localisation of cerebral function*. Cambridge University Press.
- Cannon, W. B., & Britton, S. W. (1924). Pseudoaffective medulliadrenal secretion. *American Journal of Physiology*, 72, 283–294.
- Cauda, F., Geminiani, G. C., & Vercelli, A. (2014). Evolutionary appearance of von Economo's neurons in the mammalian cerebral cortex. *Frontiers in Human Neuroscience*, 14(8), 104. <https://doi.org/10.3389>
- Felleman, D. J., & van Essen, D. C. (1991). Distributed hierarchical processing in the primate cerebral cortex. *Cerebral Cortex*, 1, 1–47.
- Finn, E. S., Shen, X., Scheinost, D., Rosenberg, M. D., Huang, J., Chun, M. M., Papademetris, X., & Constable, R. T. (2015). Functional connectome fingerprinting: Identifying individuals using patterns of brain connectivity. *Nature Neuroscience*, 18(11), 1664–1671.
- Flechsig, P. (1920). *Anatomie des menschlichen Gehirns und Rückenmarks*. Georg Thieme.
- Ghazanfar, A. A., Maier, J. X., Hoffman, K. L., & Logothetis, N. K. (2005). Multisensory integration of dynamic faces and voices in rhesus monkey auditory cortex. *Journal of Neuroscience*, 25, 5004–5012.
- Ghazanfar, A. A., & Schroeder, C. E. (2006). Is neocortex essentially multisensory? *Trends in Cognitive Science*, 10, 278–285.
- Goltz, F. (1960). On the functions of the hemispheres. In G. von Bonin (Ed.), *The cerebral cortex*. Charles C. Thomas.
- Grill, H. J., & Norgren, R. (1978). Neurological tests and behavioral deficits in chronic thalamic and chronic decerebrate rats. *Brain Research*, 143, 299–312.
- Grillner, S. (1973). Locomotion in the spinal cat. In R. B. Stein (Ed.), *Control of posture and locomotion*. Plenum.
- Herculano-Houzel, S. (2012). The remarkable, yet not extraordinary, human brain as a scaled-up primate brain and its associated cost. *Proceedings of the National Academy of Sciences U.S.A.*, 109 (Suppl 1), 10661–10668.
- Hodge, R. D., Bakken, T. E., Millner, J. A., Smith, K. A., Barkan, E. R., Graybiel, L. T., Close, J. L., Long, B., Johansen, N., Penn, O., Yao, Z., Eggermont, J., Höllt, T., Levi, B. P., Shehata, S. I., Aevermann, B., Beller, A., Bertagnolli, D., Brouner, K., Casper, T., et al. (2019). Conserved cell types with divergent feature in human versus mouse cortex. *Nature*, <https://doi.org/10.1038/s41586-019-1506-7>
- Jerison, H. J. (1991). *Brain size and the evolution of mind*. American Museum of Natural History.
- Jung, R., & Hassler, R. (1960). The extrapyramidal system. In J. Field, H. W. Magoun, & V. E. Hall (Eds.), *Handbook of physiology* (Vol. 2, pp. 863–927). American Physiological Society.
- Kliemann, D., Adolphs, R., Tyszk, J. M., Fischl, B., Yeo, B. T., Nair, R., Dubois, J., & Paul, L. K. (2019). Intrinsic functional connectivity of the brain in adults with a single cerebral hemisphere. *Cell Reports*, <https://doi.org/10.1016/j.celrep.2019.10.067>.
- Krubitzer, L., & Kaas, J. (2005). The evolution of the neocortex in mammals: How is phenotypic diversity generated? *Current Opinion in Neurobiology*, 15, 444–453.
- Luria, A. R. (1973). *The working brain*. Penguin.
- Meehan, T. P., & Bressler, S. L. (2012). Neurocognitive networks: Findings, models, and theory. *Neuroscience and Biobehavioral Reviews*, 36, 2232–2247.
- Oakley, D. A. (1979). Cerebral cortex and adaptive behavior. In D. A. Oakley & H. C. Plotkin (Eds.), *Brain, evolution and behavior*. Methuen.
- Pandya, D. N., & Yeterian, E. H. (1985). Architecture and connections of cortical association areas. In A. Peters & E. G. Jones (Eds.), *Cerebral cortex* (Vol. 4). Plenum Press.
- Peters, A., & Jones, E. G. (1984–1999). *Cerebral cortex*, Vols. 1–14. Plenum.
- Purves, D., Riddle, D. R., & LaMantia, A.-S. (1992). Iterated patterns of brain circuitry (or how the brain gets its spots). *Trends in Neuroscience*, 15, 362–368.
- Shepherd, G. M. (1979). *The synaptic organization of the brain*, 2nd ed. Oxford University Press.
- Szentagothai, J. (1969). Architecture of the cerebral cortex. In H. H. Jasper, A. A. Ward, & A. Pope (Eds.), *Basic mechanisms of the epilepsies*. Little, Brown.
- Türk, E., van den Heuvel, M. I., Bender, M. J., de Heus, R., Franx, A., Manning, J. H., Hect, J. L., Hernandez-Andrade, E., Hassan, S. S., Romero, R., Kahn, R. S., Thomason, M. E., & van den Heuvel, M. P. (2019). Functional connectome of the fetal brain. *Journal of Neuroscience*, 39(49), 9716–9724.
- van Essen, D. C., Donahue, C. J., & Glasser, M. F. (2018). Development and evolution of cerebral and cerebellar cortex. *Brain, Behaviour, & Evolution*, 91, 158–169.
- Wang, D., Buckner, R. L., Fox, M. D., Holt, D. J., Holmes, A. J., Stoecklein, S., Langs, G., Pan, R., Qian, T., Li, K., Baker, J. T., Stufflebeam, S. M., Wang, K., Wang X., Hong, B., & Liu, H. (2015). Parcellating cortical functional networks in individuals. *Nature Neuroscience*, 18(12), 1853–1860.
- Whishaw, I. Q. (1989). The decorticate rat. In B. Kolb & R. Tees (Eds.), *The neocortex of the rat*. MIT Press.
- Yeo, B. T., Krienen, F. M., Sepulcre, J., Sabuncu, M. R., Lashkari, D., Hollinshead, M., Roffman, J. L., Smoller, J. W., Zöllei, L., Polimeni, J. R., Fischl, B., Liu, H., & Buckner, R. L. (2011). The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *Journal of Neurophysiology*, 106(3), 1125–1165. <https://doi.org/10.1152/jn.00338.2011>
- Zeki, S. (1993). *A vision of the brain*. Blackwell Scientific.