3 | The Behavioral Geography of the Brain

So much is now known about the brain—and yet so little. The structure of the brain is well visualized with current technology and minute details of cell structure can be seen with electron microscopy. Even structural changes in the neuron associated with learning have been photographed (Eichenbaum and Cohen, 2001; Engert and Bonhoeffer, 1999). Neuronal pathways have been traced to and from major regions of the brain (for some pathway examples, see Markowitsch, 2000, for memory; Frackowiak et al., 1997, chap. 5, for the somatosensory system; Lichter and Cummings, 2001, *passim,* for frontal-subcortical circuitry; Rolls, 1999, for emotions; Shepherd, 1998, for a review of synaptic circuits; Spencer, 2000b, chap. 1, for neurotoxicity; and Steinmetz et al., 2001, for connections underlying learning).

With the remarkable developments in functional neuroimaging, investigators are exploring the complex interaction of regions of the brain during specific experiences and behaviors through measurement of brain blood flow or metabolism (for some imaging examples of complex behaviors, see Andreasen, 2001, for sensory and motor activation in controls and psychiatric patients; Driver and Baylis, 1998, for an assortment of visual responses; Frackowiak et al., 1997 for reading, higher cortical processes including emotions, and varieties of memory, in chaps. 13, 14, 15; Haxby, Courtney, and Clark, 1998, for different aspects of active attention; and Lumer, 2000, for visuoperceptual discriminations). The combination of functional neuroimaging with methods for detecting the temporal order of brain activation in multiple brain regions, such as electroencephalography (EEG) and magnetoencephalography (MEG) (Andreassi, 1995; Daube, 2002), allows for an understanding of the sequence in which brain regions are put "on line" during a mental task.

This beginning understanding of the complexities of brain activation lays the foundation for a neuroscience-based revision of the big questions self-conscious humans have asked for centuries: What is the neural (anatomic, physiologic) nature of consciousness (e.g., R. Carter, 2002; Dehaene, 2002, *passim;* L. Weiskrantz, 1997)? What are the relative contributions and interactions of genotype and experience (e.g., P.R. Huttenlocher, 2002; B.F. Pennington, 2002). What are the neuroanatomic bases of "self" (Metzinger, 2000, *passim,* 2003, *passim*)?

New technology has supported many traditional beliefs about the brain and challenged others. The long-held belief that neurons do not proliferate after early stages of development has been shaken by considerable evidence showing that new neurons are produced in the adult brains of a number of mammalian species, perhaps playing a role in brain injury repair and new learning (H.S. Levin and Grafman, 2000; Sohlberg and Mateer, 2001; D.G. Stein et al., 1995). In the past few years it has been shown that adult-produced neurons are found in the dentate gyrus of the hippocampus and neocortex in the monkey (Gould, Reeves, Fallah et al., 1999; Gould, Reeves, Graziano, and Gross, 1999), and the hippocampal formation of the human is capable of generating neurons throughout life (Eriksson et al., 1998). The implications of these findings for human aging and diseases are unknown.

In addition, the roles of many brain regions are far more complex than previously thought. The basal ganglia and cerebellum, once believed to be motor control centers, are now being appreciated for their influences on cognition and psychiatric disorders (Barlow, 2002; Crosson, Moore, and Wierenga, 2003; D.M. Jacobs, Levy, and Marder, 1997; Lichter and Cummings, 2001, *passim*). Even the motor cortex appears to play an active role in processing abstract learned information (A.F. Carpenter et al., 1999).

This chapter presents a brief (and necessarily superficial) sketch of some of the structural arrangements in the human central nervous system that are intimately connected with behavioral function. This sketch is followed by a review of anatomical and functional interrelationships that appear with enough regularity to have psychologically meaningful predictive value. More detailed information on neuroanatomy and its behavioral correlates is available in such standard references as Afifi and Bergman (1998), Hendelman (2000), and Nolte (1999). A.R. Damasio and Tranel (1991), Mesulam (2000c), and Tranel (2002) provide excellent reviews of brain–behavior relationships. Reviews of the

brain correlates for a variety of neuropsychological disorders can be found in Feinberg and Farah (2003a), Heilman and Valenstein (2003), Kolb and Whishaw (1996), Naugle, Cullum, and Bigler (1997), and Yudofsky and Hales (2002).

The role of physiological and biochemical events in behavioral expression adds another important dimension to neuropsychological phenomena. Most of the work in these areas is beyond the scope of this book. Readers wishing to learn how biochemistry and neurophysiology relate to behavioral phenomena can consult Andreassi (1995), Cacioppo et al. (2000), Shepherd (1998), and P.F. Smith and Darlington (1996).

BRAIN PATHOLOGY AND PSYCHOLOGICAL FUNCTIONS

> There is no localizable single store for the meaning of a given entity or event within a cortical region. Rather, meaning is achieved by widespread multiregional activation of fragmentary records pertinent to a given stimulus and according to a combinatorial code specific or partially specific to the entity . . . the meaning of an entity, in this sense, is not stored anywhere in the brain in permanent fashion; instead it is re-created anew for every instantiation.
>
> *Daniel Tranel and Antonio R. Damasio, 2000*

The relationship between brain and behavior is exceedingly intricate and frequently puzzling. Our understanding of this fundamental relationship is still very limited, but the broad outlines and many details of the correlations between brain and behavior have been sufficiently well explained to be clinically useful. Any given behavior is the product of a myriad of complex neurophysiological and biochemical interactions involving the whole brain. Complex acts, such as swatting a fly or reading this page, are the products of countless neural interactions involving many, often far-flung sites in the neural network; their neuroanatomical correlates are not confined to any local area of the brain (Luria, 1966; Sherrington, 1955; see also Fuster, 2003; Parks, Levine, and Long, 1998).

Yet discrete psychological activities such as the perception of a pure tone or the movement of a finger can be disrupted by *lesions* (localized abnormal tissues changes) involving approximately the same anatomical structures in most human brains. Additionally, one focal lesion may affect many functions when the damaged neural structure is involved with more or less different functions thus producing a neurobehavioral *syndrome,* a cluster of deficits that tend to occur together with some regularity (Benton, 1977b [1985]; Bogousslavsky and Caplan, 2001, *passim;* H. Damasio and Damasio, 1989; E. Goldberg, 1995). This disruption of complex behavior by brain lesions occurs with such consistent anatomical regularity that inability to understand speech, to recall recent events, or to copy a design, for example, can often be predicted when the site of the lesion is known (Benton, 1981[1985]; Filley, 1995; Geschwind, 1979; Rapp, 2001; Strub and Black, 2000). Knowledge of the *localization of dysfunction,* as this correlation between damaged neuroanatomical structures and behavioral functions may be called, also enables neuropsychologists and neurologists to make educated guesses about the site of a lesion on the basis of abnormal patterns of behavior. However, similar lesions may have quite dissimilar behavioral outcomes (Bigler, 2001b). Markowitsch (1984) described the limits of prediction: "[a] straightforward correlation between a particular brain lesion and observable functional deficits is . . . unlikely . . . as a lesioned structure is known not to act on its own, but depends in its function on a network of input and output channels, and as the equilibrium of the brain will be influenced in many and up to now largely unpredictable ways by even a restricted lesion" (p. 40).

Moreover, localization of dysfunction cannot imply a "push-button" relationship between local brain sites and specific behaviors as the brain's processing functions take place at multiple levels (e.g., encoding a single modality of a percept, energizing memory search, recognition, attribution of meaning) within complex, integrated, interactive, and often widely distributed systems. Thus lesions at many different brain sites may alter or extinguish a single complex act (Luria, 1973b; Nichelli, Grafman, et al., 1994; Sergent, 1988b), as can lesions interrupting the neural pathways connecting areas of the brain involved in the act (Geschwind, 1965; Tranel and Damasio, 2000). E. Miller (1972) reminded us that,

> It is tempting to conclude that if by removing a particular part of the brain we can produce a deficit in behavior, e.g., a difficulty in verbal learning following removal of the left temporal lobe in man, then that part of the brain must be responsible for the impaired function. . . . [T]his conclusion does not necessarily follow from the evidence as can be seen from the following analogy. If we were to remove the fuel tank from a car we would not be surprised to find that the car was incapable of moving itself forward. Nevertheless, it would be very misleading to infer that the function of the fuel tank is to propel the car. (pp. 19–20)

THE CELLULAR SUBSTRATE

The nervous system makes behavior possible. It is involved in the reception, processing, storage, and transmission of information within the organism and in the

organism's exchanges with the outside world. It is a dynamic system in that its activity modifies its performance, its internal relationships, and its capacity to mediate stimuli from the outside.

The brain has two types of cells. *Neurons* conduct nerve impulses that transmit information in the brain and throughout the nervous system. Estimates of the number of nerve cells (neurons) in the brain range from "ten thousand million" (10 billion) (Beaumont, 1988b) to as much as 10^{12} (Strange, 1992). *Glia,* ten to 50 times more numerous than neurons, are supporting brain cells that lack the ability to transmit information (Kandel et al., 2000; Levitan and Kaczmarak, 2002). Their functions are not fully understood, but they are thought to have nutritional and scavenger functions and to release growth factors. *Astrocytes* are one major type of glial cell with an additional role as a component of the *blood–brain barrier* which prevents some substances in the blood from entering into brain cells (P.A. Stewart, 1997). Another major type of glial cell are *oligodendroglia,* which also form *myelin,* the substance of axonal sheaths (see below).

Nerve cells vary in shape and function (Levitan and Kaczmarek, 2002). Most have a cell body, multiple branching *dendrites* that receive stimulation from other neurons, and an *axon* that carries the electrical nerve impulse (called *action potential*). Although the neuron has only one initial segment of axon, the axon may branch to produce collateral segments. Axons vary in length. Long axons have myelin sheaths that provide insulation for high-speed conduction of nerve impulses (Andreassi, 1995; Kandell et al., 2000; Victor and Ropper, 2001).

When well-nourished and adequately stimulated, tiny transmission organs at the neuronal tips proliferate abundantly, providing the human nervous system with an astronomical multiplicity of points of interaction between nerve cells, the *synapses* (Shepherd and Koch, 1998). S. Green (1987) estimates that within the brain a single neuron may have direct synaptic contact with as many as several thousand other neurons. Extrapolating from neuronal and synaptic densities in cat cortex, Shepherd and Koch (1998) calculate that there "must be" approximately 10 billion cells in the human cortex alone, which would give rise to 60 trillion (60×10^{12}) synapses. The stimulation of a neuron can have either an excitatory or inhibitory effect. The postsynaptic cell computes its excitatory and inhibitory inputs and either fires a nerve impulse or not. Alterations in spatial and temporal excitation patterns in the brain's circuitry can add considerably more to its dynamic potential as stimulation applied to a neural pathway heightens that pathway's sensitivity and increases the efficacy with which neuronal excitation may be transmitted through its synapses (Engert and Bonhoeffer, 1999; Koch and Segev, 2000; McAllister Usrey, et al., 2002; Toni et al., 1999). Long-lasting synaptic modifications are called *long-term potentiation* and *long-term depression* (Fuster, 1995; Lynch, 2000; McGaugh, Weinberger, and Lynch, 1995, *passim*). Together these mechanisms of synaptic modification provide the neural potential for the variability and flexibility of human behavior (Levitan and Kaczmarek, 2002; Rolls and Treves, 1998; Shepherd, 1998, *passim*).

Nerve cells do not touch one another at synapses. Communication between neurons is made primarily through the medium of *neurotransmitters,* chemical agents generated within and secreted by stimulated nerve cells. These substances can bridge synaptic gaps between nerve cells to activate receptor neurons (E.S. Levine and Black, 2000; D.A. McCormick, 1998; P.G. Nelson and Davenport, 1999). The discovery of more than 100 neurotransmitters (National Advisory Mental Health Council, 1989) gives some idea of the possible range of selective activation between neurons as each neurotransmitter can bind to and thus activate only those receptor sites with the corresponding molecular conformation, and a single neuron may produce and release more than one of these chemical messengers (Hökfelt et al., 1984; Levitan and Kaczmarek, 2002). The key transmitters implicated in neurologic and psychiatric diseases are acetylcholine, dopamine, norepinephrine, serotonin, glutamate, and gamma-aminobutyric acid (Andreasen, 2001; Wilcox and Gonzales, 1995).

When a nerve cell is injured or diseased, it may stop functioning and the circuits to which it contributed will then be disrupted. Some circuits may eventually reactivate as damaged cells resume functioning or alternative patterns involving different cell populations take over (see pp. 293–294, regarding brain injury and neuroplasticity). When a circuit loses a sufficiently great number of neurons, the broken circuit can neither be reactivated nor replaced. In general, when a human neuron dies, it is not replaced, except in the capacity of the dentate gyrus of the human hippocampus to generate new neurons (Eriksson et al., 1998). Evidence of the generation of new neurons in response to injury or disease is still lacking.

During development neurons initiate a process—*apoptosis*—that kills them to enhance the organization of specific neuronal pathways, a process called *pruning* (Rakic, 2000; Yuan, 2000; Yuan and Yankner, 2000). Diseases of the nervous system may result from the apoptotic process or other forms of cell death which is normally prevented in the healthy adult state by neurotrophic factors (Leist and Nicotera, 1997; Raff, 1998; McAllister, Usrey, et al., 2002).

THE STRUCTURE OF THE BRAIN

The brain is an intricately patterned complex of small and delicate structures. Three major anatomical divisions of the brain succeed one another along the brain stem: the *hindbrain,* the *midbrain,* and the *forebrain* (see Figs. 3.1 and 3.2; for detailed graphic displays, see also Montemurro and Bruni, 1988; Netter, 1983). Structurally, the brain centers that are lowest are the most simply organized. The brain's forward development is characterized by a pronounced tendency for increased anatomical complexity and diversity culminating in the huge, elaborate structures at the brain's front end, the *cerebrum* or *cerebral hemispheres* (since most cerebral structures are laterally paired). The brain's functional organization parallels its structural development as functional complexity increases from the lower brain stem up through its succeeding parts. By and large, lower brain centers mediate simpler, more primitive functions while the forward (top in humans) part of the brain, the cerebral cortex (see p. 52ff), mediates the highest functions.

Within the brain are four fluid-filled pouches, or *ventricles,* through which *cerebrospinal fluid* (*CSF*) flows (Schmidley and Maas, 1990; see also Netter, 1983, pp. 30–31). The most prominent of the pouches, the lateral ventricles, are a pair of horn-shaped reservoirs situated inside the cerebral hemispheres, running from front to back and curving around into the temporal lobe (see Fig. 3.3, p. 42). The third ventricle is situated in the midline in the *diencephalon* ("between-brain") (see Figs. 3.3 and 3.6, p. 49). The fourth lies within the brain stem. Cerebrospinal fluid is produced by specialized tissues within all of the ventricles but mostly in the lateral ventricles. The cerebrospinal fluid serves as a shock absorber and helps to maintain the shape of the soft nervous tissue of the brain. Obstruction of the flow of cerebrospinal fluid in adults can create the condition known as *normal pressure hydrocephalus* (*NPH*) (see pp. 256–257). In conditions in which brain substance deteriorates, the ventricles enlarge to fill in the void. Thus, the size of the ventricles can be an important indicator of the brain's status.

In addition, an elaborate network of blood vessels maintains a rich supply of nutrients to the extremely oxygen-dependent brain tissue (Golanov and Reis, 1997; Hudetz, 1997; Powers, 1990). The cerebral blood supply comes from three major arterial distributions (Fig. 3.4; see Sokoloff, 1997; Tatu et al., 2001). The site of disease or damage to arterial circulation determines the area of the brain cut off from its oxygen supply and, to a large extent, the neuropathologic consequences (see Figs. 3.1 and 3.7, 3.12, pp. 53, 64; pp. 63–85 for a review of cerebral lobes and their functions; pp. 194–202 for pathologies arising from cerebrovascular disorders). The anterior and middle cerebral arteries branch from the internal carotid artery. The anterior division supplies the anterior frontal lobe and *medial* (toward the midline) regions of the brain. The middle cerebral artery feeds the lateral temporal, parietal, and posterior frontal lobes and sends branches deep into subcortical regions. The posterior circulation

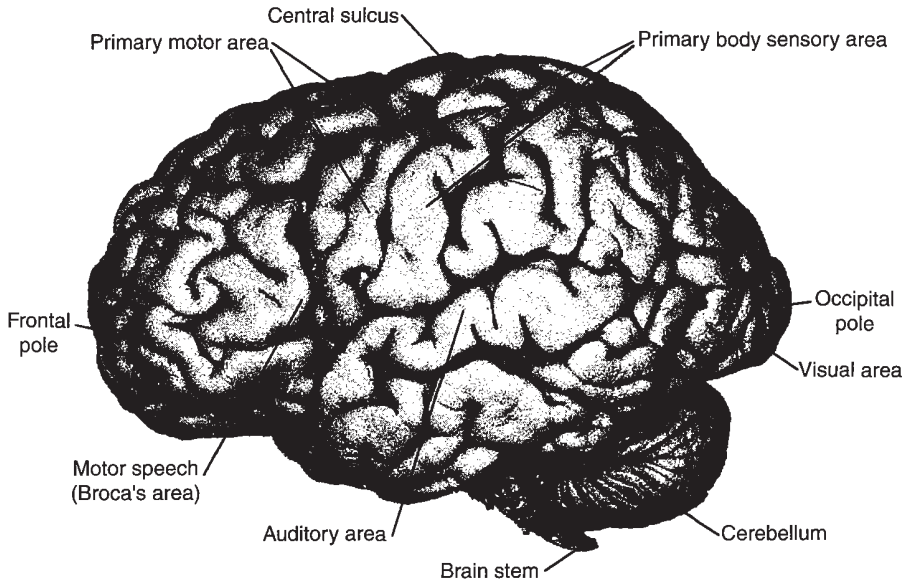

FIGURE 3.1 Lateral view of the cerebrum, cerebellum, and part of the brain stem. (From DeArmond, Fusco, and Dewey, 1976)

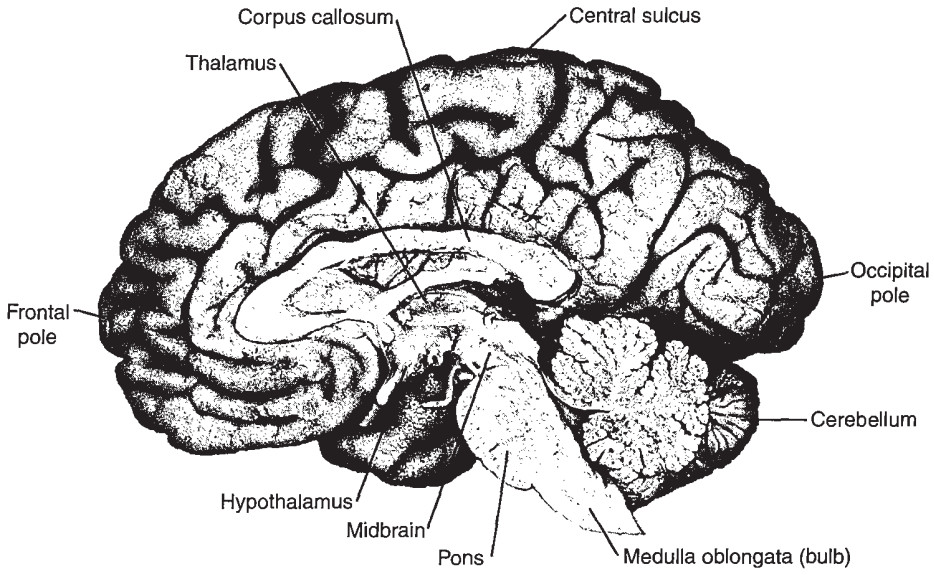

FIGURE 3.2 Medial view of the brain. (From DeArmond, Fusco, and Dewey, 1976)

originates from the vertebral arteries, which join to form the basilar artery. They provide blood to the brain stem and cerebellum. The basilar artery divides into the posterior cerebral arteries and supplies the occipital cortex and medial and inferior regions of the temporal lobe.

The Hindbrain

The medulla oblongata

The lowest part of the brain stem is the hindbrain, and its lowest section is the *medulla oblongata* or *bulb* (see Figs. 3.2 and 3.5, p. 45). The corticospinal tract, which runs down it, crosses the midline here so that each cerebral hemisphere has motor control over the opposite side of the body. The hindbrain is the site of basic life-maintaining centers for nervous control of respiration, blood pressure, and heartbeat. Significant injury to the bulb generally results in death. The medulla contains *nuclei* (clusters of functionally related nerve cells) involved in movements of mouth and throat structures necessary for swallowing, speech, and such related activities as gagging and control of drooling. Damage to lateral medullary structures can result in sensory deficits (J.S. Kim et al., 1997).

The reticular formation

Running through the bulb from the upper cord to the diencephalon is the *reticular formation,* a network of intertwined and interconnecting nerve cell bodies and

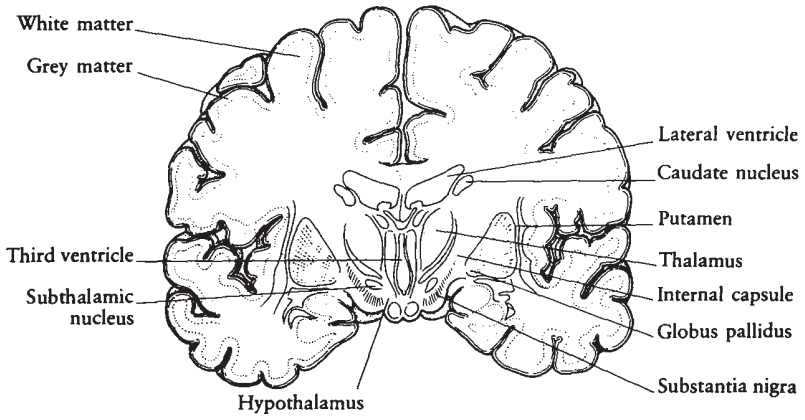

FIGURE 3.3 Coronal (vertical) section of the human brain "taken roughly through the ears" showing diencephalic and other subcortical cerebral structures. (From Strange, 1992)

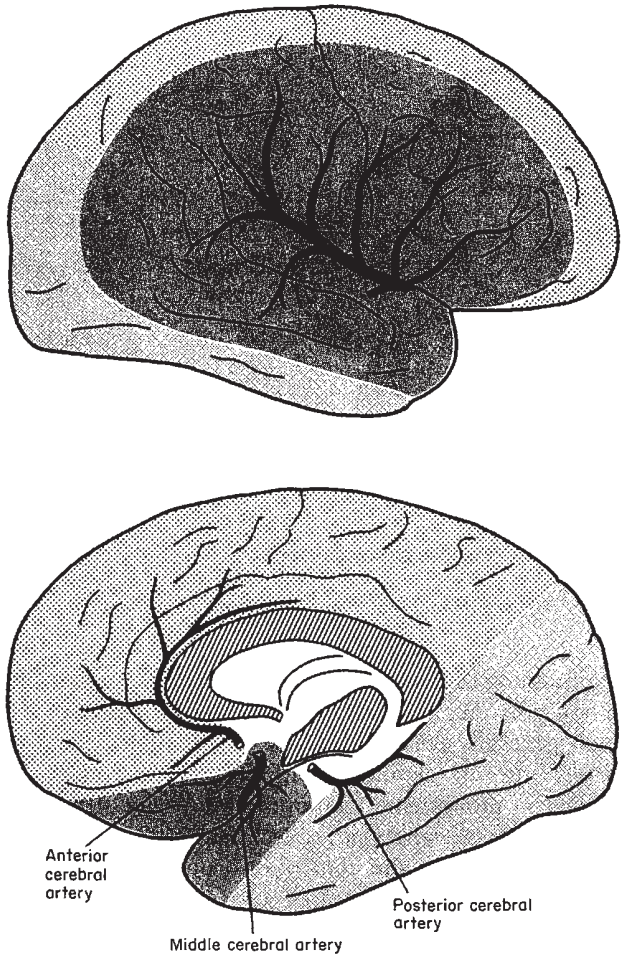

FIGURE 3.4 The parts of the brain supplied with blood from the main arterial branches. (From P. Brodal, 1992)

fibers that enter into or connect with all major neural tracts going to and from the brain (see Figs. 3.5, p. 45 and 3.17, p. 77). The reticular formation is not a single functional unit but contains many nerve centers, i.e., nuclei. These nerve centers mediate important and complex postural reflexes, contribute to the smoothness of muscle activity, and maintain muscle tone. The reticular formation, from about the level of the lower third of the pons (see below and Figs. 3.2 and 3.5) up to and including diencephalic structures, is also the site of the *reticular activating system* (*RAS*), which is the part of the network that controls wakefulness and alerting mechanisms that ready the individual to react (S. Green, 1987; Mirsky, 1989). The RAS modulates attention through its arousal of the cerebral cortex (Mesulam, 2000b; Parasuraman, Warm, and See, 1998; Van Zomeren and Brouwer, 1994). The intact functioning of this network is a precondition for conscious behavior since it arouses the sleeping or inattentive organism (G. Roth, 2000). Brain stem lesions involving the RAS give rise to sleep disturbances and to global disorders of consciousness and responsivity such as drowsiness, somnolence, stupor, or coma.

The pons

The *pons* is high in the hindbrain (Figs. 3.2 and 3.5, pp. 42, 45). It contains major pathways for fibers running between the cerebral cortex and the cerebellum (see below), which is attached to the brain stem. Together, the pons and cerebellum correlate postural and *kinesthetic* (muscle movement sense) information, refining and regulating motor impulses relayed from the cerebrum at the top of the brain stem. Lesions of the pons may cause motor, sensory, and coordination disorders (L.R. Caplan, 2001; Chung and Caplan, 2001).

The cerebellum

The *cerebellum* is at the posterior base of the brain (Figs. 3.1, 3.2, 3.5). In addition to reciprocal connections with vestibular and brain stem nuclei, the *hypothalamus* (see p. 47), and the spinal cord, it has strong connections with the motor cortex and contributes to motor control through influences on programming and execution of actions. Cerebellar damage is commonly known to produce problems of fine motor control, coordination, and postural regulation (Barlow, 2002). Dizziness (*vertigo*) and jerky eye movements may also accompany cerebellar damage.

It is becoming increasingly evident that the cerebellum has a variety of nonmotor functions involving all aspects of behavior (Schmahmann, 2003). Highly organized neural pathways from both lower and higher areas of the brain project through the pons to the cerebellum (Llinás and Walton, 1998; Schmahmann and Sherman, 1998). The cerebellum projects through the thalamus to the same cortical areas from which it receives input, including frontal, parietal, and superior temporal cortices (Botez, Gravel, Attig, and Vezina, 1985; Schmahmann and Sherman, 1998). Through its connections with these cortical areas and with subcortical sites, cerebellar lesions can disrupt abstract reasoning, verbal fluency, visuospatial abilities, attention, emotional modulation (Botez, Lalonde, and Botez-Marquard, 1996; Middleton and Strick, 2000a; Schmahmann and Sherman, 1998), and planning and time judgment (Dow, 1988; Ivry and Fiez, 2000; MacLean, 1991). The cerebellum is also involved in linguistic processing (H.C. Leiner et al., 1989), word generation (Raichle, 2000), set shifting (Le et al., 1998), working memory (Desmond et al., 1997), and memory and learning (Nyberg, 1998)—especially habit forma-

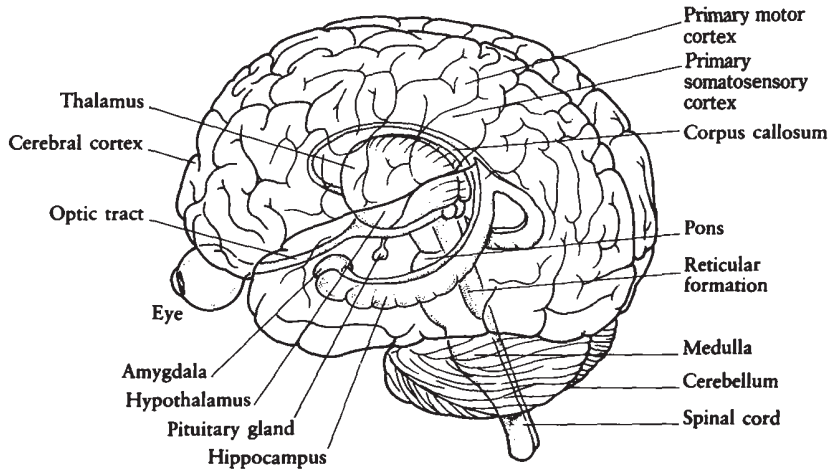

FIGURE 3.5 Diagram showing the hippocampus in relation to the rest of the brain. (From Strange, 1992)

tion (Eichenbaum and Cohen, 2001; H.C. Leiner et al., 1986; R.F. Thompson, 1988). Moreover, speed of information processing slows with cerebellar lesions (Botez, Gravel, et al., 1985). Some disruptions may be transient (Botez et al., 1985; Botez-Marquard, Leveille, and Botez, 1994; Schmahmann and Sherman, 1998). Personality changes and psychiatric disorders have also been linked to cerebellar dysfunction (Andreasen, 2001; P. Martin and Albers, 1995; J. Parvizi et al., 2001).

The Midbrain

The *midbrain* (*mesencephalon*), a small area just forward of the hindbrain, includes the major portion of the reticular activating system. Its functioning may be a prerequisite for conscious experience (Parvizi and Damasio, 2001). It also contains both sensory and motor correlation centers (see Fig. 3.2). Auditory and visual system processing that takes place in midbrain nuclei contributes to the integration of reflex and automatic responses. Midbrain lesions have been associated with specific movement disabilities such as certain types of tremor, rigidity, and extraneous movements of local muscle groups. Even impaired memory retrieval has been associated with damage to midbrain pathways projecting to structures in the memory system (E. Goldberg, Antin, Bilder, et al., 1981; Hommel and Besson, 2001).

The Forebrain: Diencephalic Structures

The most forward part of the brain has two subdivisions. The *diencephalon* ("between-brain") comprises a set of structures, including correlation and relay centers, that evolved at the *anterior,* or most forward, part of the brain stem. These structures are almost completely embedded within the two halves of the *forebrain,* the *telencephalon.*

The thalamus

From a neuropsychological viewpoint, the most important of the diencephalic structures are the *thalamus* and the *hypothalamus* (see Figs. 3.2, 3.3, p. 43, 3.5 and 3.6, p. 49). The thalamus is a small, paired, somewhat oval structure lying along the right and left sides of the third ventricle. Each half of the thalamus consists of eleven nuclei or more, depending on whether minor or peripheral structures are distinguished or included in the count. The two halves are matched approximately in size, shape, and position to corresponding nuclei in the other half. Most of the anatomic interconnections formed by these nuclei and many of their functional contributions are known. Nevertheless, growing understanding of how complex are the fine circuitry, feedback loops, and many functional systems in which the thalamus is enmeshed, and of the interplay between its neurophysiological processes, its neurotransmitters, and its structures encourages speculation and requires caution when interpreting research findings (Steriade et al., 1990).

A complete description of the complex connections of the many thalamic nuclei with cortical, brainstem, and limbic system (see pp. 49–51) structures is beyond the scope of this book. The basic organization and highlights are presented instead.

Thalamic nuclei have extensive reciprocal connections with the cortex that are topographically organized (S.M. Sherman and Koch, 1998). Sensory nuclei serve as major sensory relay centers for all senses ex-

cept smell and project to primary sensory cortices (see pp. 53–54). Body sensations in particular may be degraded or lost with damage to appropriate thalamic nuclei (L.R. Caplan, 1980; Graff-Radford, Damasio, et al., 1985), with an associated impairment of the ability to make tactile discriminations and identification of what is felt (*tactile object agnosia*) (Caselli, 1991; Bauer and Demery, 2003). Although pain sensation typically remains intact or is only mildly diminished, with some kinds of thalamic damage it may be heightened to an excruciating degree (A. Barth et al., 2001; Brodal, 1981; Clifford, 1990). Other thalamic nuclei are relay pathways for vision, hearing, and taste (J.S. Kim, 2001). Still other areas are relay nuclei for limbic structures. Motor nuclei receive input from the cerebellum and the basal ganglia and project to the motor association cortex. As the termination site for the ascending RAS, it is not surprising that the thalamus has important arousal and sleep-producing functions (S. Green, 1987; J. Newman, 1997; Steriade et al., 1990) and that it alerts—activates and intensifies—specific processing and response systems (Crosson, 1992; LaBerge, 2000; Mesulam, 2000b). Its involvement in attention shows up in diminished awareness of stimuli impinging on the side opposite the lesion (*unilateral inattention*) (Heilman, Watson, and Valenstein, 2003; Ojemann, 1984; Posner, 1988).

The thalamus also plays a significant role in regulating higher-level brain activity (S.M. Sherman and Koch, 1998). The *dorsomedial nucleus* is of particular interest because of its established role in memory and its extensive reciprocal connections with the prefrontal cortex (Graff-Radford, 2003; Mesulam, 2000b). It also receives input from the temporal cortex, *amygdala* (see pp. 49–50), hypothalamus, and other thalamic nuclei (Afifi and Bergman, 1998). That the dorsomedial nuclei of the thalamus participate in memory functions has been known ever since lesions here were associated with the memory deficit of Korsakoff's psychosis (von Cramon et al., 1985; Victor, Adams, and Collins, 1971; see pp. 262–265). In most if not all cases of memory impairment associated with the thalamus, lesions have extended to the *mammillothalamic tract* (Graff-Radford, 2003; Markowitsch, 2000; Verfaellie and Cermak, 1997). The mammillothalamic tract connects the *mammillary bodies* (small structures at the posterior part of the hypothalamus involved in information correlation and transmission [Brodal, 1981; Crosson, 1992]) to the thalamus which sends projections on a pathway to the prefrontal cortex and medial temporal lobe (Fuster, 1994; Markowitsch, 2000).

Two kinds of memory impairments tend to accompany thalamic lesions: (1) Learning is compromised (anterograde amnesia), possibly by defective encoding, which makes effective retrieval difficult if not impossible (N. Butters, 1984a; Mayes, 1988; Ojemann, Hoyenga, and Ward, 1971); possibly by a diminished capacity of learning processes to free up readily for succeeding exposures to new information (defective *release from proactive inhibition*) (N. Butters and Stuss, 1989; Parkin, 1984). A rapid loss of newly acquired information may also occur (Stuss, Guberman, et al., 1988), although usually when patients with thalamic memory impairment do learn they forget no faster than do intact persons (Parkin, 1984). (2) Recall of past information is defective (retrograde amnesia), typically in a *temporal gradient* such that recall of the most recent (premorbid) events and new information is most impaired, and increasingly older memories are increasingly better retrieved (N. Butters and Albert, 1982; Kopelman, 2001). Montaldi and Parkin (1989) suggest that these two kinds of memory impairment are different aspects of a breakdown in the use of context (encoding), for retrieval depends on establishing and maintaining "contextual relations among existing memories." Errors made by an unlettered file clerk would provide an analogy for these learning and retrieval deficits: Items filed randomly remain in the file cabinet but cannot be retrieved by directed search, yet they may pop up from time to time, unconnected to any intent to find them (see also Hodges, 1995).

Amnesic patients with bilateral diencephalic lesions, such as Korsakoff patients, tend to show disturbances in time sense and the ability to make temporal discriminations that may play a role in their prominent retrieval deficits (Graff-Radford, Tranel, et al., 1990; Squire, Haist, and Shimamura, 1989). Characteristically, memory-impaired patients with thalamic or other diencephalic lesions lack appreciation of their deficits, in this differing from many other memory-impaired persons (Mesulam, 2000b; Parkin, 1984; Schacter, 1991). In a review of 61 cases of adults with thalamic lesions, mostly resulting from stroke, half had problems with concept formation, flexibility of thinking, or executive functions (Van der Werf et al., 2000).

Differences in how the two halves of the brain process data, so pronounced at the highest—cortical—level, first appear in thalamic processing of sensory information (A. Barth et al., 2001; J.W. Brown, 1975). In its lateral asymmetry, thalamic organization parallels cortical organization in that left thalamic structures are implicated in verbal activity, and right thalamic structures in nonverbal aspects of cognitive performance. For example, patients who have left thalamic lesions or who are undergoing left thalamic electrostimulation have not lost the capacity for verbal communication but may experience dysnomia and other language disruption (Crosson, 1992; Graff-Radford,

Damasio, et al., 1985; M.D. Johnson and Ojemann, 2000). This pattern is not considered to be a true aphasia, but rather has been described as a "withering" of language functioning that sometimes leads to mutism. Apathy, confusion, and disorientation characterize this behavior pattern (J.W. Brown, 1974; see also D. Caplan, 1987; Mazaux and Orgogozo, 1982). Patients with left thalamic lesions may achieve lower scores on verbal tests than patients whose thalamic damage is limited to the right side (Graff-Radford, Damasio, et al., 1985; Vilkki, 1979). Language deficits do not appear with very small thalamic lesions, suggesting that observable language deficits at the thalamic level require destruction of more than one pathway or nucleus, as would happen with larger lesions (Wallesch, Kornhuber, et al., 1983).

Neuroimaging studies have shown that right thalamic regions are involved in identifying shapes or locations (LaBerge, 2000). Patients who have right thalamic lesions or who undergo electrostimulation of the right thalamus can have difficulty with face or pattern recognition and pattern matching (Fedio and Van Buren, 1975; Vilkki and Laitinen, 1974, 1976), maze tracing (Meier and Story, 1967), and design reconstruction (Graff-Radford, Damasio, et al., 1985). Heilman, Watson, and Valenstein (2003) provide graphic evidence of patients with right thalamic lesions who displayed left-sided inattention characteristic of patients with right-sided—particularly right posterior—cortical lesions (the "neglect syndrome"; see pp. 72–73). This phenomenon may also accompany left thalamic lesions, although unilateral inattention occurs more often with right-sided damage (Posner, 1988; Velasco et al., 1986; Vilkki, 1984). Although some studies have suggested that unilateral thalamic lesions lead to modality-specific memory deficits (Graff-Radford, Damasio, et al., 1985; M.D. Johnson and Ojemann, 2000; Stuss, Guberman, et al., 1988), conflicting data leave this question unresolved (N. Kapur, 1988b; Rousseaux et al., 1986).

Alterations in emotional capacity and responsivity tend to accompany thalamic damage, typically as apathy, loss of spontaneity and drive, and affective flattening, emotional characteristics that are integral to the Korsakoff syndrome (O'Connor et al., 1995; Schott et al., 1980; Stuss, Guberman, et al., 1988). Yet disinhibited behavior and emotions occasionally appear with bilateral thalamic lesions (Graff-Radford, Tranel, et al., 1990). Transient manic episodes may follow right thalamic infarctions, with few such reactions—or strong emotional responses—seen when the lesion is on the left (Cummings and Mega, 2003; Starkstein, Robinson, Berthier, et al., 1988). These emotional and personality changes in diencephalic amnesia patients reflect how intimately interlocked are the emotional and memory components of the limbic system.

The other limbic system structures that have been specifically implicated in impairment of the recording and consolidation processes of memory are the mammillary bodies and the *fornix* (a central forebrain structure that links the hippocampal and the mammillothalamic areas of the limbic system) (N. Butters and Stuss, 1989; Markowitsch, 2000; Tanaka et al., 1997; Warrington and Weiskrantz, 1982). Massive anterograde amnesia and some retrograde amnesia can result from diffuse lesions involving the mammillary bodies and the thalamus (Graff-Radford, Tranel, et al., 1990; Kopelman, 2002; Squire, Haist, and Shimamura, 1989). Recording of ongoing events may be impaired by lesions of the fornix (Grafman, Salazar, et al., 1985; Mayes, 2000b; Ojemann, 1966; Warrington and Weiskrantz, 1982).

The hypothalamus

Although it takes up less than one-half of one percent of the brain's total weight, the *hypothalamus* regulates such important physiologically based drives as appetite, sexual arousal, and thirst (Netter, 1983; Rolls, 1999; C.B. Saper, 1990). It receives inputs from many brain regions and coordinates autonomic and endocrine functions. Behavior patterns having to do with physical protection, such as rage and fear reactions, are also regulated by hypothalamic centers. Depending on the site of the damage, lesions to hypothalamic nuclei can result in a variety of symptoms, including obesity, disorders of temperature control, and diminished drive states and responsivity (F.G. Flynn et al., 1988). Mood states may also be affected by hypothalamic lesions (Andreason, 2001; Shepherd, 1994; Wolkowitz and Reus, 2001). Damage to the mammillary bodies in the posterior hypothalamus disrupts memory processing (Tanaka et al., 1997).

The Forebrain: The Cerebrum

The basal ganglia

The *cerebrum,* the most recently evolved, most elaborated, and by far the largest brain structure, has two hemispheres that are almost but not quite identical mirror images of each other (see Figs. 3.5, p. 45 and 3.7, p. 53). Within each *cerebral hemisphere,* at its base, are situated a number of nuclear masses known as the *basal ganglia* ("ganglion" is another term for "nucleus"). In most nomenclatures the basal ganglia refer to the *caudate, putamen,* and *globus pallidus* (see Figs. 3.3, 3.6, 3.17, pp. 45, 49, 77). In some sources, the basal gan-

glia include the amygdala, *subthalamic nucleus, substantia nigra,* and other subcortical structures (see Figs. 3.5 and 3.17, pp. 45, 77). The cerebral cortex projects directly to the caudate and putamen, and the globus pallidus and substantia nigra project back to the cerebral cortex through the thalamus. In addition to the motor cortex, the basal ganglia have reciprocal connections with at least nine other cortical areas, including subdivisions of the premotor, oculomotor, prefrontal (dorsolateral and orbitofrontal), and inferotemporal cortices (Middleton and Strick, 2000a, b; Rolls, 1999). Somatotopic representation of specific body parts (e.g., hand, foot, face) within basal ganglia structures overlap, are similar for different individuals, and are unlike the pattern of cortical body part representation (Maillard et al., 2000).

"Figuratively speaking, the *neostriatum* (caudate and putamen) can be considered as part of the system which translates cognition into action" (Divac, 1977; see also Brunia and Van Boxtel, 2000; Passingham, 1997). The basal ganglia influence all aspects of motor control, and movement disorders may be the most common and obvious symptoms of basal ganglia damage (Crosson, Moore, and Wierenga, 2003). They are not motor nuclei in a strict sense, as damage to them gives rise to various motor disturbances but does not result in paralysis. The movement disorders associated with basal ganglia disease have been thoroughly described, but what these nuclei contribute to the motor system is less well understood (Haaland and Harrington, 1990; Thach and Montgomery, 1990). In general, diseases of the basal ganglia are characterized by abnormal involuntary movements at rest. The particular effects vary with the specific site of injury. These nuclei also play an important role in the acquisition of habits and skills (Jog et al., 1999; see also Blazquez et al., 2002; Graybiel and Kubota, 2003).

Much of the understanding of the influence of the basal ganglia on movement and other aspects of behavior has been obtained by studying patients with *Parkinson's disease* and *Huntington's disease* (see pp. 225–227, 234–236). Parkinson's disease, primarily occuring with depletion of the neurotransmitter *dopamine* in the neostriatum due to degeneration of the substantia nigra, results in poverty of movement. It is interesting to note that difficulties in starting activities and in altering the course of ongoing activities characterize both motor and mental aspects of this disease (R.G. Brown, 2003). Huntington's disease, which develops with loss of neurons in the caudate nucleus, is characterized by excessive motor activity. Huntington patients, like Parkinson patients, appear to have trouble initiating cognitive processes (Brandt and Butters, 1996) and control over cognitive functions as well as movements is impaired (Richer and Chouinard, 2003). In both conditions, many cognitive abilities are impaired and emotional disturbances may be prominent.

The neostriatum appears to be a key component of the procedural memory system (Fuster, 1995; Mishkin and Appenzeller, 1987; Knowlton et al., 1996), perhaps serving as a procedural memory buffer for established skills and response patterns and participating in the development of new response strategies (skills) for novel situations (Saint-Cyr and Taylor, 1992). With damage to the basal ganglia, cognitive flexibility—the ability to generate and shift ideas and responses—is reduced (Lawrence et al., 1999; Mendez, Adams, and Lewandowski, 1989). Hemispheric lateralization becomes apparent with unilateral lesions, both in motor disturbances affecting the side of the body contralateral to the lesioned nuclei and in the nature of the concomitant cognitive disorders (L.R. Caplan, Schmahmann, et al., 1990). Several different types of aphasic and related communication disorders have been described in association with left-sided lesions (Cummings and Mega, 2003). In some patients, lesions in the left basal ganglia alone or in conjunction with left cortical lesions have been associated with defective knowledge of the colors of familiar objects (Varney and Risse, 1993). Symptoms tend to vary in a fairly regular manner with the lesion site (M.P. Alexander, Naeser, and Palumbo, 1987; Basso, Della Sala, and Farabola, 1987; A.R. Damasio, Damasio, and Rizzo, 1982; Tanridag and Kirshner, 1985), paralleling the cortical aphasia pattern of reduced output with anterior lesions, reduced comprehension with posterior ones (Crosson, 1992; Naeser, Alexander, et al., 1982). Left unilateral inattention accompanies some right-sided basal ganglia lesions (Bisiach and Vallar, 1988; Ferro, Kertesz, and Black, 1987; L.R. Caplan, Schmahmann, et al., 1990; Vallar and Perani, 1986; Villardita et al., 1983).

Dramatic and disruptive personality changes may occur in Huntington's disease as basal ganglia degeneration proceeds (see pp. 227, 235–236). Moreover, alterations in basal ganglia circuits involved with nonmotor areas of the cortex have been implicated in a wide variety of neuropsychiatric disorders including schizophrenia, obsessive-compulsive disorder, depression, Tourette's syndrome, autism, and attention deficit disorders (D.J. Stein and Hugo, 2002; Middleton and Strick, 2000b; M.A. Taylor, 1999). Emotional flattening with loss of drive resulting in more or less severe states of inertia can occur with bilateral basal ganglia damage (Bhatia and Marsden, 1994; Laplane et al., 1984; Strub, 1989). These *anergic* (unenergized, apathetic) conditions resemble those associated with some kinds of frontal damage and further emphasize the interrelationships between the basal ganglia and the

frontal lobes. Mood differences have shown up in new stroke patients with lateralized basal ganglia lesions, in that more patients with left-sided damage were depressed than those with right-sided involvement (Starkstein, Robinson, Berthier, et al., 1988).

The *nucleus basalis of Meynert* is a small basal forebrain structure lying partly within and partly adjacent to the basal ganglia (N. Butters, 1985; H. Damasio and Damasio, 1989). It is an important source of the cholinergic neurotransmitters implicated in learning. Loss of neurons here occurs in degenerative dementing disorders in which memory impairment is a prominent feature (Fuster, 1995; J.D. Rogers et al., 1985).

The Limbic System

The *limbic system* includes, among other structures, the amygdala and two phylogenetically old regions of cortex: the cingulate gyrus and the hippocampus (Dudai, 1989; Markowitsch, 2000; Papez, 1937; see also Figs. 3.5, p. 45 and 3.6). Its components are embedded in structures as far apart as the reticular activating system in the brain stem and olfactory nuclei underlying the forebrain. These structures have important roles in emotion, motivation, and memory (Damasio, 1994; Markowitsch, 2000; Mesulam, 2000b; Don M. Tucker, Derryberry, and Luu, 2000). The intimate connection between memory and emotions is illustrated by Korsakoff patients with severe learning impairments who retain emotionally laden words better than neutral ones (J. Kessler et al., 1987). This same phenomenon has been observed in some anergic TBI (traumatic brain injury) patients whose condition implicates limbic damage and whose responsiveness and learning ability increase when emotionally stimulated. Disturbances in emotional behavior occur in association with seizure activity involving these structures (see pp. 76, 322).

The amygdala

This small structure is located deep in the anterior part of the temporal lobe (Fig. 3.5, p. 45). Consisting of a number of nuclei with differing input and output pathways, it has connections with the cerebral cortex, hippocampus, basal ganglia, thalamus, hypothalamus, and brain stem nuceli. It plays important roles in emotional processing and learning (Bechara, Damasio, Damasio, and Lee, 1999; Rolls, 1999; Sarter and Markowitsch, 1985) and in the modulation of attention (Eichenbaum and Cohen, 2001).

Not surprisingly, given its rich hypothalamic interconnections, the amygdala is intimately involved with vegetative and protective drive states, movement patterns, and associated emotional responses. It has direct connections with the primitive olfaction centers (*olfactory bulbs*) (A.R. Damasio, 2001; Shepherd and Greer, 1998; see Fig. 3.5). Damage to the amygdala's interconnecting structures (e.g., the posterior septum lying between the hemispheres in front of the anterior commissure) has been associated with both hypersexuality

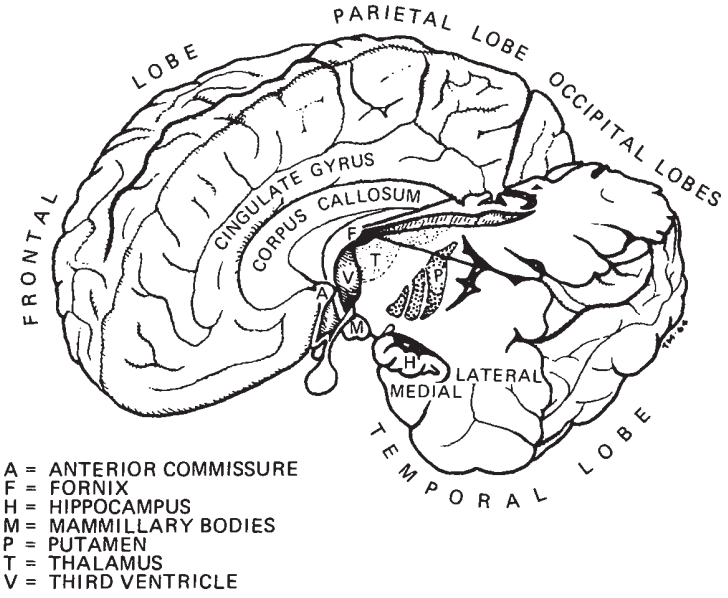

FIGURE 3.6 Cutaway perspective drawing of a human brain showing the spatial relationships of most of the regions and structures thought to be related to general memory function. (The putamen is shown only as a landmark for readers familiar with the brain.) (From Ojemann, 1966)

and diminished aggressive capacity (Brodal, 1981; Gorman and Cummings, 1992). Semiautomatic visceral activities, particularly those concerned with feeding (e.g., chewing, salivating, licking, and gagging) and with the visceral components of fear reactions, are affected by stimulation or ablation of the amygdala. This small structure may also be necessary for processing facial expressions of fear (Adolphs and Damasio, 2000; Rolls, 1999). Seizure activity and experimental stimulation of the amygdala provoke visceral responses associated with fright and mouth movements involved in feeding.

Removal of the amygdala from both hemispheres can have a "taming" effect on humans and other animals alike, with loss of the ability to make emotionally meaningful discriminations between stimuli (Cahill and McGaugh, 1998; Killcross, 2000; J. Rosen and Schulkin, 1998; Pincus and Tucker, 2003). Amygdalectomized humans become apathetic showing little spontaneity, creativity, or affective expression (Aggleton, 1993; G.P. Lee, Bechara, Adolphs, et al., 1989). In addition, the ability to make social interpretations of facial expressions is impaired in patients with bilateral amygdala lesions (Adolphs et al., 1998). Amygdala dysfunction has been implicated in autism (Baron-Cohen, 1995; Baron-Cohen et al., 2000).

The amygdala provides an emotional "tag" to memory traces (Doty, 1990; Rolls, 1990; Sarter and Markowitsch, 1985). With its connections to the orbitofrontal cortex, the amygdala appears to be necessary for learning to associate sensory stimuli with reward (Rolls and Treves, 1998). Information about rewards and emotions is sent from the amygdala to the hippocampus. Material learned by amygdalectomized patients tends to be retained, but they become more dependent on context and external structure for learning new material, for retrieval generally, and for maintaining directed attention and tracking than prior to surgery (R. Anderson, 1978). The amygdala may play an important role in memory consolidation by influencing neuroplasticity in other brain regions (McGaugh, 2000), although much remains speculative. Its specialized memory functions appear to involve object recognition (Mishkin and Appenzeller, 1987). Bilateral destruction of the amygdala in humans does not produce a prominent amnesic disorder (G.P. Lee, Meador, Smith, et al., 1988; Markowitsch, Calabrese, Wurker, et al., 1994; I.F. Small et al., 1977). However, lesions in the amygdala and nearby temporal cortex contribute to the severity of memory deficits associated with hippocampal damage (Jernigan, Ostergaard, and Fennema-Notestine, 2001). Amygdalectomized patients are slow to acquire a mind set, but once it is established it becomes hard to dislodge; yet performance on standard measures of mental abilities (e.g., Wechsler Intelligence Scale tests) remains essentially unchanged (R. Andersen, 1978).

The *Klüver-Bucy syndrome* follows bilateral destruction of the amygdala and *uncus* (the small hooked front end of the inner temporal lobe fold). This is a rare condition that can occur with disease (e.g., herpes encephalitis [see pp. 275–276]) or trauma. These placid patients lose the capacity to learn and to make perceptual distinctions, they eat excessively and indiscriminately, and they may become hypersexual, often indiscriminately so (Cummings and Mega, 2003; Hayman et al., 1998; Trimble, Mendez, and Cummings, 1997).

The cingulate cortex

The *cingulate gyrus* is located in the medial aspects of the hemispheres above the corpus callosum (Fig. 3.6). It has important influences on attention, response selection, and emotional behavior (Brunia and Van Boxtel, 2000; Chelazzi and Corbetta, 2000; Rolls, 1999). Anterior and posterior portions have different projections and roles. Together with the lateral prefrontal cortex, the anterior cingulate cortex controls behavior by detecting errors and signaling the occurrence of conflicts during information processing. These functions are critical for the regulation of behavior according to self-determined intentions. The relative contribution of the two structures is a matter of debate (J.D. Cohen et al., 2000; Gehring and Knight, 2000). Lesions of the anterior cingulate cortex interfere with selective attention, response competition monitoring, and self-initiated behavior (R.A. Cohen et al., 1999; Danckert et al., 2000; Devinsky, Morrell, and Vogt, 1995; Posner and Rothbart, 1998). The anterior cingulate is also involved in pain perception (Rolls, 1999). Whereas the anterior cingulate receives projections mainly from the amygdala, the posterior cingulate receives most projections from the hippocampus (see below) and is part of the neural pathway for memory (Desgranges et al., 1998; Mesulam, 2000b).

The hippocampus

A major component of the memory system, the *hippocampus* runs within the inside fold of each temporal lobe for much of its length (Figs. 3.5 and 3.6, pp. 45, 46). Converging evidence from lesion studies, epilepsy surgery, and functional imaging studies points to its primary role in normal learning and retention. The hippocampus is well-designed for rapid association of information from many different cortical areas (Eichenbaum and Cohen, 2001; D. Johnston and Amaral, 1998; O'Keefe and Nadel, 1978). The hippocampus has

been identified as one site of interaction between the perception and the memory systems with a particular role in spatial memory (Mishkin and Appenzeller, 1987; Zola and Squire, 2000). Only sensorimotor skill learning and simple forms of conditioning take place in other brain centers (Buckner and Tulving, 1995; Corkin, 1968; Eichenbaum and Cohen, 2001; Mayes, 2000b; Squire and Knowlton, 2000).

The hippocampus has been described as using a "snapshot" type of processing to remember a scene or episode with its unique elements and contextual features (Rolls and Treves, 1998). The hippocampus can later activate retrieval of the whole representation when a small part of the representation occurs (McClelland, 1994; Rolls and Treves, 1998). Two-way information between many areas of the cortex and the hippocampus goes through the *entorhinal cortex* as information about rewards and emotions travels from the amygdala to the hippocampus. A second pathway for outputs from the hippocampus to the cortex goes by way of the *fornix* and thalamus (Fig. 3.6).

The hippocampus and adjacent areas of the temporal lobe are critical for learning, i.e., the formation of new memories (Ogden, 1996, chap. 3; Rempel-Clower et al., 1996; Zola and Squire, 2000; see pp. 75–76). It has been suggested that the hippocampus processes new memories by assigning each experience an index corresponding to the areas of the neocortex which, when activated, reproduce the experience or memory (Alvarez and Squire, 1994; Schacter, 1998). The hippocampal index typically includes information about events and their context, such as when and where they occurred as well as emotions and thoughts associated with them. The index corresponding to a particular memory, such as a conversation or other activity, is crucial for activating the memory until the neocortex consolidates the memory by linking all the features of the experience to one another. After consolidation, direct neocortical links are sufficient for storing the memory (Schacter, Norman, and Koutstaal, 1998). Old memories do not appear to be stored in the hippocampus; rather, storage is probably distributed throughout the cortex (Fuster, 1995; Rempel-Clower et al., 1996; Rolls and Treves, 1998).

Bilateral damage to the hippocampus can produce severe anterograde amnesia (Rempel-Clower et al., 1996; Tulving and Markowitsch, 1998). The cortical regions adjacent to the hippocampus, the entorhinal cortex, parahippocampus, and other perirhinal cortices provide major input to the hippocampus. When lesions of the hippocampus extend into these regions, the severity of the memory impairment worsens and the likelihood of extensive retrograde amnesia increases (K.S. Graham and Hodges, 1997; J.M. Reed and Squire, 1998). Damage to the hippocampus and adjacent areas of the temporal lobe is responsible for the memory impairment so prominent in mild Alzheimer's disease (Cotman and Anderson, 1995; Jack et al., 1999; Kaye, Swihart, Howieson, et al., 1997). Disturbances in emotional behavior occur in association with seizure activity involving the hippocampus as well as the amygdala and uncus (Heilman, Blonder, et al., 2003; Pincus and Tucker, 2003; Wieser, 1986).

Unilateral destruction of the hippocampus can result in lateralized processing differences. Loss of the left hippocampus impairs verbal memory, and destruction of the right hippocampus results in defective recognition and recall of "complex visual and auditory patterns to which a name cannot readily be assigned" (B. Milner, 1970, p. 30; see also A.R. Damasio, 2001; Jones-Gotman, 1987). For example, London taxi drivers recalling familiar routes showed right hippocampal activation on PET scans (Maguire et al., 1997). However, rote verbal learning may be more vulnerable to left hippocampal disease than learning meaningful material (a story) (Saling et al., 1993). Story recall appears to be affected—but to a lesser degree than rote learning—by damage to either the right or left hippocampus. Additionally, learning unrelated as opposed to related word pairs is disproportionately impaired with left, rather than right, hippocampal disease (A.G. Wood et al., 2000).

Intracerebral conduction pathways

> The mind depends as much on white matter as on its gray counterpart.
>
> *Christopher M. Filley, 2001*

Much of the bulk of the cerebral hemispheres is *white matter,* consisting of densely packed conduction fibers that transmit neural impulses between cortical points within a hemisphere (*association fibers*), between the hemispheres (*commissural fibers*), or between the cerebral cortex and lower centers (*projection fibers*). Lesions in cerebral white matter sever connections between lower and higher centers or between cortical areas. White matter lesions are found in many dementing disorders and appear to be specifically associated with attentional impairments (Filley, 2001; Junqué et al., 1990).

The *corpus callosum* is the great band of commissural fibers connecting the two hemispheres (see Figs. 3.2, 3.5, and 3.6, pp. 42, 45, 49). Other interhemispheric connections are provided by some smaller bands of fibers. Interhemispheric communication maintained by the corpus callosum and other commissural fibers enforces integration of cerebral activity between

the two hemispheres (Banich, 1995; Trevarthen, 1990; E. Zaidel, Clarke, and Suyenobu, 1990).

The corpus callosum is organized with a great deal of regularity (Brodal, 1981; J.M. Clarke et al., 1998; Witelson, 1995). Fibers from the frontal cortex make up its anterior portion. The posterior portion consists of fibers originating in the posterior cortex. Fibers from the visual cortex at the posterior pole of the cerebrum occupy the posterior end portion of the callosum. Midcallosal areas contain a mixture of fibers coming from both anterior and posterior regions. Studies of sex differences in overall size of the corpus callosum have produced inconsistent results (Bishop and Wahlstein, 1997; H.L. Burke and Yeo, 1994; Davatzikos and Resnick, 1998; Salat et al., 1997; Witelson, 1989; E. Zaidel, Aboitiz, et al., 1995). Some studies have found that the corpus callosum tends to be larger in nonright-handers (Cowell et al., 1993; Habib, Gayraud, Oliva, et al., 1991; Witelson, 1985).

Surgical section of the corpus callosum cuts off direct interhemispheric communication (Baynes and Gazzaniga, 2000; Bogen, 1985; Seymour et al., 1994). When examined by special neuropsychological techniques (see E. Zaidel, Zaidel, and Bogen 1990), patients who have undergone section of commissural fibers (*commissurotomy*) exhibit profound behavioral discontinuities between perception, comprehension, and response, which reflect significant functional differences between the hemispheres. Probably because direct communication between two cortical points occurs far less frequently than indirect communication relayed through lower brain centers, especially the thalamus and the basal ganglia, these patients generally manage to perform everyday activities quite well, including tasks involving interhemispheric information transfer (J.J. Myers and Sperry, 1985; Sergent, 1990, 1991b; E. Zaidel, Clarke, and Suyenobu, 1990) and emotional and conceptual information not dependent on language or complex visuospatial processes (Cronin-Golomb, 1986). In noting that alertness remains unaffected by commissurotomy and that emotional tone is consistent between the hemispheres, Sperry (1990) suggested that both phenomena rely on bilateral projections through the intact brain stem.

Some persons with *agenesis of the corpus callosum* (a rare congenital condition in which the corpus callosum is insufficiently developed or absent altogether) are identified only when some other condition brings them to a neurologist's attention, as they normally display no neurological or neuropsychological defects (L.J. Harris, 1995; E. Zaidel, Iacoboni, et al., 2003) other than slowed motor performances, particularly of bimanual tasks (Lassonde et al., 1991). However, persons with congenital agenesis of the corpus callosum also tend to be generally slowed on perceptual and language tasks involving interhemispheric communication, and some show specific linguistic and/or visuospatial deficits (Jeeves, 1990, 1994; see also E. Zaidel and Iacoboni, 2003). In some cases, problems with higher order cognitive processes such as concept formation, reasoning, and problem solving with limited social insight have been observed (W.S. Brown and Paul, 2000). The functional disconnection between hemispheres and the effects of surgical hemispheric disconnection have been demonstrated by the same kinds of testing techniques (Bogen, 1985; Jeeves, 1990; E. Zaidel, 1990).

The cerebral cortex

The cortex of the cerebral hemispheres, the convoluted outer layer of gray matter composed of nerve cell bodies and their synaptic connections, is the most highly organized correlation center of the brain (see Figs. 3.1 and 3.2), but the specificity of cortical structures in mediating behavior is neither clear-cut nor circumscribed (R.C. Collins, 1990; Frackowiak, Friston, et al., 1997, Part Two). Predictably established relationships between cortical areas and behavior reflect the systematic organization of the cortex and its interconnections. Now modern visualizing techniques display what thoughtful clinicians had suspected: multiple cortical and subcortical areas are involved to some degree in the mediation of complex behaviors (Fuster, 1995; Mesulam, 2000b) and specific brain regions are typically multifunctional (Lloyd, 2000). The boundaries of functionally definable cortical areas, or zones, are vague. Cells subserving a specific function are highly concentrated in the primary area of a zone, thin out, and overlap with other zones as the perimeter of the zone is approached (E. Goldberg, 1989, 1995; Polyakov, 1966). Cortical activity at every level, from the cellular to the integrated system, is maintained and modulated by complex feedback loops that in themselves constitute major subsystems, some within the cortex and others involving subcortical centers and pathways as well. "Processing patterns take many forms, including *parallel, convergent* [integrative], *divergent* [spreading excitation], *nonlinear, recursive* [feeding back onto itself] and *iterative*" (H. Damasio and Damasio, 1989, p. 71). Even those functions that are subserved by cells located within relatively well-defined cortical areas have a significant number of components distributed outside the local cortical center (Brodal, 1981; Paulesu, Frackowiak, and Bottini, 1997).

THE CEREBRAL CORTEX AND BEHAVIOR

Cortical involvement appears to be a prerequisite for awareness of experience (Fuster, 1995; Köhler and Moscovitch, 1997; G. Roth, 2000). Patterns of func-

tional localization in the cerebral cortex are broadly organized along two spatial planes. The *lateral plane* cuts through *homologous* (in the corresponding position) areas of the right and left hemispheres. The *longitudinal plane* runs from the front to the back of the cortex, with a relatively sharp demarcation between functions that are primarily localized in the forward portion of the cortex and those whose primary localization is behind the *central sulcus* or *fissure of Rolando*.

Lateral Organization

Lateral symmetry

The two cerebral hemispheres are nearly symmetrical. The primary sensory and motor centers are homologously positioned within the cerebral cortex of each hemisphere in a mirror-image relationship. With certain exceptions, such as the visual and auditory systems, the centers in each cerebral hemisphere predominate in mediating the activities of the *contralateral* (other side) half of the body (see Fig. 3.7). Thus, an injury to the primary *somesthetic* or *somatosensory* (sensations on the body) area of the right hemisphere results in decreased or absent sensation in the corresponding left-sided body part; an injury affecting the left motor cortex results in a right-sided weakness or paralysis (*hemiplegia*).

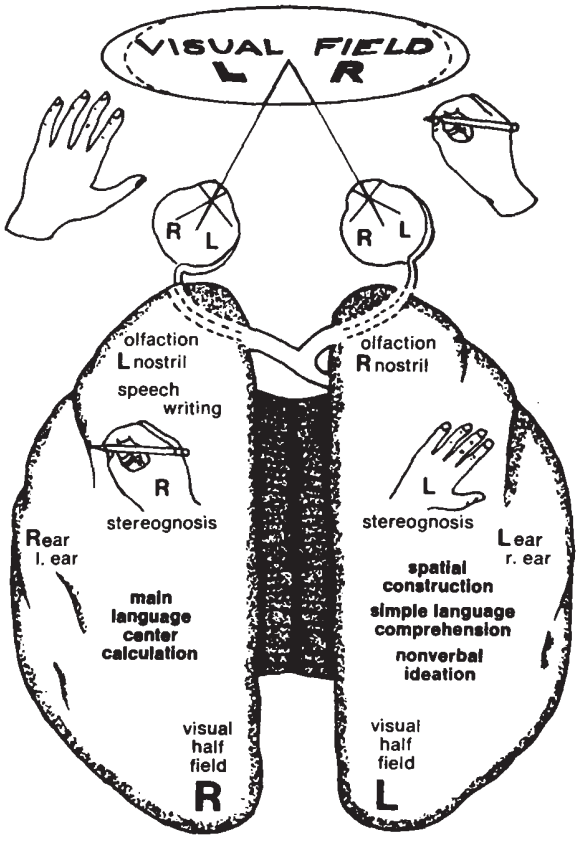

FIGURE 3.7 Schematic diagram of visual fields, optic tracts, and the associated brain areas, showing left and right lateralization in humans. (From Sperry, 1984)

Point-to-point representation on the cortex. The organization of both the primary sensory and primary motor areas of the cortex provides for a point-to-point representation of the body. The amount of cortex identified with each body portion or organ is proportional to the number of sensory or motor nerve endings in that part of the body rather than to its size. For example, the areas concerned with sensation and movement of the tongue or fingers are much more extensive than the areas representing the elbow or back.

The visual system is also organized on a contralateral plan, but it is one-half of each *visual field* (the entire view encompassed by the eye) that is projected onto the contralateral visual cortex (see Fig. 3.7). Fibers originating in the right half of each retina, which registers stimuli in the left visual field, project to the right visual cortex; fibers from the left half of the retina convey the right visual field image to the left visual cortex. Thus, destruction of either eye leaves both halves of the visual field intact. Destruction of the right or the left primary visual cortex or of all the fibers leading to either side results in blindness for that side of both visual fields (*homonymous hemianopia*). Lesions involving a portion of the visual projection fibers or visual cortex result in circumscribed *field defects,* such as areas of blindness (*scotoma,* pl. *scotomata*) within the visual field of one or both eyes, depending on whether the lesion involves the visual pathway before or after its fibers cross on their route from the retina of the eye to the visual cortex. The precise point-to-point arrangement of projection fibers from the retina to the visual cortex permits especially accurate localization of lesions within the primary visual system (Sterling, 1998). Visual recognition is mediated by (at least) two different systems, each with different pathways involving different parts of the cortex (Goodale, 2000; Mesulam, 2000b; see Fig. 3.14, p. 68). One system processes visuospatial analysis, and one is dedicated to pattern analysis and object recognition; movement perception may involve a third system (Iwata, 1989; Zihl et al., 1983).

Some patients with brain injuries that do not impair visual acuity or recognition complain of blurred vision or degraded percepts, particularly with sustained activity, such as reading, or when exposure is very brief (Hankey, 2001; Sergent, 1984; Zihl, 1989). These problems reflect the complexity of an interactive net-

work system in which the effects of lesions resonate throughout the network, slowing and distorting multiple aspects of cerebral processing with these resultant visual disturbances.

A majority of the nerve fibers transmitting auditory stimulation from each ear are projected to the primary auditory centers in the opposite hemisphere; the remaining fibers go to the *ipsilateral* (same side) auditory cortex. Thus, the contralateral pattern is preserved to a large degree in the auditory system too. As a result of this mixed projection pattern, destruction of one of the primary auditory centers does not result in loss of hearing in the contralateral ear. A point-to-point relationship between sense receptors and cortical cells is also laid out on the primary auditory cortex, with cortical representation arranged according to pitch, from high tones to low ones.

Destruction of a primary cortical sensory or motor area results in specific sensory or motor deficits but generally has little effect on the higher cortical functions. For instance, an adult-onset lesion limited to the primary visual cortex produces loss of visual awareness (cortical blindness, blindsight; see p. 66) while reasoning ability, emotional control, and even the ability for visual conceptualization may remain intact (Farah, 2003b; Güzeldere et al., 2000; Weiskrantz, 1986). Some mild decrements in movement speed and strength of the hand on the same side as lesions in the motor cortex have been reported (Smutok et al., 1989; see also Cramer, Finklestein, Schaechter et al., 1999, for a discussion of ipsilateral and bilateral motor control).

Association areas of the cortex. Cortical representation of sensory or motor nerve endings in the body takes place on a direct point-to-point basis, but stimulation of the *primary* cortical area gives rise only to meaningless sensations or nonfunctional movements (Brodal, 1981; Luria, 1966). Modified and complex functions involve the cortex adjacent to primary sensory and motor centers (E. Goldberg, 1989, 1990; Passingham, 1997; Paulesu et al., 1997). Neurons in these *secondary* cortical areas integrate and refine raw percepts or simple motor responses. *Tertiary* association or overlap zones are areas peripheral to functional centers where the neuronal components of two or more different functions or modalities are interspersed. The posterior association cortex, in which supramodal integration of perceptual functions takes place has also been called the *multimodal* (Pandya and Yeterian, 1990) or *heteromodal* (Mesulam, 2000b; Strub and Black, 1988) cortex. These processing areas are connected in a "stepwise" manner such that information-bearing stimuli reach the cortex first in the primary sensory centers. They then pass through the cortical association areas in order of increasing complexity, interconnecting with other cortical and subcortical structures along the way to frontal and limbic system association areas and finally expression in action, thought, and feeling (Arciniegas and Beresford, 2001; Mesulam, 2000b; Pandya and Yeterian, 1990, 1998). These projection systems have both forward and reciprocal connections at each step in the progression to the frontal lobes; and each sensory association area makes specific frontal lobe connections which, too, have their reciprocal connections back to the association areas of the posterior cortex (Rolls, 1998).

Unlike damage to primary cortical areas, a lesion involving association areas and overlap zones typically does not result in specific sensory or motor defects; rather, the behavioral effects of such damage will more likely appear as a pattern of deficits running through related functions or as impairment of a general capacity (E. Goldberg, 1989, 1995). Thus, certain lesions that are implicated in drawing distortions also tend to affect the ability to do computations on paper; lesions of the auditory association cortex do not interfere with hearing acuity per se but with the appreciation of patterned sounds.

Asymmetry between the hemispheres

A second kind of organization across the lateral plane differentiates the two hemispheres with respect to the localization of primary cognitive functions and to significant qualitative aspects of behavior processed by each of the hemispheres. Although no two human brains are exactly alike in their structure, in most people the right frontal area is wider than the left and the right frontal pole protrudes beyond the left while the reverse is true of the occipital pole: the left occipital pole is frequently wider and protrudes further posteriorly than the right but the central portion of the right hemisphere is frequently wider than the left (Damasio and Geschwind, 1984; Jänke and Steinmetz, 2003). Men show greater degrees of frontal and occipital asymmetry than women (Bear, Schiff, et al., 1986). These asymmetries exist in fetal brains (de Lacoste et al., 1991; Weinberger, Luchins, et al., 1982; Witelson, 1995). The left *Sylvian fissure,* the fold between the temporal and frontal lobes, is larger than the right in most people (Witelson, 1995), even in newborns (Seidenwurm et al., 1985). Much attention has focused on the asymmetry of the posterior portion of the superior surface of the temporal lobe, the *planum temporale.* This region, which is involved in auditory processing, is larger on the left side in most right-handers (Beaton, 1997; E. Strauss, LaPointe, et al., 1985). Differences in the neurotransmitters found in each hemisphere have

also been associated with differences in hemisphere function (Berridge et al., 2003; Direnfeld et al., 1984; Glick et al., 1982; R.G. Robinson and Starkstein, 2002) and sex (Arato et al., 1991). These differences may have an evolutionary foundation, for they have been found in primates and other animals (Corballis, 1991; Geschwind and Galaburda, 1985; Nottebohm, 1979). The lateralized size differential in primates is paralleled in some species by left lateralization for vocal communication (MacNeilage, 1987).

Lateralized cerebral differences may also occur at the level of cellular organization (B. Anderson et al., 1999; Galuske et al., 2000; Gazzaniga, 2000b; Peled et al., 1998). As early as 1963, Hécaen and Angelergues, on careful review of the neuropsychological symptoms associated with lesions of the right or left hemisphere, speculated that neural organization might be more closely knit and integrated on the left, more diffuse on the right. In accounting for findings that the spatial performance of right hemisphere damaged patients is adversely affected by lesions occurring anywhere in a fairly wide area while only those left hemisphere damaged patients with relatively severe damage to a well-defined area show impaired performance on spatial tasks, De Renzi and Faglioni (1967), too, hypothesized more diffuse representation of functions in the right hemisphere and more focal representation in the left. A similar conclusion follows from findings that patients with right hemisphere damage tend to have a reduced capacity for tactile discrimination and sensorimotor tasks in both hands while those with left hemisphere damage experience impaired tactile discrimination only in the contralateral hand (Hom and Reitan, 1982; Semmes, 1968), although contradictory data have been reported (Benton, 1972). Hemispheric bias extends to fine motor control, but differs from the usual perceptual bias in that left hemisphere damage is associated with bilateral motor response deficits, and damage to the right produces only contralateral impairment (Haaland, Cleeland, and Carr, 1977; Harrington and Haaland, 1991a; Jason, 1990; Okuda et al., 1995). Moreover, lesions outside the right hemisphere's sensorimotor area can contribute to motor deficits, but in the left hemisphere motor deficits occur only with lesions involving the sensorimotor area (Haaland and Yeo, 1989).

Additional data supporting a hypothesis that the right hemisphere is more diffusely organized than the left have been provided by evidence that visuospatial and constructional disabilities of patients with right hemisphere damage do not differ significantly regardless of the extensiveness of damage (Kertesz and Dobrowolski, 1981). Hammond (1982) reports that damage to the left hemisphere tends to reduce acuity of time discrimination more than right-sided damage, suggesting that the left hemisphere has a capacity for finer temporal resolution than the right. Also, the right hemisphere does not appear to be as discretely organized as the left for visuoperceptual and associated visual memory operations (Fried et al., 1982; Wasserstein, Zappula, Rosen, and Gerstman, 1984). Kolb and Whishaw (1996, pp. 204–207) offer several interpretations of these observations.

Functional specialization of the hemispheres. The supramodal nature of hemisphere specialization shows up in a number of ways: One is the organization of the left hemisphere for "linear" processing of sequentially presenting stimuli such as verbal statements, mathematical propositions, and the programming of rapid motor sequences. The right hemisphere is superior for "configurational" processing required by material that cannot be described adequately in words or strings of symbols, such as the appearance of a face or three-dimensional spatial relationships (Bogen, 1969a,b; Carlesimo and Caltagirone, 1995; Lezak, 1994; Swithenby et al., 1998). The two hemispheres process global/local or whole/detail information differently (L.C. Robertson and Rafal, 2000; Rossion et al., 2000), what Delis, Kiefner, and Fridlund (1988) refer to as the level of hierarchical analysis. When asked to copy or read a large-scale stimulus such as the shape of a letter or other common symbol composed of many different symbols in small scale (see Fig. 3.8), patients with left hemisphere disease will tend to ignore the small bits and interpret the large-scale figure; those whose lesions are on the right are more likely to overlook the big symbol but respond to the small ones. This can be interpreted as indicating a left hemisphere superiority in processing detailed information, a right hemisphere predilection for large-scale or global percepts.

Yet another processing difference between the hemispheres has to do with stimulus familiarity, as the right hemisphere appears to be best suited to handling novel information while the left tends to be more adept with familiar material such as "well-routinized codes" (E. Goldberg, 1990; E. Goldberg and Costa, 1981). Other studies have associated the right hemisphere with early, less detailed stages of processing, which may also be those that emerge first in the course of development, leaving the left hemisphere to perform later stage op-

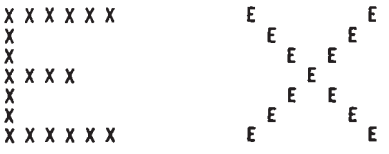

FIGURE 3.8 Examples of global/local stimuli.

erations on more detailed features (Bouma, 1990; Sergent, 1984, 1988a).

However, laboratory studies of normal subjects and "split brain" patients have shown that which hemisphere processes what depends on the relative weighting of many variables (Beaumont, 1997). In addition to underlying hemispheric organization, these include the nature of the task (e.g., modality, speed factors, complexity), the subject's set of expectancies, prior experiences with the task, previously developed perceptual or response strategies, and inherent subject variables such as sex and handedness (Bouma, 1990; Bryden, 1978; Kuhl, 2000; S.C. Levine, 1995). Thus, in these subjects the degree to which hemispheric specialization occurs at any given time is a relative phenomenon rather than an absolute one (Hellige, 1995; L.C. Robertson, 1995; Sergent, 1991a; E. Zaidel, Clarke, and Suyenobu, 1990). Moreover, it is important to recognize that normal behavior is a function of the whole brain with important contributions from both hemispheres entering into every activity and emotional state. Only laboratory studies of intact or split brain subjects or studies of persons with lateralized brain damage demonstrate the differences in hemisphere function.

The most obvious functional difference between the hemispheres is that the left hemisphere in most people is *dominant* for speech (i.e., language functions are primarily mediated in the left hemisphere) and the right hemisphere predominates in mediating complex, difficult-to-verbalize stimuli. Absence of words does not make a stimulus "nonverbal." Pictorial, diagrammatic, or design stimuli—sounds, sensations of touch and taste, etc.—may be more or less susceptible to verbal labeling depending on their meaningfulness, complexity, familiarity, potential for affective arousal, and other characteristics such as patterning or number. Thus, when classifying a wordless stimulus as verbal or nonverbal, it is important to take into account how readily it can be verbalized.

For most people the left hemisphere is the primary mediator of verbal functions (Indefrey and Levelt, 2000), including reading and writing, understanding and speaking, verbal ideation, verbal memory, and even comprehension of verbal symbols traced on the skin. The left hemisphere also mediates the numerical symbol system. Moreover, left hemisphere lateralization extends to control of posturing and of sequencing hand and arm movements, and of the musculature of speech, although bilateral structures are involved. Processing the linear and rapidly changing acoustic information needed for speech comprehension is better with the left than the right hemisphere (Beeman and Chiarello, 1998; Howard, 1997; J. Schwartz and Tallal, 1980). Males show a stronger left hemisphere lateralization for phonological processing than females (Shaywitz et al., 1995; E. Zaidel, Aboitiz, et al., 1995).

Right hemisphere language capacities have been demonstrated for comprehension of speech and written material. One significant contribution is the appreciation and integration of relationships in verbal discourse and narrative materials (Beeman and Chiarello, 1998, *passim;* Delis, Wapner, et al., 1983; Kiehl et al., 1999), which is a capacity necessary for enjoying a good joke (Beeman, 1998; H. Gardner, 1994). The right hemisphere also appears to provide the possibility of alternative meanings, getting away from purely literal interpretations of verbal material (Bottini et al., 1994; Brownell and Martino, 1998; Fiore and Schooler, 1998). Following commissurotomy, when speech is directed to the right hemisphere, much of what is heard is comprehended so long as it remains simple (Baynes and Eliassen, 1998; Searleman, 1977). Although functional imaging studies show a preponderance of left cerebral activity in reading (C.J. Price, 1997), not surprisingly, given its visuospatial components, reading also engages the right hemisphere, activating specific areas (Banich and Nicholas, 1998; Gaillard and Converso, 1988; Huettner et al., 1989; Indefrey and Levelt, 2000; Ornstein et al., 1979). In contrast to the ability for rapid, automatic processing of printed words by the intact left hemisphere, the healthy right hemisphere takes a slower and generally inefficient letter by letter approach (C. Burgess and Lund, 1998; Chiarello, 1988), which may be useful when word shapes have unfamiliar forms (Banich and Nicholas, 1998). The right hemisphere appears to have a reading lexicon (Bogen, 1997; Coslett and Saffran, 1998), but the more verbally adept left hemisphere normally blocks access to it so that the right hemisphere's knowledge of words becomes evident only through laboratory manipulations or with left hemisphere damage (Landis and Regard, 1988; Landis, Regard, et al., 1983). The right hemisphere seems to be sensitive to speech intonations (Borod, Bloom, and Santschi-Haywood, 1998; Ivry and Lebby, 1998), and is necessary for voice recognition (Van Lancker, Kreiman, and Cummings, 1989).

Less can be said for the verbal expressive capacities of the right hemisphere since they are quite limited, as displayed—or rather, not displayed—by split brain patients who make few utterances in response to right brain stimulation (Baynes and Gazzaniga, 2000; E. Zaidel, 1978). The right hemisphere appears to play a role in organizing verbal production conceptually (Brownell and Martino, 1998; Joanette et al., 1990), with specific temporal and prefrontal involvement in comprehending story meanings (Nichelli, Grafman, et al., 1995). It may be necessary for meaningfully ex-

pressive speech intonation (*prosody*) (Borod, Bloom, and Santschi-Haywood, 1998; Filley, 1995; E.D. Ross, 2000). The right hemisphere contributes to the maintenance of context-appropriate and emotionally appropriate verbal behavior (Brownell and Martino, 1998; Joanette et al., 1990), although this contribution is not limited to communications but extends to all behavior domains (Lezak, 1994). That the right hemisphere has a language capacity can also be inferred in aphasic patients with left-sided lesions who showed improvement from their immediate post-stroke deficits accompanied by measurably heightened right hemisphere activity (Frackowiak, 1997; B.T. Gold and Kertesz, 2000; Heiss et al., 1999; Murdoch, 1990; Papanicolaou et al., 1988).

The right hemisphere has also been erroneously called the "minor" or "nondominant" hemisphere because the often subtle character of right hemisphere disorders led early observers to believe that it played no specialized role in behavior.[1] However, although limited linguistically, the right hemisphere is "fully human with respect to its cognitive depth and complexity" (J. Levy, 1983).

The right hemisphere dominates the processing of information that does not readily lend itself to verbalization. This includes the reception and storage of visual data, tactile and visual recognition of shapes and forms, perception of spatial orientation and perspective, and copying and drawing geometric and representational designs and pictures. The left hemisphere seems to predominate in metric distance judgments (Hellige, 1988; McCarthy and Warrington, 1990), while the right hemisphere has superiority in metric angle judgments (Benton, Sivan, et al., 1994; Mehta and Newcombe, 1996). Thus both hemispheres contribute to processing spatial information, with some differences in what they process most efficiently (Banich, 1995; Sergent, 1991b). Arithmetic calculations (involving spatial organization of the problem elements as distinct from left hemisphere–mediated linear arithmetic problems involving, for instance, stories or equations with an $a + b = c$ form [Dehaene, 2000]) have a significant right hemisphere component (Grafman and Rickard, 1997; H.S. Levin, Goldstein, and Spiers, 1993). Some aspects of musical ability are also localized on the right, as are abilities to recognize and discriminate nonverbal sounds (Bauer, 1993; Bauer and McDonald, 2003). The right hemisphere has bilateral involvement in somatosensory sensitivity and discrimination. It may be superior in distinguishing odors (Zatorre and Jones-Gotman, 1990).

Data from a variety of sources suggest right hemisphere dominance for spatial attention specifically, if not attention generally: Patients with compromised right hemisphere functioning tend to have diminished awareness of or responsiveness to stimuli presented to their left side; reaction times mediated by the right hemisphere are faster than those mediated by the left; and the right hemisphere is activated equally by stimuli from either side in contrast to more exclusively contralateral left hemisphere activation (Heilman and Van Den Abell, 1980; Heilman, Watson, and Valenstein, 2003; Meador, Loring, Lee, et al., 1988; Mesulam, 2000b). However, other studies suggest that neither hemisphere has an attentional advantage, but rather that each hemisphere directs attention contralaterally (Mirsky, 1989; Posner, 1990), and that they are equally capable of detecting stimuli (Prather et al., 1992). The right hemisphere appears to direct attention to far space while the left hemisphere directs attention to near space (Heilman, Chatterjee, and Doty, 1995). The appearance of right hemisphere superiority for attention in some situations may stem from its ability to integrate complex, nonlinear information rapidly.

Facial recognition studies exemplify the processing differences underlying many aspects of hemisphere specialization. When pictured faces are presented normally to each field separately they are processed more rapidly when presented to the left field/right hemisphere than to the right field/left hemisphere; but no right hemisphere advantage appears when faces are inverted (Tovée, 1996). "It seems that, in the right hemisphere, upright faces are processed in terms of their feature configuration, whereas inverted faces are processed in a piecemeal manner, feature by feature. . . . In the left hemisphere, both upright and inverted faces seem to be processed in a piecemeal manner." (pp. 134–135)

Cognitive alterations with lateralized lesions. Time-bound relationships of sequence and order characterize many of the functions that are vulnerable to left hemisphere lesions (Harrington and Haaland, 1991a, 1992). The most obvious cognitive defect associated with left hemisphere damage is aphasia (Feinberg and Farah, 2003b; Wernicke, 1874/1977). This complex of disorders reflects a very basic underlying capacity of the left hemisphere that is not dependent on hearing, as deaf persons who sign can develop an aphasia for their nonauditory language in the areas associated with aphasia in hearing persons (Bellugi et al., 1983; Poizner et al., 1990). Other left hemisphere disorders include verbal memory or verbal fluency deficits, concrete

[1]Because the left hemisphere is usually dominant for speech in both right- and left-handed persons (see pp. 305–306), it became customary to refer to it as the "dominant" hemisphere before the dominant functions of the right hemisphere were appreciated (Benton, 1972). The most common pattern, in which the left and right hemispheres predominate for verbal and nonverbal functions, respectively, is generally assumed in writing about the hemispheres today and will be assumed here.

thinking, specific impairments in reading or writing, and impaired arithmetic ability characterized by defects or loss of basic mathematical concepts of operations and even of number (Grafman and Rickard, 1997; Delazer and Bartha, 2001). Patients with left hemisphere damage may make defective constructions largely because of tendencies toward simplification and difficulties in drawing angles, but they also may display deficits in visuospatial orientation and short-term recall (Mehta et al., 1989). Their ability to perform complex manual—as well as oral—motor sequences may be impaired (Harrington and Haaland, 1992; Meador, Loring, Lee et al., 1999; Schluter et al., 2001).

The diversity of behavioral disorders associated with right hemisphere damage continues to thwart efforts to devise a neat classification system for them (S. Clarke, 2001; Cutting, 1990; Feinberg and Farah, 2003c; Filley, 1995). Pimental and Kingsbury (1989) reviewed syndrome classifications offered by other writers and proposed one of their own with seven major classes encompassing 18 lower level categories, of which some contain further subclasses of symptoms. The many different presentations of right hemisphere dysfunction may be understood as determined in large part by the specific area(s) of damage in terms of gradients of cortical specialization (E. Goldberg, 1989, 1995; see p. 65). No attempt to include every kind of impairment reported in the literature will be made here. Rather, the most prominent features of right hemisphere dysfunction will be described, with more detailed presentations in the sections on the functional organization of the cerebral cortex.

Patients with right hemisphere damage may be quite fluent, even verbose (Brookshire, 1978; Cutting, 1990; Rivers and Love, 1980), but illogical and given to loose generalizations and bad judgment (Stemmer and Joanette, 1998). They are apt to have difficulty ordering, organizing, and making sense out of complex stimuli or situations, and thus many display planning defects and some are no longer able to process the components of music. These organizational deficits can impair appreciation of complex verbal information so that verbal comprehension may be compromised by confusion of the elements of what is heard, by personalized intrusions, by literal interpretations, and by a generalized loss of gist in a morass of details (Beeman and Chiarello, 1998, *passim*). Their speech may be uninflected and aprosodic, paralleling their difficulty in comprehending speech intonations (E.D. Ross, 2003). These patients are vulnerable to difficulty in maintaining a high level of alertness (Ladavas et al., 1989), which may be akin to the association of right hemisphere lesions with *impersistence*—the inability to sustain facial or limb postures (Pimental and Kingsbury, 1989b). Perceptual deficits, particularly left-sided inattention phenomena and those involving degraded stimuli or unusual presentations, are not uncommon (McCarthy and Warrington, 1990). The visuospatial perceptual deficits that trouble many patients with right-lateralized damage can affect different cognitive activities (Farah and Feinberg, 2003b, *passim;* Vuilleumier, 2001). Arithmetic failures are most likely to appear in written calculations that require spatial organization of the problems' elements (Grafman and Rickard, 1997; see Fig. 3.16, p. 72). Visuospatial and other perceptual deficits show up in these patients' difficulty copying designs, making constructions, and matching or discriminating patterns or faces. Patients with right hemisphere damage may have particular problems with spatial orientation and visuo-spatial memory such that they get lost, even in familiar surroundings, and can be slow to learn their way around a new area. Their constructional disabilities may reflect both their spatial disorientation and defective capacity for perceptual or conceptual organization. Stereoscopic vision may be affected (Benton and Hécaen, 1970). Their reaction times are slowed.

The painful efforts of a right hemisphere stroke patient to arrange plain and diagonally colored blocks according to a pictured pattern (Fig. 3.9a, p. 59) illustrate the kind of solutions available to a person in whom only the left hemisphere is fully intact. This glib 51-year-old retired salesman constructed several simple 2 × 2 block design patterns correctly by verbalizing the relations. "The red one (block) on the right goes above the white one; there's another red one to the left of the white one." This method worked so long as the relationships of each block to the others in the pattern remained obvious. When the diagonality of a design obscured the relative placement of the blocks, he could neither perceive how each block fit into the design nor guide himself with verbal cues. He continued to use verbal cues, but at this level of complexity his verbalizations only served to confuse him further. He attempted to reproduce diagonally oriented designs by lining up the blocks diagonally (e.g., "to the side," "in back of") without regard for the squared (2 × 2 or 3 × 3) format. He could not orient any one block to more than another single block at a time, and he was unable to maintain a center of focus to the design he was constructing.

On the same task, a 31-year-old mildly dysphasic former logger who had had left hemisphere surgery involving the visual association area had no difficulty until he came to the first 3 × 3 design, the only one of the four nine-block designs that lends itself readily to verbal analysis. On this design, he reproduced the overall pattern immediately but oriented one corner block erroneously. He attempted to reorient it but then turned a correctly oriented block into a 180° error. Though dissatisfied with this solution, he was unable to localize his error or define the simple angulation pattern (Fig. 3.9b).

As illustrated in Figure 3.9, the distinctive processing qualities of each hemisphere become evident in the mediation of spatial relations. Left hemisphere processing

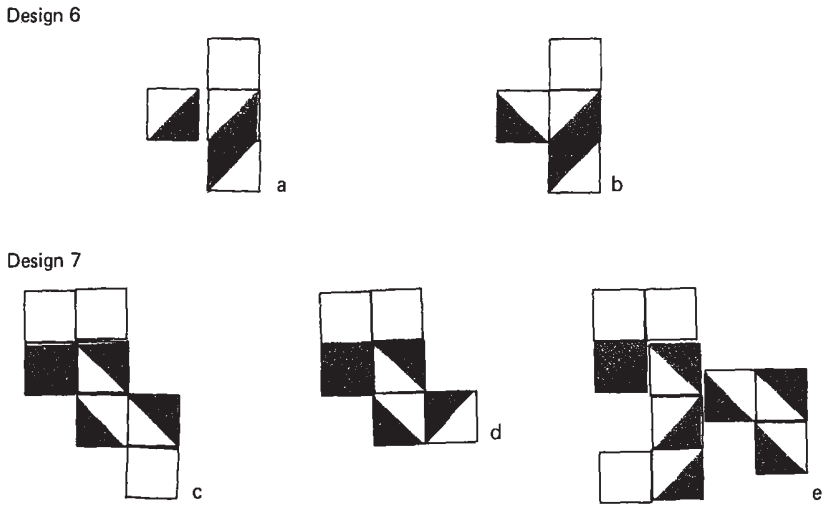

FIGURE 3.9a Attempts of a 51-year-old right hemisphere stroke patient to copy pictured designs with colored blocks. (*a*) First stage in the construction of a 2 × 2 chevron design. (*b*) Second stage: the patient does not see the 2 × 2 format and gives up after four minutes. (*c*) First stage in construction of 3 × 3 pinwheel pattern (see below). (*d*) Second stage. (*e*) Third and final stage. This patient later told his wife that he believed the examiner was preparing him for "architect school."

FIGURE 3.9b Attempts of a 31-year-old patient with a surgical lesion of the left visual association area to copy the 3 × 3 pinwheel design with colored blocks. (*f*) Initial soluation: 180° rotation of upper left corner block. (*g*) "Corrected" solution: upper left corner block rotated to correct position and lower right corner rotated 180° to incorrect position.

tends to break the visual percept into details that can be identified and conceptualized verbally in terms of number or length of lines, size and direction of angles, etc. In the right hemisphere the tendency is to deal with the same visual stimuli as spatially related wholes. Thus, for most people, the ability to perform such complex visual tasks as the formation of complete impressions from fragmented percepts (the closure function), the appreciation of differences in patterns, and the recognition and remembering of faces depends on the functioning of the right hemisphere. Together the two processing systems provide recognition, storage, and comprehension of discrete and continuous, serial and simultaneous, detailed and holistic aspects of experience across at least the major sensory modalities of vision, audition, and touch.

Although greatly oversimplified, this model has clinical value. Loss of tissue in a hemisphere tends to impair its particular processing capacity. When a lesion has rendered lateralized areas essentially nonfunctional, the intact hemisphere may process activities normally handled by the damaged hemisphere (W.H. Moore, 1984; Papanicolaou et al., 1988; Fig. 3.9a is an example of this phenomenon). Moreover, a diminished contribution from one hemisphere may be accompanied by augmented or exaggerated activity of the other when released from the inhibitory or competitive constraints of normal hemispheric interactions (Lezak, 1994; Novelly et al., 1984; Shimizu et al., 2000; Starkstein and Robinson, 1997). This phenomenon appears in the verbosity and overwriting of many right hemisphere damaged patients (Cutting, 1990; Lezak and Newman, 1979; Yamadori et al., 1986; see Fig. 3.10, p. 60). The functional difference between hemispheres also appears in the tendency for patients with left-sided damage to be more accurate in remembering large visually presented forms than the small details making up those forms; but when the lesion is on the right, recall of the details is more accurate than recall of the whole composed figure (Delis, Robertson, and Efron, 1986) (see Fig. 3.8, p. 55). These examples suggest that one hemisphere's function is enhanced when the other hemisphere is impaired. In an analogous manner, patients with left hemisphere disease tend to reproduce the essential configuration but leave out details when copying drawings (see Fig. 3.11, p. 61), and they may perform some visuoperceptual tasks better than intact subjects (Y. Kim et al., 1984; Wasserstein, Zappulla, Rosen, et al., 1987).

Memory and learning also show hemispheric differences. Loss of the left hippocampus and nearby corti-

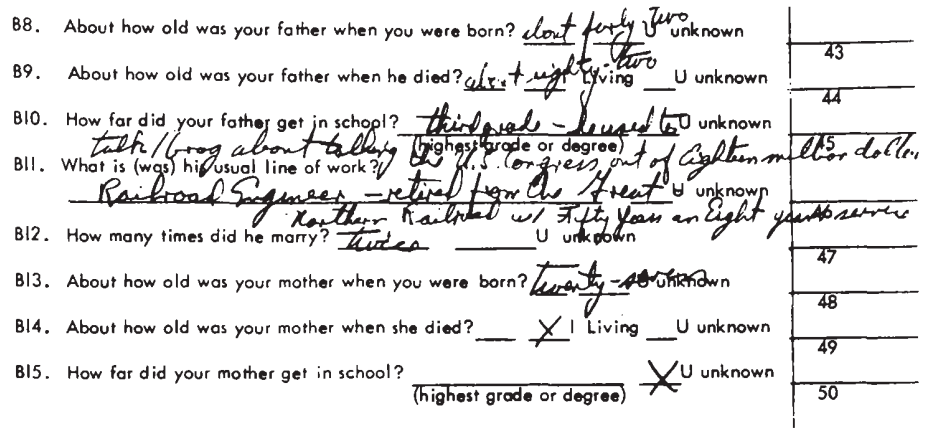

FIGURE 3.10 Overwriting (hypergraphia) by a 48-year-old college-educated retired police investigator suffering right temporal lobe atrophy secondary to a local right temporal lobe stroke.

cal areas impairs verbal memory, and destruction of the right hippocampus results in defective recognition and recall of "complex visual and auditory patterns to which a name cannot readily be assigned" (B. Milner, 1970, p. 30; see also Abrahams et al., 1997; Jones-Gotman, Zatorre, Olivier, et al., 1997; R.G. Morris, Abrahams, and Polkey, 1995; Pillon, Bazin, Deweer, et al., 1999; Sass, Buchanan, Kraemer, et al., 1995).

The subjects for most studies of memory and the temporal lobe are patients who have had portions of one or both temporal lobes excised, usually for seizure control. These studies show that memory deficits with temporal lobe lesions also differ according to the side of the lesion (G.P. Lee, Loring, and Thompson, 1989; B. Milner, 1972; R.G. Morris, Abrahams, and Polkey, 1995; Pillon, Bazin, Deweer, et al., 1999; M.L. Smith, 1989). Impaired verbal memory appears with surgical resection of the left temporal lobe (Seidenberg, Hermann, et al., 1998) and nonverbal (auditory, tactile, visual) memory disturbances accompany right temporal lobe resection. With left temporal lobectomies, deficits have been found for different kinds of verbal memory, including episodic (both short-term and learning), semantic, and remote memory (Frisk and Milner, 1990; Loring and Meador, 2003b; M.L. Smith, 1989). These patients also lag behind normal controls in learning de-

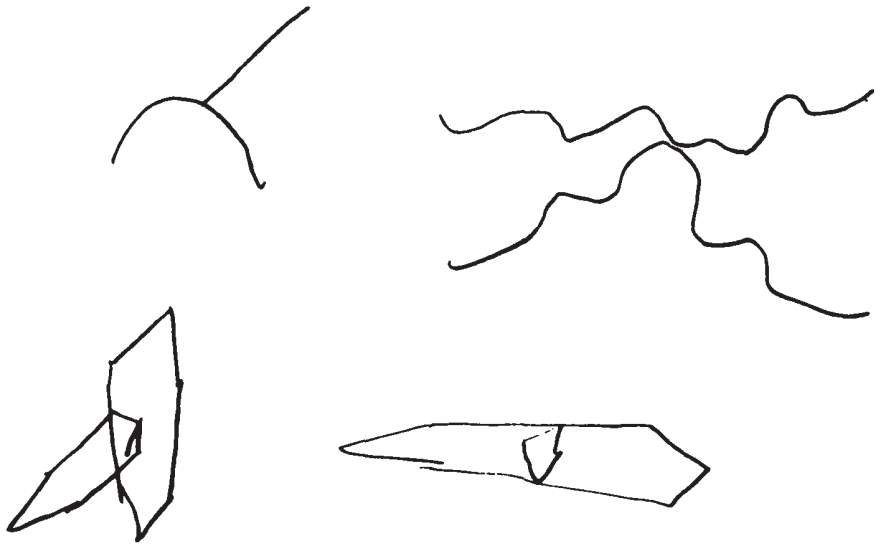

FIGURE 3.11 Simplification and distortions of four Bender-Gestalt designs by a 45-year-old assembly line worker with a high school education. These drawings were made four years after he had incurred left frontal damage in an industrial accident.

signs, although once learned their retention is good, unlike patients with right temporal lesions, who fail both aspects of this memory task (Jones-Gotman, 1986). Reduced access to verbal labeling may explain the left temporal patients' slowed learning. Learning manual sequences becomes more difficult following left but not right temporal lobectomy (Jason, 1987). Cortical stimulation of the anterior left temporal cortex interferes with verbal learning without affecting speech, while stimulation of the posterior left temporal cortex is more likely to result in retrieval (word finding) problems and *anomia* (literally, no words) (Fedio and Van Buren, 1974; Ojemann, 1978). Lesions in different areas of the left temporal lobe differentially affect the degree and nature of impairment in immediate auditory recall of tones or digits (W.P. Gordon, 1983).

Memory deficits documented for patients with right temporal lobectomies and other temporal lobe lesions involve designs, faces, melodies, and spatial formats such as those used in maze learning (e.g., Abrahams et al., 1997). In short, these patients display memory impairments when perceptions or knowledge cannot be readily put into words (B.E. Shapiro, Grossman, and Gardner, 1981; M.L. Smith, 1989). This left–right difference has been found in brain activation studies comparing the effect of stimulus material on temporal lobes (Dolan et al., 1997; Ojemann, 1978) and on the prefrontal cortex's role in memory (A.C. Lee et al., 2000; K.B. McDermott, Ojemann, et al., 1999; A.D. Wagner et al., 1998). However, current evidence suggests that the relationship between the type of material (verbal vs. nonverbalizable) to be learned or modality of stimulus input and hemisphere involvement is not simple. Functional neuroimaging data demonstrate that both hemispheres may be activated by a verbal memory task (Buckner et al., 1998; S.C. Johnson et al., 2001).

Emotional alterations with lateralized lesions. The complementary modes of processing that distinguish the cognitive activities of the two hemispheres extend to emotional behavior as well (Bear, 1983; Borod, Bloom, and Santschi-Haywood, 1998; Gainotti, 1984, 2000; Gainotti, Caltagirone, and Zoccolotti, 1993; Heilman, Blonder, et al., 2003). The configurational processing of the right hemisphere lends itself most readily to the handling of the multidimensional and alogical stimuli that convey *emotional tone,* such as facial expressions (Benowitz, Bear, et al., 1983; Borod, Haywood, and Koff, 1997; Ivry and Lebby, 1998; Moreno et al., 1990) and voice quality (Blumstein and Cooper, 1974; Joanette et al., 1990; Ley and Bryden, 1982). The analytic, bit-by-bit processing of the left hemisphere deals best with the words of emotion. A face distorted by fear and the exclamation "I'm scared to death" both convey affective meaning, but the meaning of each is normally processed well by only one hemisphere (Hansch and Pirozzolo, 1980; Safer and Leventhal, 1977). Thus, patients with right hemisphere damage tend to experience relative difficulty in discerning the emotional features of stimuli, whether visual or auditory, with corresponding diminution in their emotional responsivity (Adolphs and Damasio, 2000; Borod, Cicero et al., 1998; Cicone et al., 1980; Ruckdeschel-Hibbard et al., 1986; Van Lancker and Sidtis, 1992). While impairments in affective recognition appear to be supramodal, deficits in recognizing different kinds of affective communication (e.g., facial expressions, gestures, prosody) can occur independently of one another (Bowers et al., 1993). Patients with such deficits are limited in both their comprehension and their enjoyment of humor (H. Gardner 1994; H. Gardner et al., 1975). Patients with left hemisphere lesions have less difficulty appreciating facial expressions and voice intonation, and most are normally responsive to uncaptioned cartoons but do as poorly as right hemisphere patients when the stimulus is verbal (see also Heilman, Scholes, and Watson, 1975). Self-reference processing and self-evaluation appear to have mostly right hemisphere involvement (J.P. Keenan et al., 2000), although both hemispheres contribute to processing of aspects of personal information (Kircher et al., 2001).

Differences in emotional expression can also distinguish patients with lateralized lesions (Borod, 1993; Etcoff, 1986). Right hemisphere–lesioned patients' range and intensity of affective intonation are frequently inappropriate (Borod, Koff, Lorch, and Nicholas, 1985; Borod, St. Clair, et al., 1990; Joanette et al., 1990; B.E. Shapiro and Danly, 1985). In the controversy over whether their facial behavior is less expressive than that of persons with left hemisphere damage or of normal control subjects, Brozgold and colleagues (1998) and Montreys and Borod (1998) say it is while Pizzamiglio and Mammucari (1989) say it is not. The preponderance of research on normal subjects indicates heightened expressiveness on the left side of the face (Borod, Kent, et al., 1988; Dopson et al., 1984; Sackeim, Gur, and Saucy, 1978). These findings are generally interpreted as indicating right hemisphere superiority for affective expression.

There is disagreement as to whether right hemisphere damaged patients experience emotions any less than other people. Some studies have found reduced autonomic responses to what would normally be an emotional stimulus (Gainotti, 1997). However, given their impaired appreciation of emotionally charged stimuli, this may raise a chicken–egg question concerning what

is the fundamental deficit here. Others, myself [mdl] included, have observed strong—but not necessarily appropriate—emotional reactions in patients with right-lateralized damage, leading to the hypothesis that their experience of emotional communications and their capacity to transmit the nuances and subtleties of their own feeling states differ from normal affective processing (Barbizet, 1974; Lezak, 1994; Morrow, Vrtunski, et al., 1981; E.D. Ross and Rush, 1981), leaving them out of joint with those around them.

Hemispheric differences have been reported for the emotional and even personality changes that may accompany brain injury (Gainotti, 1993; Prigatano, 1987; Sackeim, Greenburg, et al., 1982). Patients with left hemisphere lesions can exhibit a *catastrophic reaction* (extreme and disruptive transient emotional disturbance). The catastrophic reaction may appear as acute—often disorganizing—anxiety, agitation, or tearfulness, disrupting the activity that provoked it. Typically, it occurs when patients are confronted with their limitations, as when taking a test (Prigatano, 1987; R.G. Robinson and Starkstein, 2002). They tend to regain their composure as soon as the source of frustration is removed. Anxiety is also a common feature of left hemisphere involvement (Gainotti, 1972; Galin, 1974). It may show up as undue cautiousness (Jones-Gotman and Milner, 1977) or oversensitivity to impairments and a tendency to exaggerate disabilities (Keppel and Crowe, 2000). Yet, despite tendencies to be overly sensitive to their disabilities, many patients with left hemisphere lesions ultimately compensate for them well enough to make a satisfactory adjustment to their disabilities and living situations (Tellier et al., 1990).

In contrast, patients whose injuries involve the right hemisphere are less likely to be dissatisfied with themselves or their performances than are those with left hemisphere lesions (Keppel and Crowe, 2000) and less likely to be aware of their mistakes (McGlynn and Schacter, 1989). They are more likely to be apathetic (Andersson et al., 1999), to be risk takers (L. Miller, and Milner, 1985), and to have poorer social functioning (Brozgold et al., 1998). At least in the acute or early stages of their condition, they may display an *indifference reaction,* tending to deny or make light of the extent of their disabilities (Gainotti, 1972; Pimental and Kingsbury, 1989). In extreme cases, patients are unaware of such seemingly obvious defects as crippling left-sided paralysis or slurred and poorly articulated speech. In the long run these patients tend to have difficulty making satisfactory psychosocial adaptations, with those whose lesions are anterior being most maladjusted in all areas of psychosocial functioning (Tellier et al., 1990).

What can be considered an experimental model of these changes stems from use of the *Wada technique* of intracarotid injections of sodium amytal for pharmacological inactivation of one side of the brain to evaluate lateralization of function before surgical treatment of epilepsy (Jones-Gotman, 1987; Rausch and Risinger, 1990; Wada and Rasmussen, 1960). The emotional reactions of these patients tend to differ depending on which side is inactivated (Ahern et al., 1994; Davidson and Henriques, 2000; G.P. Lee, Loring, et al., 1990; Nebes, 1978). Patients whose left hemisphere has been inactivated are tearful and tell of feelings of depression more often than their right hemisphere counterparts, who are more apt to laugh and feel euphoric. In the same vein, Regard and Landis (1988) found that pictures exposed to the left visual field were disliked and those to the right were liked. Since the emotional alterations seen with some stroke patients and in lateralized pharmacological inactivation have been interpreted as representing the tendencies of the disinhibited intact hemisphere, some investigators have hypothesized that each hemisphere is specialized for positive (the left) or negative (the right) emotions, suggesting relationships between the lateralized affective phenomena and psychiatric disorders (e.g., Flor-Henry, 1986; G.P. Lee, Loring, et al., 1990).

However, studies of depression in stroke patients have produced inconsistent results (A.J. Carson et al., 2000; Sato et al., 1999; Singh et al., 2000). Shimoda and Robinson (1999) found that hospitalized stroke patients with the greatest incidence of depression were those with left anterior hemisphere lesions. At short-term follow-up (3–6 months), proximity of the lesion to the frontal pole and lesion volume correlated with depression in both right and left hemisphere stroke patients. At long-term follow-up (1–2 years), depression was significantly associated with right hemisphere lesion volume and proximity of the lesion to the occipital pole. Moreover, the incidence of depression in patients with left hemisphere disease dropped over the course of the first year (R.G. Robinson and Manes, 2000). Impaired social functioning was most evident in those patients who remained depressed. Consistent with these findings are reports of a higher incidence of depression in patients with anterior lesions 2–4 months poststroke (J.S. Kim and Choi-Kwon, 2000; Singh et al., 2000) and with right hemisphere lesions at six months poststroke (MacHale et al., 1998). Women are more likely to be depressed in the acute stages of a left hemisphere stroke than men (Paradiso and Robinson, 1998).

Gainotti, Caltagirone, and Zoccolotti (1993) suggest that the emotional processing tendencies of the two hemispheres are complementary: "The right hemi-

sphere seems to be involved preferentially in functions of emotional arousal, intimately linked to the generation of the autonomic components of the emotional response, whereas the left hemisphere seems to play a more important role in functions of intentional control of the emotional expressive apparatus" (pp. 86–87). These authors hypothesize that language development tends to override the left hemisphere's capacity for emotional immediacy while, in contrast, the more spontaneous and pronounced affective display characteristic of right hemisphere emotionality gives that hemisphere the appearance of superior emotional endowment.

The differences in presentation of depression in right and left hemisphere damaged patients would seem to support this hypothesis. With left hemisphere damaged patients, depression seems to reflect awareness of deficit; the more severe the deficit and acute the patient's capacity for awareness, the more likely it is that the patient will be depressed. As awareness of deficit is often muted or lacking with right hemisphere lesions (K. Carpenter et al., 1995; Meador, Loring, Feinberg, et al., 2000; Pederson, Jorgensen, Nakayama, et al., 1996), these patients tend to be spared the agony of severe depression particularly early in the course of their condition. When the lesion is on the right, the emotional disturbance does not seem to arise from awareness of defects so much as from the secondary effects of the patient's diminished self-awareness and social insensitivity. Patients with right hemisphere lesions who do not appreciate the nature or extent of their disability tend to set unrealistic goals for themselves or to maintain previous goals without taking their new limitations into account. As a result, they frequently fail to realize their expectations. Their diminished capacity for self-awareness and for emotional spontaneity and sensitivity can make them unpleasant to live with and thus more likely to be rejected by family and friends than are patients with left hemisphere lesions. Depression in patients with right-sided cortical damage may take longer to develop than it does in patients with left hemisphere involvement since it is less likely to be an emotional response to immediately perceived disabilities than to a more slowly evolving reaction to their secondary consequences. When depression does develop in patients with right-sided disease, however, it can be more chronic, more debilitating, and more resistive to intervention.

These descriptions of differences in the emotional behavior of right and left hemisphere damaged patients reflect observed tendencies that are not necessary consequences of unilateral brain disease (Gainotti, 1993). Neither are the emotional reactions reported here associated only with unilateral brain lesions. Mourning reactions naturally follow the experience of personal loss of a capacity whether it be due to brain injury, a lesion lower down in the nervous system, or amputation of a body part. Inappropriate euphoria and self-satisfaction may accompany lesions involving other than right hemisphere areas of the cortex (McGlynn and Schacter, 1989). Further, premorbid personality colors the quality of patients' responses to their disabilities. Thus, the clinician should never be tempted to predict the site of damage from the patient's mood alone.

While knowledge of the asymmetrical pattern of cerebral organization adds to the understanding of many cognitive and emotional phenomena associated with unilateral lesions or demonstrated in laboratory studies of normal subjects or commissurotomized patients, it is inappropriate to generalize these findings to the behavior of persons whose brains are intact (Sergent, 1984; Springer and Deutsch, 1989). In normal persons, the functioning of the two hemispheres is tightly yoked by the corpus callosum so that neither can be engaged without significant activation of the other (Lezak, 1982b). As much as cognitive styles and personal tastes and habits might seem to reflect the processing characteristics of one or the other hemisphere, these qualities appear to be integral to both hemispheres (Arndt and Berger, 1978; Sperry et al., 1979). "In the normal intact state, the conscious activity is typically a unified and coherent bilateral process that spans both hemispheres through the commissures" (Sperry, 1976). Even when the hemispheres have been surgically separated, the "brain works as a single and unified organism" (Sergent, 1987).

Advantages of hemisphere interaction. Simple tasks in which the processing capacity of one hemisphere is sufficient are performed faster and with more advantage than if both hemispheres are engaged (Belger and Banich, 1998; Ringo et al., 1994). However, very few tasks rely exclusively on one hemisphere. Interaction between the hemispheres also has important mutually enhancing effects. Complex mental tasks such as reading, arithmetic, and word and object learning are performed best when both hemispheres can be actively engaged (Belger and Banich, 1998; Gaillard, 1990; Huettner et al., 1989; Moscovitch, 1979; A. Rey, 1959; Weissman and Banich, 2000). Other mutually enhancing effects of bilateral processing show up in the superior memorizing and retrieval of both verbal and configurational material when simultaneously processed (encoded) by the verbal and configurational systems (B. Milner, 1978; Moscovitch, 1979); in enhanced cognitive efficiency of normal subjects when hemispheric activation is bilateral rather than unilateral (J.M. Berger and Perret, 1986; J.M. Berger, Perret, and Zimmer-

mann, 1987); and in better performances of visual tasks by commissurotomized patients when both hemispheres participate than when vision is restricted to either hemisphere (Sergent, 1991a,b; E. Zaidel, 1979).

The cerebral processing of music illuminates the differences in what each hemisphere contributes, the complexities of hemispheric interactions, and how experience can alter hemispheric roles. The left hemisphere tends to predominate in the processing of sequential and discrete tonal components of music (Botez and Botez, 1996; Breitling et al., 1987; Gaede et al., 1978). Inability to use both hands to play a musical instrument (*bimanual instrument apraxia*) has been reported with left hemisphere lesions that spare motor functions (Benton, 1977a). The right hemisphere predominates in melody recognition and in melodic singing (H.W. Gordon and Bogen, 1974; Kumkova, 1990; Samson and Zatorre, 1988; Yamadori et al., 1977). Its involvement with chord analysis is generally greatest for musically untrained persons (Gaede et al., 1978). Training can alter these hemispheric biases so that, for musicians, the left hemisphere predominates for melody recognition (Bever and Chiarello, 1974; Messerli, Pegna, and Sordet, 1995), tone discrimination (Mazziota et al., 1982; Shanon, 1981), and musical judgments (Shanon, 1980, 1984). Moreover, intact, untrained persons tend not to show lateralized effects for tone discrimination or musical judgments (Shanon, 1980, 1981, 1984). Taken altogether, these findings suggest that while cerebral processing of different components of music is lateralized with each hemisphere predominating in certain aspects, both hemispheres are needed for musical appreciation and performance (Bauer and McDonald, 2003).

The bilateral integration of cerebral function is most clearly exhibited by creative artists, who typically have intact brains. Excepting singing, harmonica playing, and the small repertoire of piano pieces written for one hand, making music is a two-handed activity. Moreover, for instruments such as guitars and the entire violin family, the right hand performs those aspects of the music that are mediated predominantly by the right hemisphere, such as expression and tonality, while the left hand interprets the linear sequence of notes best deciphered by the left hemisphere. Right-handed artists do their drawing, painting, sculpting, and modeling with the right hand, with perhaps an occasional assist from the left. Thus, by its very nature, the artist's performance involves the smoothly integrated activity of both hemispheres. The contributions of each hemisphere are indistinguishable and inseparable as the artist's two eyes and two ears guide the two hands or the bisymmetrical speech and singing structures that together render the artistic production.

Longitudinal Organization

Although no two human brains are exactly alike in their structure, all normally developed brains share the same major distinguishing features (see Fig. 3.12). The external surface of each half of the cerebral cortex is wrinkled into a complex of ridges or convolutions called *gyri* (sing., *gyrus*), which are separated by two deep fissures and many shallow clefts, the *sulci* (sing., *sulcus*). The two prominent fissures and certain of the major sulci divide each hemisphere into four lobes, the occipital, parietal, temporal, and frontal lobes. (For detailed delineations of cortical features and landmarks, see Brodal, 1981; Kolb and Whishaw, 1996; Mesulam, 2000b.)

The *central sulcus* divides the cerebral hemispheres into anterior and posterior regions. Immediately in front of the central sulcus lies the precentral gyrus which contains much of the *primary motor* or *motor*

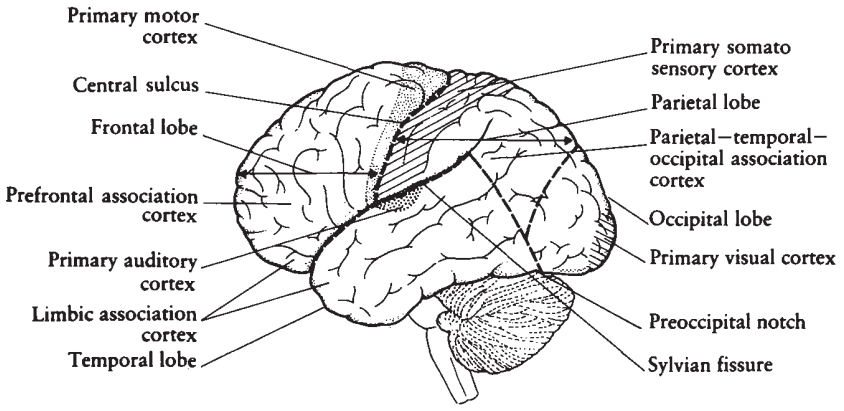

FIGURE 3.12 The lobe divisions of the human brain and their functional anatomy. (From Strange, 1992)

projection area. The entire area forward of the central sulcus is known as the *precentral* or *prerolandic* area. The bulk of the *primary somesthetic* or *somatosensory projection* area is located in the gyrus just behind the central sulcus. The area behind the central sulcus is also known as the *retrorolandic* or *postcentral* area.

Certain functional systems have primary or significant representation on the cerebral cortex with sufficient regularity that the lobes do provide a useful anatomical frame of reference for functional localization, much as a continent provides a geographical frame of reference for a country. However, because the lobes were originally defined solely on the basis of their gross appearance, some functionally definable areas overlap two and even three lobes. For example, the boundary between the parietal and occipital lobes is arbitrarily defined by a minor sulcus, the *parieto-occipital sulcus,* lying in what is now known to be an overlap zone for visual and spatial functions.

A two-dimensional organization of cortical functions lends itself to a schema that offers a framework for conceptualizing cortical organization. The posterior parts of the cortex behind the central sulcus are primarily involved in the analysis, coding, and storage of information, while the area anterior to the central sulcus is involved in the formation of intentions and programs for behavior (Luria, 1970). That is, information analyzed by the retrorolandic cortex is sent to prerolandic regions for planning and action. Prerolandic areas also receive information from subcortical areas regarding past experiences and emotions, which is used in decision making about actions. The actual interweaving of different functional components complicates this simple model as the right hemisphere has some involvement with verbal functions, some nonverbal behavior is mediated by the left cortex, and neural pathways between anterior and posterior regions ensure other extensive interactions.

FUNCTIONAL ORGANIZATION OF THE POSTERIOR CORTEX

Primary sensory areas are located in the posterior cortex. The primary visual cortex is located on the occipital lobes at the most posterior portion of the cerebral hemisphere (see Fig. 3.12, p. 64). The postcentral gyrus, at the most forward part of the parietal lobe, contains the primary sensory (somatosensory) projection area. The primary auditory cortex is located on the uppermost fold of the temporal lobe close to where it joins the parietal lobe. Kinesthetic and vestibular functions are mediated by areas low on the parietal lobe near the occipital and temporal lobe boundary regions. Sensory information undergoes extensive associative elaboration through reciprocal connections with other cortical and subcortical areas (Kolb and Whishaw, 1996; Mesulam, 1998).

No clear-cut demarcations exist among any of the functions localized on the posterior cortex. Rather, although the primary centers of the major functions served by the posterior cerebral regions are relatively distant from one another, secondary association areas gradually fade into tertiary overlap, or heteromodal, zones in which auditory, visual, and body-sensing components commingle.

As a general rule, the character of the defects arising from lesions of the association areas of the posterior cortex varies according to the extent to which the lesion involves each of the sense modalities. Any disorder with a visual component, for example, may implicate some occipital lobe involvement. If a patient with visual agnosia also has difficulty estimating close distances or feels confused in familiar surroundings, then parietal lobe areas serving spatially related kinesthetic and vestibular functions may also be affected. Knowledge of the sites of the primary sensory centers and of the behavioral correlates of lesions to these sites and to the intermediate association areas enables the clinician to infer the approximate location of a lesion from the patient's behavioral symptoms (see E. Goldberg, 1989, 1990, for a detailed elaboration of this functional schema).

The Occipital Lobes and Their Disorders

The visual pathway travels from the retina through the *lateral geniculate nucleus* of the thalamus to the primary visual cortex. A lesion anywhere in the path between the lateral geniculate and primary visual cortex can produce a homonymous hemianopia (see p. 53). Lesions of the primary visual cortex result in discrete blind spots in the corresponding parts of the visual fields but do not alter the comprehension of visual stimuli or the ability to make a proper response to what is seen.

Blindness and associated problems

The nature of the blindness that accompanies total loss of function of the primary visual cortex, and the patient's response to it, varies with the extent of involvement of subcortical or associated cortical areas. Some visual discriminations may take place at the thalamic level, but the cortex is necessary for the conscious experience of visual phenomena (Celesia et al., 1991; Koch and Crick, 2000; Weiskrantz, 1986). Although it is rare for damage or dysfunction to be restricted to the

primary visual cortex, when this does occur bilaterally the patient appears to have lost the capacity to distinguish forms or patterns while remaining responsive to light and dark, a condition called *cortical blindness* (Barton and Caplan, 2001; Luria, 1966). Patients may exhibit visually responsive behavior without experiencing vision, a phenomenon called *blindsight* (Farah, 2003b; Weiskrantz, 1986, 1996; Zeki, 1997). This phenomenon suggests that limited information in the blind visual field may project through alternate pathways to visual association areas. Total blindness due to brain damage appears to require large bilateral occipital cortex lesions (Barton and Caplan, 2001), and some patients have had destruction of thalamic areas as well as the visual cortex or the pathways leading to it (Teuber, 1975). In *denial of blindness* due to brain damage (*visual anosognosia*), patients lack appreciation that they are blind and attempt to behave as if sighted, making elaborate explanations and rationalizations for difficulties in getting around, handling objects, etc. (Redlich and Dorsey, 1945; Feinberg, 2003). Denial of blindness, sometimes called *Anton's syndrome,* may occur with several different lesion patterns; but typically the lesions are bilateral and involve the occipital lobe (Goldenberg, Mullbacher, and Nowak, 1995; McGlynn and Schacter, 1989). Such denial appears to be associated with disruption of corticothalamic connections and breakdown of sensory feedback loops.

Visual agnosias and other visual distortions

Lesions involving the visual association areas of the occipital lobes give rise to *visual agnosias,* or visual distortions (Benson, 1989; A.R. Damasio, Tranel, and Rizzo, 2000; Farah, 2003b; E. Goldberg, 1990; Mazaux, Dehail, et al., 1999). Only rarely do visuoperceptual disturbances result from lesions of other lobes or subcortical structures without occipital cortical damage as well. More often, impairments of visual awareness or visual recognition are associated with disturbances of other perceptual modalities; for example, when lesions in parietal regions extend to the occipital lobe disorders of visuospatial functions may occur.

Visual agnosia refers to a variety of relatively rare visual disturbances in which some aspect(s) of visual perception is defective in persons who can see and who are normally knowledgeable about information coming through other perceptual channels (Benson, 1989; A.R. Damasio, Tranel, and Damasio, 1989; Farah, 1999; Lissauer, [1888] 1988). They typically occur with bilateral occipital lesions (Vuilleumier, 2001).

In *apperceptive visual agnosia,* patients cannot synthesize what they see (M. Grossman, Galetta, and D'Esposito, 1997; see also Humphreys, 1999). They may indicate awareness of discrete parts of a word or a phrase, or recognize elements of an object without organizing the discrete percepts into a perceptual whole. Drawings by these patients are fragmented: bits and pieces are recognizable but are not put together. They cannot recognize an object presented in unconventional views, such as recognizing an object usually seen from the side (e.g., a teapot) but now viewed from the top (Davidoff and Warrington, 1999). These patients often display general cognitive deterioration as well (Bauer, 1993). Patients with *associative visual agnosia* (or *visual object agnosia*) can perceive the whole of a visual stimulus, such as a familiar object, but cannot recognize it although they may be able to identify it by touch, sound, or smell (Ogden, 1996; see also Farah and Feinberg, 2003a). The examiner can distinguish visual object agnosia from a naming impairment by asking the patient who cannot name the object to give any identifying information, such as what function it has.

Simultaneous agnosia, or *simultanagnosia*—also known as *Balint's syndrome*—appears as an inability to perceive more than one object or point in space at a time (Bauer, 1993; A.R. Damasio, Tranel, and Rizzo, 2000; Rafal, 1997a). This extreme perceptual limitation impairs these patients' ability to move about; they get lost easily, and even reaching for something in their field of vision becomes difficult (L.C. Robertson and Rafal, 2000). Some workers highlight abnormalities in control of eye movements, resulting in difficulty in shifting visual attention from one point in the visual field to another (Pierrot-Deseilligny, 2001; Tranel and Damasio, 2000), but L.R. Robertson and Rafal (2000) discuss it in terms of reduced access to "spatial representations that normally guide attention from one object to another in a cluttered field." Both explanations appear to be valid, as patients with Balint's syndrome have difficulty directing their gaze *and* shifting from a fixation point (Barton and Caplan, 2001; Benson, 1989; Rizzo and Robin, 1990). *Color agnosia,* the inability to appreciate differences between colors or to relate colors to objects in the presence of intact color vision, may occur in association with other visual agnosias (Gloning et al., 1968; Lennie, 2001), particularly color naming and recognition defects (A.R. Damasio, Tranel, and Rizzo, 2000). However, in describing five patients with occipital lesions, each presenting a different pattern of visual agnosia, Warrington (1986b) demonstrated that agnosic color, shape, and location deficits are fully dissociable. Inability to comprehend pantomimes (*pantomime agnosia*), even when the ability to copy them remains intact, has been reported with lesions confined to the occipital lobes (Rothi, Mack, and Heilman, 1986).

Some visual agnosias are particularly associated with right- or left-sided damage (see Chaves and Caplan, 2001). *Associative visual agnosia* usually occurs with lesions of the left occipitotemporal region (De Renzi, 2000). Patients with lesions in the left occipital cortex and its subcortical connections may have a reading problem that stems from defects of visual recognition, organization, and scanning rather than from defective comprehension of written material, which usually occurs only with parietal damage or in aphasia (R.B. Friedman et al., 1993; Köhler and Moscovitch, 1997). Defective color naming frequently accompanies this kind of reading disability and is also typically associated with damage to the left occipital lobe or to underlying white matter containing visual system pathways (Benson, 1989; A.R. Damasio and Damasio, 1983). Beauvois and Saillant (1985) identified an *optic aphasia for colors* in which "the functional interactions between verbal and visual representations" are impaired. One form of *acalculia* (literally, "no counting"), a disorder that Grewel (1952) considered a primary type of impaired arithmetic ability in which the calculation process itself is affected, may result from visual disturbances of symbol perception associated with left occipital cortex lesions.

Visual inattention refers to imperception of stimuli. Material in one visual field—usually the left—can be seen but remains unnoticed unless the patient's attention is drawn to it (Chaves and Caplan, 2001; see Fig. 3.13). This form of visual inattention, also known as *unilateral sensory* or *spatial neglect,* typically occurs when there is right parietal lobe involvement as well as occipital lobe damage. Right occipital lesions are less likely to give rise to inattention. The so-called "visual inattention" associated with occipital lobe damage is similar to simultaneous agnosia in that the patient spontaneously perceives only one thing at a time. It differs from simultaneous agnosia in that the patient will see more than one object if others are pointed out; this is not the case in a true simultaneous agnosia.

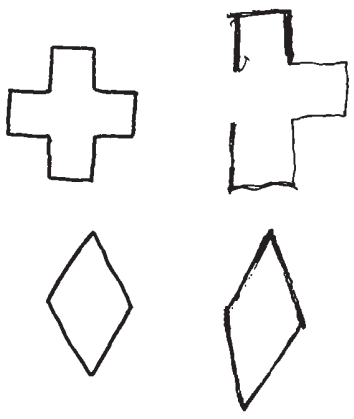

FIGURE 3.13 Example of inattention to the left visual field by a 57-year-old college graduate with a right parieto-occipital lesion.

Other visuoperceptual anomalies associated with occipital lesions include achromatopsia (loss of color vision in one or both visual half-fields), astereopsis (loss of stereoscopic vision), metamorphopsias (visual distortions), monocular polyopias (double, triple, or more vision in one eye), optic allesthesia (misplacement of percepts in space), and palinopsia (perseverated visual percept) (Barton and Caplan, 2001; Benson, 1989; A.R. Damasio, 1988; Zihl, 1989). These are very rare conditions but of theoretical interest as they may provide clues to cortical organization and function. Lesions associated with these conditions tend to involve the parietal cortex as well.

Prosopagnosia

Some workers report that another kind of visual agnosia, *prosopagnosia* (inability to recognize faces), occurs only when the cortex on the undersides of the occipital and temporal lobes is damaged bilaterally (A.R. Damasio, 1985; Geschwind, 1979; Mesulam, 2000b, p. 337), although other investigators have observed this phenomenon when the damage is restricted to the right hemisphere (De Renzi, 1997a; De Renzi, Perani, Carlesimo et al., 1994; Landis, Cummings, et al., 1986; Vuilleumier, 2001). It can present with just occipital lesions, but often temporal lobe lesions and sometimes parietal damage accompany the lesions (e.g., see A.R. Damasio, 1985; Tranel, Damasio, and Damasio, 1988). In normal subjects, only *ventromedial* areas (at the base of the brain toward the midline of the posterior right hemisphere) are specifically activated during a face recognition task (G. McCarthy, 2000; Sergent, Ohta, and MacDonald, 1992).

Difficulty in discriminating and matching unfamiliar faces may accompany left as well as right hemisphere lesions (Benton, 1980; Benton, Sivan, Hamsher, et al., 1994), although impairment tends to be greater when the lesion is on the right (Sergent, 1989). It is less frequent among patients with left hemisphere damage, affecting only aphasic patients who have comprehension defects at about the same rate of occurrence for all patients with right hemisphere damage. Capitani et al. (1978) reported that among patients unable to recognize unfamiliar faces, those with parietal rather than occipital lobe involvement were significantly more error prone on a color discrimination task, with the right-lesioned patients making almost twice as many errors as those whose lesions were on the left.

Oliver Sacks richly described the extraordinary condition of prosopagnosia for familiar faces in his book *The Man who Mistook His Wife for a Hat* (1987). Like many prosopagnosics, his patient suffered visual agnosia on a broad scale, with inability to recognize faces as just one of many recognition deficits. This defect may show up whenever these patients must use vision to make a specific identification of an item in a category of objects or creatures, e.g., a bird watcher unable to identify birds or a farmer unable to recognize specific animals he once knew by name (A.R. Damasio, 1985).

Characteristic hemisphere processing differences show up in face recognition performances of patients with unilateral occipital lobe lesions (A.R. Damasio, Tranel, and Rizzo, 2000). Left occipital lesioned patients using right hemisphere processing strategies form their impressions quickly but may make semantic (i.e., naming) errors. With right occipital lesions, recognition proceeds slowly and laboriously in a piecemeal manner, but is often successful. A.R. Damasio, Damasio, and Tranel (1990) described other problems of perceptual fragmentation that can appear with prosopagnosia.

Reports on prosopagnosia in the literature indicate that it is about four times more common in men than in women, a finding that may reflect sex differences in cerebral organization (Mazzucchi and Biber, 1983; see pp. 301–303). Although impaired recognition of both familiar and unfamiliar faces is often treated as a single condition, these two forms of prosopagnosia can occur separately and thus their cerebral organization differs (D.R. Malone et al., 1982; R.A. McCarthy and Warrington, 1990). Some patients with this condition can appreciate the facial expressions, age, and sex of faces they may not recognize (A.R. Damasio, Tranel, and Rizzo, 2000). Lesions in occipital sites can result in the most flagrant and circumscribed face recognition deficits, but storage and processing also appear to take place at many other cortical and subcortical sites. Inability to recognize familiar faces may result from inaccessibility of memory traces for known faces stored in other brain regions (Carlesimo and Caltagirone, 1995). Thus the neuroanatomic model for face recognition suggests a pattern for the "multiple representation of visual stimuli" generally (A.R. Damasio, Damasio, and Tranel, 1990) and of information from the other sensory modalities as well (C.G. Phillips et al., 1984).

Two visuoperceptual systems

Another anatomic dimension that differentiates visual functions has to do with a *dorsal* (top side of the cerebrum)–*ventral* (under side) distinction (see Fig. 3.14). Two now well-identified visual systems have separate pathways with different cortical loci (Barton and Caplan, 2001; Goodale, 2000; Mesulam, 2000b). One runs dorsally from the occipital to the parietal lobe. This parieto-occipital pathway is involved with spatial analysis, providing for spatial orientation: it gives visual "where" information. The temporo-occipital pathway, which takes a ventral route from the occipital lobe, conveys information about shapes and patterns, the "what" of visual perception. In clarifying their different contributions, D.N. Levine and his colleagues (1985) note that damage to either pathway can result in spatial disorientation but for different reasons: with damage to the dorsal pathway, patients will experience visual disorientation; when the damage involves the ventral pathway, "patients lose their way because they cannot recognize landmarks." Many of these latter patients have difficulty with face and object recognition (Hermann, Seidenberg, et al., 1993).

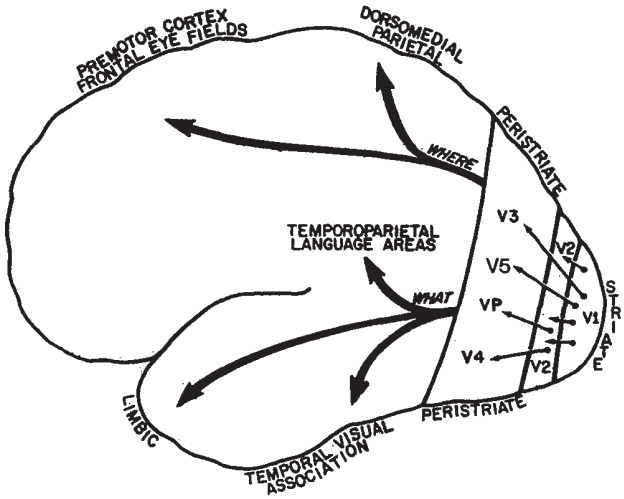

FIGURE 3.14 Organization of the two major visual pathways in the human brain. (From Mesulam, 2000b)

The Posterior Association Cortex and Its Disorders

Association areas in the parieto-temporo-occipital region are situated just in front of the visual association areas and behind the primary sensory strip (see Fig. 3.12, p. 64). They run from the *longitudinal fissure,* sometimes called the *sagittal fissure* (the deep cleft separating the two hemispheres) laterally into the areas adjacent to and just above the temporal lobe where temporal, occipital, and parietal elements commingle. These association areas include much of the parietal and occipital lobes and some temporal association areas. Functionally they are the site of cortical integration for all behavior involving vision, touch, body awareness and spatial orientation, verbal comprehension, localization in space, abstract and complex cog-

nitive functions of mathematical reasoning, and the formulation of logical propositions that have their conceptual roots in basic visuospatial experiences such as "inside," "bigger," "and," or "instead of." It is within these areas that intermodal sensory integration takes place, making this region "an association area of association areas" (Geschwind, 1965) or "heteromodal association cortex" (Mesulam, 2000b) or "multimodal sensory convergence areas" (Heilman, 2002).

A variety of *apraxias* (inability to perform learned purposeful movements) and agnosias have been ascribed to parieto-temporo-occipital lesions. Most of them have to do with verbal or with nonverbal stimuli but not with both and thus are asymmetrically localized. A few occur with lesions in either hemisphere.

Defects arising from posterior lesions in either hemisphere

Constructional disorders are among the predominantly parietal lobe disabilities that appear with lesions on either side of the midline (F.W. Black and Bernard, 1984; De Renzi, 1997b), reflecting the involvement of both hemispheres in processing spatial information (Sergent, 1991a,b). They involve impairment of the "capacity to draw or construct two or three dimensional figures or shapes from one and two dimensional units" (Strub and Black, 2000). They seem to be closely associated with perceptual defects (Pillon, 1981a,b; Sohlberg and Mateer, 2001). Constructional disorders take different forms depending on the hemispheric side of the lesion (Consoli, 1979; Cutting, 1990; Walsh and Darby, 1999; Warrington, James, and Kinsbourne, 1966). Left-sided lesions are apt to disrupt the programming or ordering of movements necessary for constructional activity (Hécaen and Albert, 1978). Visuospatial defects associated with impaired understanding of spatial relationships or defective spatial imagery tend to underlie right hemisphere constructional disorders (Pillon, 1979). Diagonality in a design or construction can be particularly disorienting to patients with right hemisphere lesions (B. Milner, 1971; Warrington, James, and Kinsbourne, 1966). Defects in copying designs appear in the drawings of patients with left hemisphere lesions as simplification and difficulty in making angles, and in the drawings of patients with right-sided involvement as a tendency to a counterclockwise tilt (rotation), fragmented percepts, irrelevant overelaborativeness, and inattention to the left half of the page or the left half of elements on the page (Diller and Weinberg, 1965; Ducarne and Pillon, 1974; Warrington, James, and Kinsbourne, 1966). (See Fig. 3.15a,b for freehand drawings of left and right hemisphere damaged patients showing typical hemispheric defects.) Assembling puzzles in two- and three-dimensional space may be affected by both right and left hemisphere lesions (E. Kaplan, 1988; E. Kaplan, Fein, et al., 1991).

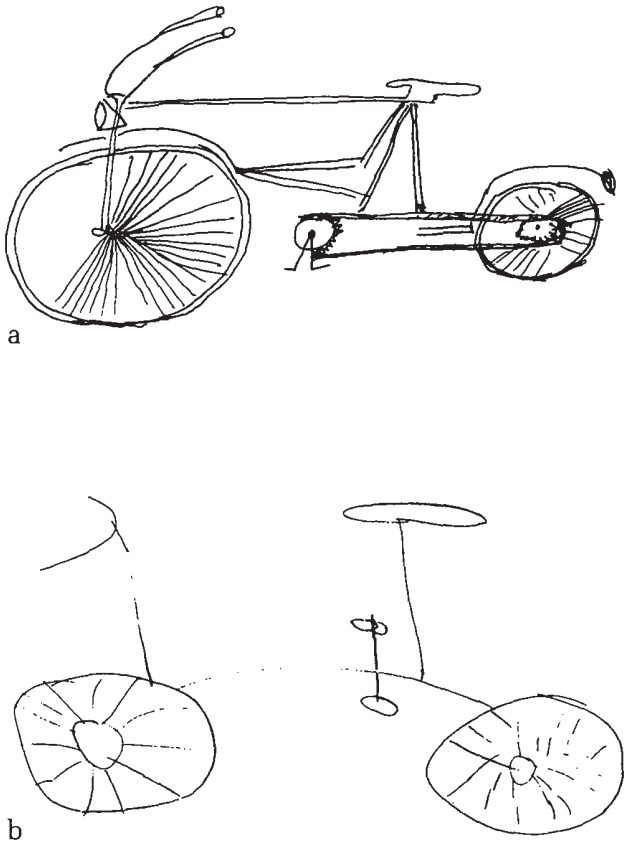

FIGURE 3.15*a* This bicycle was drawn by the same 51-year-old retired salesman who constructed the block designs of Figure 3.9 (*a–e*). This drawing demonstrate that neglect of the left visual field is not due to carelessness as the patient painstaking provided details and was very pleased with his performance. *b:* This bicycle was drawn by a 24-year-old college graduate almost a year after he received a severe injury to the left side of his head. He originally drew the bike without pedals, adding them when asked, "How do you make it go?"

Some studies have not shown any difference in the frequency with which left and right hemisphere damaged patients have constructional disorders (e.g., Arena and Gainotti, 1978; F.W. Black and Bernard, 1984; Dee et al., 1970); others (Belleza et al., 1979; Y. Kim et al., 1984; Warrington, James, and Maciejewski, 1986) have reported more constructional disabilities among right brain damaged patients. Although Arena and Gainotti (1978) attribute differences in findings to the number of aphasic patients included in the left hemisphere damaged samples, other differences between the studies may also account for the apparently conflicting findings. For example, Benton (1984) used a difficult three-dimensional construction task while Arena and Gainotti (1978) had their patients copy rel-

atively simple geometric designs. Another factor is time since injury. When examined six months after stroke, a left hemisphere group showed more improvement and better performance than a right hemisphere group (Sunderland, Tinson, and Bradley, 1994).

The integration of sensory, motor, and attentional signals that takes place within the posterior parietal cortex enables the direction and shifting of attention and response which are prerequisites for effectively dealing with space (J.F. Stein, 1991; see also Farah, Wong, et al., 1989; Mesulam, 1983). One identified function mediated in the parietal lobes is the ability to disengage attention in order to be able to reengage it rapidly and correctly: parietal lobe damage significantly slows the disengagement process (L.C. Robertson and Rafal, 2000), with the greatest slowing occurring when the lesion is on the right (Morrow and Ratcliff, 1988; Posner et al., 1984; Roy, Reuter-Lorenz, Roy, et al., 1987).

A short-term memory disorder, associated with lesions in that portion of the parietal lobe lying just above the posterior temporal lobe (the *inferior parietal lobule*), reflects the usual auditory/visual lateralization pattern (N. Butters, Samuels, et al., 1970; Mayes, 2000b; Vallar and Papagno, 2002). Thus, with left-sided lesions in this area, the number of digits, tones (W.P. Gordon, 1983), or words (Risse et al., 1984) that can be recalled immediately upon hearing them is abnormally low; patients with right-sided lesions here show reduced short-term recall for geometric patterns. Direct cortical stimulation studies (Mayes, 1988; Ojemann, 1980; Ojemann, Cawthon, and Lettich, 1990) and functional imaging (C.R. Clark et al., 2000) have also implicated this region in short-term memory.

Hécaen (1969) associated difficulties in serial ordering with impairment of the parieto-temporo-occipital area of both the left and right hemispheres. Perception of the temporal order in which stimuli are presented is much more likely to be impaired by left than right hemisphere lesions involving the posterior association areas (Carmon and Nachson, 1971; von Steinbüchel et al., 1999), except when the stimulus array also includes complex spatial configurations, for then the patients with right hemisphere lesions do worse than those with left-sided lesions (Carmon, 1978). Disruption of the sequential organization of speech associated with left hemisphere lesions may result in the language formulation defects of aphasia. Right-sided lesions of the parieto-temporo-occipital area appear to interfere with the comprehension of order and sequence so that the patient has difficulty seeing or dealing with temporal relationships and is unable to make plans (Milberg, Cummings, et al., 1979).

Damage to the crossed optic radiations underlying either parietal cortex results in loss of vision in the contralateral lower visual field quadrant (Barton and Caplan, 2001; Pearlman, 1990). Lesions in either hemisphere involving the somatosensory association areas posterior to the postcentral gyrus can produce a *tactile agnosia* or *astereognosis* (inability to identify an object by touch) to the body side opposite the lesion (Caselli, 2003). Some patients with right-sided lesions here may experience bilateral astereognosis (Vuilleumier, 2001). Sensitivity to the size, weight, and texture of hand-held objects is also diminished contralaterally by these lesions (A.R. Damasio, 1988). Left-sided inattention appears to exacerbate the problem and, with severely reduced left hand sensitivity, bilateral tactile agnosia may appear (Caselli, 1991). Semmes' (1968) findings that right hemisphere lesions may be associated with impairment of shape perception in both hands have received support (e.g., Boll, 1974), but a high incidence of bilateral sensory defects has also been noted among patients with unilateral lesions of either hemisphere (B. Milner, 1975). Parietal lesions in either hemisphere may disrupt the guidance of movements insofar as they depend on somatosensory contributions (Jason, 1990).

Other neuropsychological abnormalities historically associated with just one side of the cortex do show up with lesions on the unexpected side in right-handed patients. In the succeeding pages, those that are typically associated with a hemispheric side will be presented in accord with their characteristic lateralization, with significant exceptions noted.

Defects arising from left posterior hemisphere lesions

The posterior language areas are situated at the juncture of the temporal and parietal lobes. Fluent aphasia and related symbol-processing disabilities are generally the most prominent symptoms of left parieto-temporo-occipital lesions. This form of aphasia is usually characterized by incomprehension, jargon speech, *echolalia* (parrotted speech), and apparent lack of awareness of the communication disability. It commonly follows cortical damage within this area where "the great afferent systems" of audition, vision, and body sensation overlap (M.P. Alexander, 2003; Benson, 1988; A.R. Damasio and Damasio, 2000; Dronkers et al., 2000; see pp. 32–33). W.R. Russell (1963) pointed out that even very small cortical lesions in this area can have widespread and devastating consequences for verbal behavior. Howard (1997) offers an interpretation of imaging data, noting that language capabilities are more widespread and occur in less well-delineated cortical areas than is assumed in classical localization theory (see also Kertesz and Gold, 2003).

Communication disabilities arising from lesions in the left parieto-temporo-occipital region may involve im-

paired or absent recognition or comprehension of the semantic—and logical—features of language (Bachman and Albert, 1988; Howard, 1997; E. Goldberg, 1990; McCarthy and Warrington, 1990). Lesions overlapping both the parietal and occipital cortex may give rise to reading defects (R.B. Friedman et al., 1983). Writing ability can be disrupted by lesions in a number of cortical sites (Luria, 1966), mostly on the left and often in the posterior association cortex (Roeltgen, 2003). The nature of the writing defect depends on the site and extent of the lesion (Roeltgen, 2003). In many cases the defects of written language reflect the defects of a concomitant aphasia or apraxia (Bub and Chertkow, 1988; Luria, 1970).

Apraxias characterized by disturbances of nonverbal symbolization, such as gestural defects or inability to demonstrate an activity in pantomime or to comprehend pantomimed activity, are usually associated with lesions involving language comprehension areas and the overlap zone for kinesthetic and visual areas of the left hemisphere, occurring less often with anterior lesions (Haaland and Yeo, 1989; Heilman and Rothi, 2003; Jason, 1990; Kareken et al., 1998; Meador, Loring, Lee, et al., 1999). Defective ability to comprehend gestures has been specifically associated with impaired reading comprehension in some aphasic patients, with constructional disorders in others (Ferro, Santos, et al., 1980). Impairments in sequential hand movements are strongly associated with left parietal lesions (Haaland and Yeo, 1989). Apraxias often occur with aphasia and may be obscured by or confused with the language disorder. De Renzi, Motti, and Nichelli (1980) observed that while 50% of patients with left-sided lesions were apraxic, so too were 20% of those damaged on the right, although right-lesioned patients had milder deficits. That apraxia and aphasia can occur separately implicates different but anatomically close or overlapping neural networks (Heilman and Rothi, 2003; Kertesz, Ferro, and Shewan, 1984).

Like writing, arithmetic abilities depend on intact cortex at several sites (Rosselli and Ardila, 1989; Rickard et al., 2000; Spiers, 1987). Acalculia is most common and most severe with lesions of the left posterior cortex (Dehaene, 2000; Grafman and Rickard, 1997) and pure *agraphia* (inability to write) may also result from lesions in this area (Schomer, Pegna, et al., 1998). This area contributes to knowledge of arithmetic operations (Langdon and Warrington, 1997; Warrington, 1982) such that lesions here may disrupt computational operations in patients who can make reasonable quantity estimates. Left posterior lesions may also involve defective number reading and writing (H.S. Levin, Goldstein, and Spiers, 1993) or errors due to spatial disorientation (Grafman, 1988; Grafman, Passafiume, et al., 1982; Walsh and Darby, 1999).

Acalculia and agraphia generally appear in association with other communication disabilities. When they occur with left–right spatial disorientation and an inability to identify one's own fingers, to orient oneself to one's own fingers, to recognize or to name them (*finger agnosia*), the symptom cluster is known as *Gerstmann's syndrome* (Gerstmann, 1940, 1957) and the lesion is likely to involve the left parieto-occipital region. Acalculia associated with finger agnosia typically disrupts such relatively simple arithmetic operations as counting or ordering numbers. The frequency with which these individual symptoms occur together reflects an underlying cortical organization in which components involved in the different impaired acts are in close anatomical proximity. Other deficits—including aphasia—are also frequently associated with one or more of these symptoms (Benton, 1977b; Denburg and Tranel, 2003). Moreover, both finger agnosia and right–left disorientation can be present when cortical damage is on the right (Benton, 1977b [1985]; Denburg and Tranel, 2003). Thus, rather than achieving the stature of a syndrome with an underlying functional unity (e.g., Orgogozo, 1976), the symptoms identified by Gerstmann may best be understood together as a "cluster" which may provide valuable localizing information (Geschwind and Strub, 1974).

Agnosias arising from left hemisphere lesions just anterior to the visual association area may appear as disorientation of either extrapersonal or personal space and are likely to have either a symbolic or left–right component (Benton, 1973 [1985]; E. Goldberg, 1990). Not only may disorders of extrapersonal or personal space occur separately, but different kinds of personal space deficits and disorientations can be distinguished (Lishman, 1997; Newcombe and Ratcliff, 1989). However, visuospatial perception tends to remain accurate (Belleza et al., 1979).

Disabilities arising from left hemisphere lesions tend to be more severe when the patient is also aphasic. Although all of these disturbances can occur in the absence of aphasia, it is rare for any of them to appear as the sole defect.

Defects arising from right posterior hemisphere lesions

A commonly seen disorder associated with the right parietal lobe is impaired constructional ability (Benton, 1967 [1985]; De Renzi, 1997b; Farah, 2003a). Vestibular and oculomotor disorders, defective spatial orientation, or impaired visual scanning contribute to the constructional disability. A right hemisphere *dyscalculia* shows up on written calculations as an inability to manipulate numbers in spatial relationships, such as us-

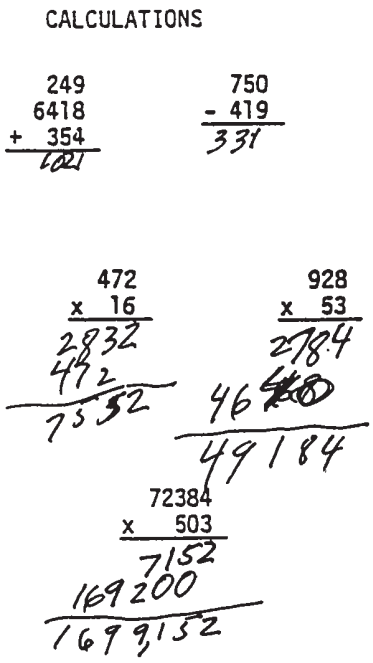

FIGURE 3.16 Example of spatial dyscalculia by the traumatically injured pediatrician described on pp. 80–81 whose reading inattention is shown in Figure 10.7. Note neglect of the 6 on the left of the problem in the upper left corner; errors on left side of bottom problem which appear to be due to more than simple neglect; labored but finally correct working out of problem in middle right side of page. This test was taken with no time limit.

ing decimal places or "carrying," although the patient retains mathematical concepts and the ability to do problems mentally (Denburg and Tranel, 2003; see Fig. 3.16). Spatial (or visuospatial) dyscalculia is frequently associated with constructional deficits (H.S. Levin, Goldstein, and Spiers, 1993; Rosselli and Ardila, 1989) and seems to follow from more general impairments of spatial orientation or organization. *Apraxia for dressing,* in which the patient has difficulty relating to and organizing parts of his body to parts of his clothing, may accompany right-sided parietal lesions (Damasio, Tranel, and Rizzo, 2000; Hier, Mondlock, and Caplan, 1983a,b; Pimental and Kingsbury, 1989). It is not a true apraxia but rather symptomatic of spatial disorientation coupled, in many instances, with left visuospatial inattention (Poeck, 1986; see below). Other performance disabilities of patients with right parietal lobe involvement are also products of a perceptual disorder, such as impaired ability to localize objects in left hemispace (Mesulam, 2000b). For example, the chief complaint of a middle-aged rancher with a right parieto-occipital lesion was difficulty in eating because his hand frequently missed when he put it out to reach the cup or his fork overshot his plate.

Many of the perceptual disorders arising from lesions of the right posterior association cortex are related to the phenomenon of inattention or *sensory neglect,* the tendency for decreased or absent awareness of events presented to the half of the body contralateral to the hemisphere side of the lesion that is not the result of a sensory defect (Bisiach and Vallar, 1988; S. Clarke, 2001; Heilman, Watson, and Valenstein, 2003; Mesulam, 2000b; Rafal, 1997b). The most common lesion site for chronic inattention is the temporoparietal cortex, with severity of the deficit directly related to lesion size. Kertesz and Dobrowolski (1981) observed left-sided inattention occurring more prominently among patients whose lesions involved the area around the central sulcus (including posterior frontal and some temporal lobe tissue) than among patients whose lesions were confined to the parietal lobe; yet Vallar and Perani's studies (1986, 1987) implicated the parietal lobe as the most common lesion site associated with inattention. Egelko, Gordon, and their colleagues (1988) noted that each of the three posterior lobes could be involved, with "a lack of specificity in the relationship between the regions of right neuroanatomic damage and visual–spatial inattention."

A few left hemisphere damaged patients experience this problem (Köhler and Moscovitch, 1997), usually during the acute stage of their illness (Colombo et al., 1976). Inattention has been reported in association with lesions on either side when patients with lateralized brain damage are given tasks too difficult for them to perform; for example, auditory letter matching elicited inattention from left hemisphere lesioned patients, while on a difficult visual discrimination task both right- and left-lesioned patients displayed inattention (Leicester et al., 1969). When inattentive patients were primed with a picture displayed to the neglected field, the amount of time they took to make a lexical decision was significantly shortened when the picture and word were semantically related, indicating that processing was taking place unconsciously in the impaired field (McGlinchey-Berroth et al., 1993). Inattention can occur in any perceptual modality but rarely involves all of them (S. Clarke, 2001; Umilta, 1995).

Inattention may be manifested in a number of ways. It may occur as a relatively discrete and subtle disorder apparent only to the examiner. When stimulated bilaterally with a light touch to both cheeks or fingers wiggled in the outside periphery of each visual field simultaneously, inattentive patients tend to ignore the stimulus on the left (*double simultaneous stimulation*), although they have no apparent difficulty noticing the stimuli when presented one at a time. This form of inattention has been variously called *sensory inattention, sensory extinction, sensory suppression,* or *perceptual*

rivalry (Walsh and Darby, 1999). Visual extinction is frequently associated with other manifestations of inattention in patients with right-sided lesions, but these two phenomena can occur separately (Barbieri and De Renzi, 1989; S. Clarke, 2001). They are often accompanied by similar deficits with different names, extinction and inattention are probably two aspects of the same pathological process (Bisiach, 1991; Mesulam, 2000; Rafal, 2000). In this book, "inattention" refers to all aspects of unilaterally depressed awareness.

Although usually presenting as one syndrome, inattention for personal and extrapersonal space do not always occur together (Bisiach, Perani, et al., 1986). In its more severe forms, inattention for personal space may amount to a complete agnosia for the half of space or for the half of the patient's body opposite the side of the lesion (*hemisomatognosia*). Mild inattention to one's own body may appear as simple negligence: the patient with right-sided damage rarely uses the left hand spontaneously, may bump into objects on the left, or may not use left-side pockets. In more extreme cases, usually associated with left hemiplegia, patients may appear completely unaware of the left half of the body, even to the point of denying left-side disabilities (*anosognosia*) or being unable to recognize that the paralyzed limbs belong to them (Cutting, 1990; Feinberg, 2003). Most cases of anosognosia involve the inferior parietal cortex, but it can occur with purely subcortical lesions or with frontal damage (Bisiach and Geminiani, 1991). S.W. Anderson and Tranel (1989) found that all of their patients with impaired awareness of physical disabilities also lacked awareness of their cognitive defects. Anosognosia creates a serious obstacle to rehabilitation as these patients typically see no need to exert the effort or submit to the discomforts required for effective rehabilitation.

In left visuospatial inattention, not only may patients not attend to stimuli in the left half of space, but they may also fail to draw or copy all of the left side of a figure or design and tend to flatten or otherwise diminish the left side of complete figures (see Figs. 3.13; 10.9). When copying written material, the patient with unilateral inattention may omit words or numbers on the left side of the model, even though the copy makes less than good sense (see Chapter 10, Fig. 10.8, p. 385). Increasing the complexity of the drawing task increases the likelihood of eliciting the inattention phenomenon (Pillon, 1981a). In reading, words on the left side of the page may be omitted although such omissions alter or lose the meaning of the text (Mesulam, 2000b; see Chapter 10, Fig. 10.7, p. 384). This form of visual imperception typically occurs only when the right parietal damage extends to occipital association areas. Left visual inattention is frequently, but not necessarily, accompanied by left visual field defects, most usually a left homonymous hemianopsia. Some patients with obvious left-sided inattention, particularly those with visual inattention, display a gaze defect such that they do not spontaneously scan the left side of space, even when spoken to from the left. These are the patients who begin reading in the middle of a line of print when asked to read and who seem unaware that the words out of context of the left half of the line make no sense. Most such right hemisphere damaged patients stop reading on their own, explaining that they have "lost interest," although they can still read with understanding when their gaze is guided. Even in their mental imagery, some of these patients may omit left-sided features (Bisiach and Luzzatti, 1978; Meador, Loring, Bowers, and Heilman, 1987).

A 45-year-old pediatrician sustained a large area of right parietal damage in a motor vehicle accident. A year later he requested that his medical license be reinstated so he could resume practice. He acknowledged a visual deficit which he attributed to loss of sight in his right eye and the left visual field of his left eye and for which he wore a little telescopic monocle with a very narrow range of focus. He claimed that this device enabled him to read. He had been divorced and was living independently at the time of the accident, but since then he has stayed with his mother. He denied physical and cognitive problems other than a restricted range of vision which he felt would not interfere with his ability to return to his profession.

On examination he achieved scores in the *superior* to *very superior* range on tests of old verbal knowledge although he performed at only *average* to *high average* levels on conceptual verbal tasks. Verbal fluency (the rapidity with which he could generate words) was just *low average,* well below expectations for his education and verbal skills. On written tests he made a number of small errors, such as copying the word bicycle as "bicyclicle," Harry as "Larry," and mistrust (on a list immediately below the word displease, which he copied correctly) as "distrust." Despite a *very superior* oral arithmetic performance, he made errors on four of 20 written calculation problems, of which two involved left spatial inattention (see Fig. 3.16). Verbal memory functions were well *within normal limits.*

On visuoperceptual and constructional tasks, his scores were generally *average* except for slowing on a visual reasoning test which dropped his score to *low average.* In his copy of a set of line drawn designs (see Chapter 14, Fig. 14.1, p. 533), left visuospatial inattention errors were prominent as he omitted the left dot of a dotted arrowhead figure and the left side of a three-sided square. Although he recalled eight of the nine figures, on both immediate and delayed recall trials, he continued to omit the dot and forgot the incomplete figure altogether. On Line Bisection, 13 of 19 "midlines" were pushed to the right. On an oral reading task arranged to be sensitive to left-side inattention, in addition to misreading an occasional word he omitted several words or phrases on the left side of the page (see Fig. 10.7, p. 384) whether reading

with or without his monocle. Essentially the performances did not differ.

In a follow-up interview he acknowledged unawareness of the inattention problem, but then reported having had both inattention and left-sided hemiparesis immediately after the accident. In ascribing his visuoperceptual problems to compromised vision, this physician demonstrated that he had been unaware of their nature. Moreover, despite painstaking efforts at checking and rechecking his performances—as was evident on the calculation page and other paper-and-pencil tasks—he did not self-monitor effectively, another aspect of not being aware of his deficits. The extent of his anosognosia and associated judgmental impairments became apparent when he persisted in his ambition to return to medical practice after being informed of his limitations.

Visuospatial disturbances associated with lesions of the parieto-occipital cortex include impairment of topographical or spatial thought and memory (Benson, 1989; De Renzi, 1997b; Newcombe and Ratcliff, 1989). Some workers identify temporo-occipital sites as the critical lesion area for object recognition (Dolan et al., 1997; Habib and Sirigu, 1987; Landis, Cummings, Benson, and Palmer, 1986). Another problem is perceptual fragmentation (Denny-Brown, 1962). A severely left hemiparetic political historian, for instance, when shown photographs of famous people he had known, named bits and pieces correctly, e.g., "This is a mouth . . . this is an eye," but was unable to organize the discrete features into recognizable faces. Warrington and Taylor (1973) also related difficulties in perceptual classification, specifically, the inability to recognize an object from an unfamiliar perspective, to right parietal lesions (see also McCarthy and Warrington, 1990). Appreciation of facial expressions may also be impaired (Adolphs and Damasio, 2000).

The Temporal Lobes and Their Disorders

Temporal cortex functions: information processing and lesion-associated defects

The primary auditory cortex is located on the upper posterior transverse folds of the temporal cortex (*Heschel's gyrus*), for the most part tucked within the *Sylvian fissure* (see Figs. 3.1 and 3.12, pp. 42, 64). This part of the superior temporal gyrus receives input from the *medial geniculate nucleus* of the thalamus. Much of the temporal lobe cortex is concerned with hearing and related functions, such as auditory memory storage and complex perceptual organization.

The superior temporal cortex and adjacent areas are critical for central auditory processing (Mesulam, 2000b; Vuillemier, 2001). The auditory pathways transmit information about sound in all parts of space to both hemispheres through major contralateral and minor ipsilateral projections (see Fig. 3.7, p. 53). The condition of cortical deafness occurs with bilateral destruction of the primary auditory cortices, but most cases with severe hearing loss also have subcortical lesions (Bauer and McDonald, 2003). Patients whose lesions are limited to the cortex are typically not deaf but their auditory recognition will be deficient (Kolb and Whishaw, 1996). Thus "cortical deafness" is a misnomer as these patients retain some hearing capacity (Coslett, Brashear, and Heilman, 1984; Hécaen and Albert, 1978).

The importance of the temporal lobes to central auditory processing becomes evident following surgical removal of either anterior temporal lobe (Efron and Crandall, 1983; Efron, Crandall, et al., 1983). In these patients, dominance for tonal pitch becomes heightened for sound heard ipsilateral to the lobectomy relative to diminished dominance on the contralateral side. This operation impairs the ability to discriminate and focus on one sound in the midst of many—the "cocktail party" effect—again for the side opposite the lesioned lobe. Cortical association areas of the left temporal lobe mediate the perception of such verbal material as word and number and voice recognition (B. Milner, 1971; Van Lancker, Cummings, et al., 1988). The farther back a lesion occurs on the temporal lobe, the more likely it is to produce alexia and verbal apraxias.

Polster and Rose (1998) describe disorders of auditory processing that parallel those of visual processing. *Pure word deafness* is an inability to comprehend spoken words despite intact hearing, speech production, reading ability, and recognition of nonlinguisitic sounds which occurs mostly with left temporal lesions. *Auditory agnosia* is an inability to recognize auditorily presented environmental sounds independent of any deficit in processing spoken language and is primarily associated with a right temporal lobe lesion. However, lesion localization is variable from case to case and often these conditions involve bilateral lesions (Bauer and McDonald, 2003). *Phonagnosia* is an inability to recognize familiar voices which may develop with a lesion in the right parietal lobe. Anatomically distinct "what" and "where" systems, also analogous to the visual processing system, have been described (Clarke, Bellman, Meuli et al., 2000; Rauschecker and Tian, 2000).

Considerable interindividual variability exists for the aphasias and associated language and other cognitive disorders, both with respect to anatomic differences in functionally relevant sites and with respect to differences in anatomic lesion patterns which, together, make the identification of deficit sites a matter of frequency of occurrence (M.P. Alexander, 2003; Dronkers et al., 2000). Any individual case is likely to deviate from the common frequency patterns (D. Caplan, 1987; De Bleser, 1988; Ojemann, 1980). Interindividual vari-

ability holds true for most other cortical functions, but few have been mapped as often or as carefully as the language functions.

Perhaps the most crippling of the communication disorders is *Wernicke's aphasia* (also called *sensory, fluent,* or *jargon aphasia;* see Chapter 2, Table 2.1, p. 33) since these patients can understand little of what they hear, although motor production of speech remains intact (Benson, 1993; A.R. Damasio and Geschwind, 1984; A.R. Damasio and Damasio, 2000; Dronkers et al., 2000). Many such patients prattle grammatically and syntactically correct nonsense. The auditory incomprehension of patients with lesions in Wernicke's area does not extend to nonverbal sounds for they can respond appropriately to sirens, squealing brakes, and the like. Moreover, these patients are frequently anosognosic, neither appreciating their deficits nor aware of their errors, and thus unable to self-monitor, self-correct, or benefit readily from therapy (Lebrun, 1987; Rubens and Garrett, 1991).

Lesions in the left temporal lobe may disrupt retrieval of words which, when severe, can seriously disrupt fluent speech (*dysnomia*) (A.R. Damasio and Damasio, 2000; Fuster, 1999; Indefrey and Levelt, 2000; Kremin, 1988). Anatomically separate regions tend to process words for distinct kinds of items, such as animals or tools (A. Martin, Wiggs, Ungerleider, and Haxby, 1996).

Many patients with a naming disorder find it hard to remember or comprehend long lists, sentences, or complex verbal material; and their ability for new verbal learning may be greatly diminished or even abolished. After left temporal lobectomy, patients tend to perform complex verbal tasks somewhat less well than prior to surgery, verbal memory tends to worsen (Ivnik, Sharbrough, and Laws, 1988), and they do poorly on tests that simulate everyday memory skills (Ivnik, Malec, Sharbrough, et al., 1993). What they do recall tends to be confounded with their associations, appearing as intrusion errors in their responses (Crosson, Sartor, et al., 1993).

Patients with cortical lesions of the right temporal lobe are unlikely to have language disabilities. These patients may have trouble organizing complex data or formulating multifaceted plans (Fiore and Schooler, 1998). Impairments in sequencing operations (Canavan et al., 1989; Milberg et al., 1979) have also been associated with right temporal lobe lesions. Temporal lobe damage may result in some form of *amusia* (literally, no music), particularly involving receptive aspects of musicianship such as the abilities to distinguish tones, tonal patterns, beats, or timbre, often but not necessarily with resulting inability to enjoy music or to sing or hum a tune or rhythmical pattern (Alajouanine, 1948; Benton, 1977a; Samson and Zatorre, 1988; Shankweiler, 1966). Odor perception may require intact temporal lobes (Eskenazi et al., 1986; Jones-Gotman and Zatorre, 1988) and is particularly vulnerable to right temporal lesions (Abraham and Mathai, 1983; Martinez et al., 1993).

The temporal lobes also contain some components of the visual system (Eichenbaum and Cohen, 2001) including the crossed optic radiations from the upper quadrants of the visual fields, so that temporal lobe damage can result in a visual field defect (Barton and Caplan, 2001; Kolb and Whishaw, 1996). Damage in ventral posterior portions of the temporal cortex can produce a variety of visuoperceptual abnormalities, such as deficits in visual discrimination and visual word and pattern recognition that occur without deficits on visuospatial tasks (Fedio, Martin, and Brouwers, 1984; Kolb and Whishaw, 1996; B. Milner, 1958). This pattern of impaired object recognition with intact spatial localization appeared following temporal lobectomies that involved "the anterior portion of the occipitotemporal object recognition system" (Hermann, Seidenberg, et al., 1993). Left–right asymmetry follows the verbal–nonverbal pattern of the posterior cortex.

The olfactory cortex is located in the medial temporal lobe near the tip and involves the uncus. It receives its input from the olfactory bulb at the base of the frontal lobe.

Memory in the temporal lobes and associated disorders

Along with the limbic system (pp. 49–51), many regions of the temporal lobes are critical for normal learning and retention (see Fig. 3.6, p. 49). Lesions of the left temporal lobe disrupt verbal memory and right temporal lobe lesions interfere with memory for many different nonverbal tasks (Tranel and Damasio, 2002; Jones-Gotman, Zatorre, Olivier, et al., 1997; Markowitsch, 2000). In some cases lesions of the temporal neocortex may impair learning and retention by disconnecting the hippocampus from cortical input (Jones-Gotman et al., 1997).

Cortical regions appear to be organized for long-term storage of memories (Fuster, 1999). Awake patients undergoing brain surgery report vivid auditory and visual recall of previously experienced scenes and episodes upon electrical stimulation of the exposed temporal lobe cortex (Gloor et al., 1982; Penfield, 1958). Nauta (1964) speculated that these memories involve widespread neural mechanisms and that the temporal cortex and, to a lesser extent, the occipital cortex play roles in organizing the discrete components of memory for orderly and complete recall. Information involving each modality appears to be stored in the association cortex adjacent to its primary sensory cortex (A.R.

Damasio, Damasio, and Tranel, 1990; Killackey, 1990; A. Martin, Haxby, Lalonde, et al., 1995). Thus, retrieval of visual information is impaired by lesions of the visual association cortex of the occipital lobe, impaired retrieval of auditory information follows lesions of the auditory association cortex of the temporal lobe, and so on. Some patients with cortical lesions have shown selective deficits in retrieving highly specific types of information, such as items in certain categories but not others (Gabrieli, 1998; A. Martin et al., 1997). This finding suggests that cortical representation of knowledge is highly organized. Loss of facts, knowledge of objects, and meaning of words have been reported with selective damage to the inferolateral temporal gyri of one or both temporal lobes, with sparing of the hippocampal and parahippocampal gyri (K.S. Graham and Hodges, 1997). Thus, while the hippocampus and medial limbic structures are involved in the processing of newly learned information that has not yet consolidated, the temporal cortex appears to house old learned information.

A variety of emotional disorders are common with temporal as well as limbic lesions, including anxiety, delusions, and mood disorders (Heilman, Blonder, et al., 2000; Trimble et al., 1997). Abnormal electrical activity of the brain associated with *temporal lobe epilepsy* (*TLE*) typically originates within the temporal lobe. Specific problems associated with temporal lobe epilepsy include alterations of mood, obsessional thinking, changes in consciousness, hallucinations, and perceptual distortions in all sensory modalities including pain, and stereotyped, often repetitive and meaningless motor behavior that may comprise quite complex activities (Filley, 1995; Schomer, O'Connor, et al., 2000; G.J. Tucker, 2002). Other names for these disturbances are *psychomotor epilepsy* and *psychomotor* or *complex partial seizures* (Pincus and Tucker, 2003; see p. 322 for a fuller discussion of the cognitive and personality/emotional features of temporal lobe epilepsy).

THE PRECENTRAL (ANTERIOR) CORTEX: FRONTAL LOBE DISORDERS

In the course of the brain's evolution, the frontal lobes developed most recently to become its largest structures. It was only natural for early students of brain function to conclude that the frontal lobes must therefore be the seat of the highest cognitive functions. Thus, when Hebb reported in 1939 that a small series of patients who had undergone surgical removal of frontal lobe tissue showed no loss in IQ score on a standard intelligence test, he provoked a controversy. In his comprehensive review of the literature on the psychological consequences of frontal lobe lesions, Klebanoff (1945) noted the seemingly unresolvable discrepancies between studies reporting on the cognitive status of patients with frontal lobe lesions. He found that since Fritsch and Hitzig ([1870] 1969) first reported mental deterioration in patients with traumatic frontal lesions, more authors had described cognitive deficits in patients with frontal lobe damage than denied the presence of such deficits in their patients.

The large number of World War II missile wound survivors and the popularity of psychosurgery on the frontal lobes for treatment of psychiatric disorders in the 1940s and 1950s ultimately provided enough cases of frontal brain damage to eliminate speculative misconceptions about frontal lobe functions. We know now that many cognitive and social behaviors may be disrupted by frontal lobe damage. Hebb's observations were limited both by his use of structured tests that primarily measured old learning and well-established skills rather than abilities to solve unfamiliar problems or exercise judgment, for example, and by his choice of summed IQ scores for his comparison criteria rather than subtest scores or qualitative aspects of the patient's performance. It may be that the frontal lobes are the closest neural representation of popular notions of "intelligence" or Spearman's *g* because of their important role in contributing to success on diverse cognitive tasks (J. Duncan et al., 2000). The three major divisions of the frontal lobes differ functionally although each is involved more or less directly with behavior output (Fig. 3.17; E. Goldberg, 1990; Pandya and Barnes, 1987; Stuss and Benson, 1986; Stuss, Eskes, and Foster, 1994; see H.C. Damasio, 1991, for a detailed delineation of the anatomy of the frontal lobes and Pandya and Yeterian, 1998, for diagrams of interconnections within the frontal lobes and with other regions of the brain).

Precentral Division

The most posterior, precentral, division lies in the first two ridges in front of the central sulcus. This is the primary motor cortex, which mediates movement (not isolated muscles) and as such has important connections with the cerebellum, the basal ganglia, and the motor divisions of the thalamus. Lesions here result in (weakness) *paresis* or paralysis of the corresponding body parts (Eslinger and Reichwein, 2001; Mesulam, 2000b). Inside the fold of the frontal and temporal lobes formed by the Sylvian fissure is the primary taste cortex (Pritchard, 1999).

Premotor Division

Situated just anterior to the precentral area, the *premotor* and *supplementary motor* areas have been iden-

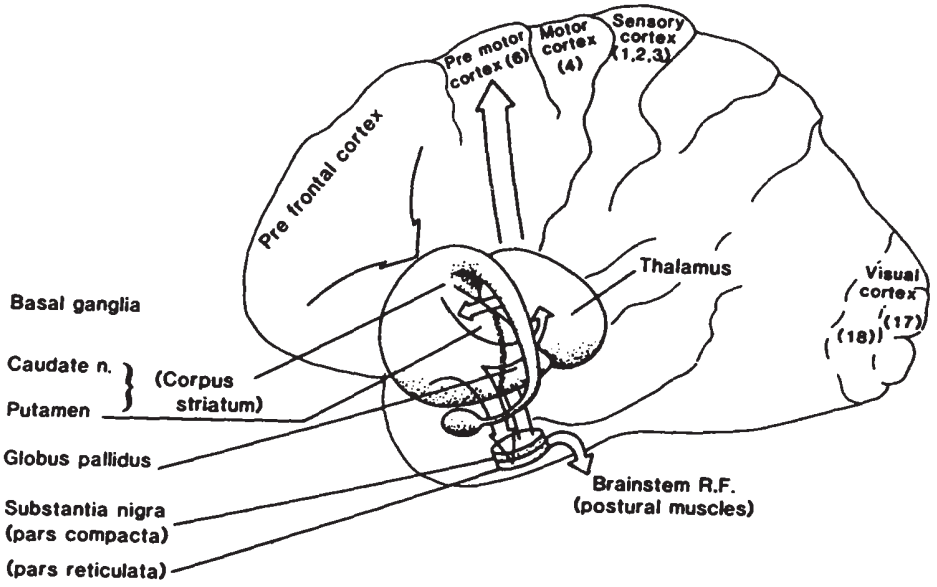

FIGURE 3.17 The three subdivisions of the frontal lobes with their most prominent subcortical connections indicated. (From J.F. Stein, 1985)

tified as the site in which the integration of motor skills and learned action sequences takes place (A.R. Damasio and Anderson, 2003; Eslinger and Geddes, 2001; Kolb and Whishaw, 1996; Nilsson et al., 2000). Premotor areas participate in afferent/efferent loops with the basal ganglia and thalamus; the looped interconnections are probably targeted to specific sites on both cortical and subcortical structures (Middleton and Strick, 2001; Passingham, 1997). Lesions here do not result in loss of the ability to move, but rather disrupt the integration of the motor components of complex acts, producing discontinuous or uncoordinated movements and impaired motor skills, and may also affect limb strength (Jason, 1990; Mesulam, 2000b). The supplemental motor area appears to mediate preparatory arousal to action at a preconscious stage in the generation of movement; thus lesions in this area may disrupt movement initiation as well (J.W. Brown, 1987). The ability to copy rapidly executed hand movements may be associated with right- or left-sided lesions in this area (Jason, 1986). Left premotor cortex has been implicated in the motor planning aspect of rapid word generation (Condon et al., 1997).

In the left hemisphere, lesions in the portion of the motor association area that mediates the motor organization and patterning of speech may result in speech disturbances that have as their common feature disruption of speech production with intact comprehension. These deficits may range in severity from total suppression of speech (D. Caplan, 1987; Eslinger and Reichwein, 2001; Jonas, 1987) to mild slowing and reduced spontaneity of speech production (Stuss and Benson, 1984, 1990). Other alterations in speech production may include stuttering, poor or monotonous tonal quality, or diminished control of the rate of speech production. Luria (1966, 1970; see also Dronkers et al., 2000) described a motor pattern apraxia of speech (*oral apraxia*) which may include difficulty imitating simple oral gestures in connection with lesions in this area, although this condition can also occur with somewhat more posterior lesions (Tognola and Vignolo, 1980). Patients with this condition display disturbances in organizing the muscles of the speech apparatus to form sounds or in patterning groups of sounds into words. This may leave them incapable of fluent speech production, although their ability to comprehend language is not necessarily impaired. Closely associated with this *supplemental motor area* mediating speech mechanisms are those involved in the initiation and programming of fine hand movements (Jonas, 1987; Vuilleumier, 2001), so it is not surprising that severe agraphia can follow lesions here (D. Caplan, 1987; Roeltgen, 1997). The anterior language center, *Broca's area,* is lower on the lateral slope of the prefrontal cortex (Benson, 1988, 1993; Broca, 1865, in Berker, Berker, and Smith, 1986; A.R. Damasio and Geschwind, 1984) (see Fig. 3.1, p. 42). It serves as "the final common path for the generation of speech impulses" (Luria, 1970, p. 197). Lesions to this area give rise to *Broca's,* or *efferent, motor aphasia* (see Chapter 2, Table 2.1, p. 33), which involves defective symbol formulation as well as a breakdown in the orderly production of speech. Ver-

bal learning can be compromised by lesions in this region (Risse et al., 1984).

Lesions in corresponding areas on the right may contribute to fragmented or piecemeal *modus operandi,* reflected most clearly in impairments of perceptual organization and of planning (see example, p. 134). *Expressive amusia* or *avocalia* (inability to sing) has been seen with lesions of either frontal lobe but occurs most often in association with aphasia when lesions are on the left (Benton, 1977a; Botez and Botez, 1996). Other activities disturbed by lesions involving the right premotor area include diminished grip strength for both men and women (Leonard et al., 1988) and *motor impersistence* (reduced ability to maintain a motor act, such as eye closure or tongue protrusion) (Ben-Yishay, Diller, Gerstman, and Haas, 1968; Eslinger and Reichwein, 2001; Kertesz, Nicholson, Cancelliere, et al., 1985).

Prefrontal Division

The cortex and underlying white matter of the frontal lobes is the site of interconnections and feedback loops between the major sensory and motor systems, linking and integrating all components of behavior at the highest level (Fuster, 1995; Kolb and Whishaw, 1996; Middleton and Strick, 2001a,b; Pandya and Barnes, 1987). Pathways carrying information about the external environment from the posterior cortex—of which about 60% comes from the heteromodal association cortex and only 25% from secondary association areas (Strub and Black, 1988)—and information about internal states from the limbic system converge in the anterior portions of the frontal lobes, the *prefrontal cortex.* Thus, the anterior frontal lobes are where already correlated incoming information from all sources—external and internal, conscious and unconscious, memory storage and visceral arousal centers—is integrated and enters ongoing activity (Dubois, Pillon, et Sirigu, 1994; Fuster, 2003). "The human prefrontal cortex attends, integrates, formulates, executes, monitors, modifies, and judges all nervous system activities" (Stuss and Benson, 1987). Perecman (1987) refers to it as "the seat of consciousness." G.A. Miller and his colleagues (1960) called it the "organ of civilization," a definition that speaks to the fragility of complex behavioral patterns and socially acquired attitudes in the damaged brain (Eslinger, 1998b; E. Goldberg and Bilder, 1987) and to its central role in the normal experience of self (Frith, 1998; Stuss, 1991b). In modern jargon, E. Goldberg (2001) refers to it as "the brain's CEO."

Lesions of the frontal lobes tend not to disrupt cognitive functions as obviously as do postcentral lesions. Rather, frontal lobe damage may be conceptualized as disrupting reciprocal relationships between the major functional systems—the sensory systems of the posterior cortex; the limbic-memory system with its interconnections to subcortical regions involved in arousal, affective, and motivational states; and the effector mechanisms of the motor system. Nauta (1971) characterized frontal lobe disorders as "derangement of behavioral programming." Fuster (1994) drew attention to a breakdown in the temporal organization of behavior with frontal lobe lesions, resulting both in deficient integration of immediate past experience (situational context) with ongoing activity and in defective planning. Frontal lobe disorders involve *how* a person responds, which can certainly affect the "*what,*" the content of the response. Frontal lobe patients' failures on test items are more likely to result from an inappropriate approach to problems than from lack of knowledge or from perceptual or language incapacities *per se.* For example, patients with frontal lobe damage (almost always involving the right frontal lobe) occasionally will call item one on the Hooper Visual Organization Test "a duck" (see Chapter 10, Fig. 10.19, p. 400) and demonstrate that they understand the instructions (to figure out what the cut-up drawings would represent if put together) by answering items two and three correctly. In such cases, the completed "flying duck" shape of the top piece in item one appears to be a stronger stimulus than the directions to combine the pieces. These patients demonstrate accurate perception and facility and accuracy in naming or writing but get stalled in carrying out all of an intentional performance—in this case by one strong feature of a complex stimulus. Others (e.g., Luria, 1966; Ochsner and Schacter, 2000; Stuss and Benson, 1984, 1987; Walsh and Darby, 1999) have called attention to the dissociation between what these patients say or appear to see or comprehend and what they do or seem to feel.

Prefrontal subdivisions

The prefrontal portion of the frontal lobes is also subdivided, with different functions (or rather, different behavioral disorders associated with specific lesion sites) mediated in different cortical regions (Fuster, 1995; Pandya and Barnes, 1987; Stuss and Benson, 1984; Walsh and Darby, 1999; Walsh, 1991). Typically, three major subdivisions are identified, each with connections to different thalamic nuclei (Brodal, 1981; Mayes, 1988; Pribram, 1987) as well as interconnections with other cortical and subcortical structures. Most of these are two-way connections with neural pathways projecting both to and from prefrontal cortex (Strub and Black, 2000).

Defects in the control, regulation, and integration of cognitive activities tend to predominate in patients with *dorsolateral* lesions, i.e., when the lesion is on the top or outer sides—the convexity—of the frontal lobes. According to Goldman-Rakic (1998), the dorsolateral prefrontal cortex has a generic function—"on-line" processing of information or working memory in the service of a wide range of cognitive functions. This process occurs through multiple neural circuits to relevant sensory, motor, and limbic areas that integrate attention, memory, motor, and possibly affective dimensions of behavior. The *medial regions* (also called *cingulate* or *limbic cortex*) are located on the sides of the lobes between the hemispheres. Lesions here or subcortical lesions that involve pathways connecting the cortex between and just under the hemispheres with the drive and affective integration centers in the diencephalon are most apt to affect emotional and social behavior by dampening or nullifying altogether capacities for emotional experience and for drive and motivation (Barrash et al., 2000; A.R. Damasio and Van Hoesen, 1983). The degree to which emotions and drive are compromised tends to be highly correlated, suggesting that affect and drive are two sides of the same coin: Frontally damaged patients with loss of affective capacity will have low drive states, even for such basic needs as food or drink; with only mildly muted emotionality, life-sustaining drives will remain intact but sexual interest may be reduced, along with interest in initiating and maintaining social or vocational activities.

The *orbital* (*basal, ventral*) frontal cortex plays a key role in impulse control and in regulation and maintenance of set and of ongoing behavior (P. Malloy, Bihrle, et al., 1993; Stuss, Benson, Kaplan, et al., 1983). In healthy persons this region is involved in the expression of aggressive behavior (Pietrini et al., 2000). Damage here can give rise to disinhibitions and impulsivity, with such associated behavior problems as aggressive outbursts and sexual promiscuity (Eslinger, 1999a; Grafman, Schwab, et al., 1996). Lesions here also can disrupt a patient's ability to be guided by future consequences of their actions (Bechara, Damasio, Damasio, and Anderson, 1994) and lead to poor decisions (Bechara, Damasio, Damasio, and Lee, 1999). Left-sided traumatic damage to this area has been associated with prolonged unconsciousness (Salazar, Martin, and Grafman, 1987). Frontal lobe disturbances thus tend to have repercussions throughout the behavioral repertoire (Luria, 1973a; Stuss, Gow, and Hetherington, 1992).

Because the structures involved in the primary processing of olfactory stimuli are situated at the base of the frontal lobes, odor discrimination is affected by orbitofrontal lesions—in both nostrils when the lesion is on the right but only in the left nostril with left-sided lesions (Eslinger, Damasio, and Van Hoesen, 1982; Zatorre and Jones-Gotman, 1991). Thus, impaired odor detection frequently accompanies the behavioral disorders associated with orbitofrontal damage (Eslinger, 1999b; P. Malloy, Bihrle, et al., 1993; Stuss, 1993; Varney and Menefee, 1993). Diminished odor discrimination may also occur with lesions in the limbic system nuclei lying within the temporal lobes and with damage to temporal lobe pathways connecting these nuclei to the orbitofrontal olfactory centers. This effect typically appears with right but not left temporal pathway lesions (Martinez et al., 1993). Temporal lobe connections to the orbitobasal forebrain are further implicated in cognitive functioning. Patients with lesions here are similar to patients with focal temporal lobe damage in displaying prominent modality-specific learning problems along with some less severe diminution in reasoning abilities (Salazar, Grafman, Schlesselman, et al., 1986).

Lateralization of frontal functions

Although lateralization of cognitive activity is less frequently described in patients with frontal damage, many of the usual distinctions between left and right hemisphere functions obtain here too. As noted above, decreased verbal fluency and impoverishment of spontaneous speech tend to be associated with left frontal lobe lesions, although mildly depressed verbal fluency can occur with right frontal lobe lesions (R.W. Butler, Rorsman, et al., 1993; Frisk and Milner, 1990; Laine, 1988; Perret, 1974). Other verbal problems associated with left anterior damage involve the organization of language and include disrupted and confused narrative sequences, simplified syntax, incomplete sentences and clauses, descriptions reduced to single words and distorted by misnaming and perseveration, and a general impoverishment of language with mutism as the extreme case (M.P. Alexander, Benson, and Stuss, 1989; Kaczmarek, 1984, 1987). Stuss and Benson (1990) emphasize that prefrontal language problems arise from self-regulatory and organizing deficits that are "neither language nor cognitive problems" (p. 43) but are the product of impaired executive functions. Patients with left frontal lesions do poorly in learning sequential manual positions and in generating different finger positions (gestural fluency), although both left and right frontal lesions can compromise the ability to make meaningful gestures, such as the sign for hitchhiking (Jason, 1985a, 1987). Deficits in making spatial analyses, including orientation and rotation problems, can occur with left frontal lesions (Y. Kim et al., 1984) but also may appear with right anterior lesions (e.g., Lezak, 1989).

Constructional deficits have been noted in patients with right frontal lobe lesions who have difficulty with the motor rather than the perceptual components of the task (Benton, 1968). The ability to invent unique designs (design fluency) is depressed with right anterior lesions (Jones-Gotman, 1991a; Jones-Gotman and Milner, 1977). Expressive language problems also affect patients with right frontal damage (Kaczmarek, 1984, 1987). Their narrative responses too may show a breakdown in internal structure related to poor overall organization of the material. Stereotyped expressions are relatively common. The prosodic quality of speech may be muted or lost (Frisk and Milner, 1990). Picture descriptions may be faulty, mostly due to misinterpretations of elements but also of the picture as a whole. Perhaps most important, as it compromises their capacity to adapt to their disabilities, is a tendency for defective evaluation of their condition (Kaczmarek, 1987). Other kinds of impaired evaluations have also been noted in these patients, such as inaccurate estimations of prices (M.L. Smith and Milner, 1984) and of frequency of events (M. L. Smith and Milner, 1988). Stuss and colleagues have stressed the importance of the right frontal lobe in emotional expression, modulation, and appreciation (Shammi and Stuss, 1999; Stuss and Alexander, 1999; Stuss, Gow, and Hetherington, 1992). In addition, the right prefrontal cortex may be a preferential component in self-recognition and self-evaluation (H.P. Keenan et al., 2000).

In recent years several overall differences in cognitive features of the left and right prefrontal lobes have been described. B. Milner and Petrides (1984) suggested that the left prefrontal cortex is important for control of self-generated plans and strategies and the right is important for monitoring externally ordered events. Using different cognitive tasks, E. Goldberg, Podell, and Lovell (1994) found a similar distinction. In particular, they suggest that the left prefrontal system is responsible for guiding cognitive selection by working memory–mediated internal contingencies, while the right prefrontal system makes selections based on external environmental contingencies. While their data support this lateralization in men, women did not show a lateralized effect.

Many investigators have found differential prefrontal cortex involvement based on the type of memory process under consideration. Left prefrontal activation occurs with verbal learning and verbal working memory (Buckner and Tulving, 1995; Nyberg and Cabeza, 2000). A number of studies have shown that the left prefrontal cortex is primarily involved in encoding and the right is preferentially activated during retrieval (Haxby, Ungerleider, Horwitz, et al., 1996; Owen, Milner, et al., 1996; Shallice, Fletcher, Frith, et al., 1994; Tulving, Kapur, Craik, et al., 1994; Ragland, Gur, et al., 2000). However, this dichotomy has been challenged and it is likely that differences in the roles of the left and right hemispheres depend on the particular memory demands as well as the type of stimulus to be learned (Iidaka et al., 2000; S. Kapur et al., 1995; Klingberg and Roland, 1998; A. Martin, Wiggs, and Weisberg, 1997). Mesulam (2000b) notes left/right differences in working memory paralleling the common verbal/spatial lateralization pattern. Autobiographical memory, too, may preferentially engage networks within the right frontotemporal region (G.R. Fink et al., 1996; J.P. Keenan et al., 2000).

Prefrontal cortex and attention

The prefrontal cortex is among the many structures involved in attention. Significant frontal activation takes place during selective attention activities in intact subjects (Mesulam, 2000b; Swick and Knight, 1998). Prefrontal cortex mediates the capacity to make and control shifts in attention (Mirsky, 1989). Luria (1973a) observed that it "*participates decisively in the higher forms of attention,*" for example, in "*raising the level of vigilance,*" in selectivity, and in maintaining a set (see also van Zomeren and Brouwer, 1990). The prefrontal cortex and anterior cingulate appear to be engaged when subjects must concentrate on solving new problems but not when attention is no longer required because the task has become automatic (Passingham, 1997, 1998). Thus attentional functions are frequently impaired with frontal lobe lesions (Luria, 1973a; Stuss and Benson, 1984). These patients may be sluggish in reacting to stimuli, unable to maintain an attentional focus (Stuss, 1993), or highly susceptible to distractions. Vendrell and his colleagues (1995) specifically implicate the right prefrontal cortex as important for sustained attention.

Patients with frontal lesions frequently have difficulty when divided attention is required, such as performing two tasks at once (Baddeley, Della Sala, Papagno, and Spinnler, 1996). Functional neuroimaging studies also support the view that the prefrontal cortex is involved in dual task performance but not when either task is performed separately (D'Esposito et al., 1995). Working memory tasks (those that require temporary storage and manipulation of information in the brain) depend on the frontal lobes (Braver et al., 1997; Dubois, Levy, Verin, et al., 1995; Fuster, 1999; Goldman-Rakic, 1993; Rypma and D'Esposito, 1999; B.E. Swartz et al., 1995).

Problems with both working memory, and short-term memory appear to be due at least in part to the poor ability of frontal patients to withstand interfer-

ence to what they may be attempting to keep in mind, whether from the environment or from their own associations (Fuster, 1985; Kapur, 1988b; Knight and Grabowecky, 2000; Stuss, 1991a; Swick and Knight, 1998). Jonides and Smith (1997) identify two multifaceted components of working memory: one involves temporary storage of information in specific modalities with its component processes (e.g., transformation into other codes, storage, rehearsal) and the other involves the processes treating the (temporarily) stored information, such as time tagging, sequencing, prioritizing, etc.

Left visuospatial inattention can occur with right anterior lesions (Heilman, Watson, and Valenstein, 2003; Mesulam, 2000b; see also Chapter 9, Fig. 9.8, p. 348) but is much less common with frontal than with parietal involvement (Bisiach and Vallar, 1988; Rizzolatti and Camarda, 1987; Vallar and Perani, 1987). Heilman, Watson, and Valenstein (2003) suggest that frontal inattention may be associated with arousal and intentional deficits. Others have interpreted this problem as reflecting involvement with one of the multiple sites in the visuoperceptual network (Mesulam, 2000b; Rizzolatti and Gallese, 1988; S. Stein and Volpe, 1983). Some patients with frontal lesions seem stuporous unless actively stimulated. Others can be so distractible as to be hyperactive. Still other patients with frontal damage may show little or no evidence of attentional disturbances, leaving open to conjecture the contributions of subcortical and other structures in the attention impaired patients.

Prefrontal cortex and memory

Memory disorders have long been associated with prefrontal lesions. However, when carefully examined, these patients typically do not have a disorder of the memory system, but rather they have disorders of one or more functions that facilitate memory.

The phenomenon of frontal amnesia demonstrates how inertia and executive disorders in particular can interfere with cognitive processes (Stuss and Benson, 1984, 1986; Walsh, 1987). Patients with frontal amnesia, when read a story or a list of words, may seem able to recall only a little if any of what they heard and steadfastly assert they cannot remember. Yet, when prompted or given specific questions (such as, "Where did the story take place?" rather than "Begin at the beginning and tell me everything you can remember"), they may produce some responses, even quite full ones, once started. The same patients may be unable to give their age although they know the date, their year of birth, and how to solve formally presented subtraction problems. What they cannot do, in each of these examples, is spontaneously undertake the activity that will provide the answer—in the first case, selecting the requested information from memory and, in the second case, identifying a solution set for the question and acting on it. Not being able to remember to remember (*prospective memory*) creates serious practical problems for these patients—forgetting to go to work, to keep appointments, even to bathe or change clothes as needed (Cockburn, 1996a). Frontal amnesia problems constitute one of the most serious obstacles to the remediation of the behavioral problems associated with frontal lobe damage; for if it does not occur to trainees to remember what they were taught or supposed to do (or not do), then whatever was learned cannot be put to use.

A 35-year-old mechanic sustained compound depressed fractures of the "left frontal bone" with cortical lacerations when a "heavy . . . machine exploded in his face." Following intensive rehabilitation he was able to return home where he assumed household chores and the daytime care of his three-year-old son. He reported that he can carry out his duties if his wife "leaves me a note in the morning of some of the things she wants done, and if she didn't put that down it wouldn't get done because I wouldn't think about it. So I try to get what she's got on her list done. And then there's lists that I make up, and if I don't look at the list, I don't do anything on it."

Two years after the accident and shortly before this interview, this man's verbal performances on the Wechsler tests were mostly within the *average* range excepting a *borderline defective* score on Similarities (which calls on verbal concepts); on the predominantly visual tests his scores were at *average* and *high average* levels. All scores on formal memory testing (Wechsler Memory Scale–Revised) were at or above the mean for his age, and 4 of the 13 listed on the Record Form were more than one standard deviation above the mean.

The frontal lobes facilitate memory in a variety of ways. They provide structure to stimulus encoding (Fletcher et al., 1998). Thus, some of these patients' memory problems may be related to diminished capacity to integrate temporally separated events (Fuster, 1980, 1985), such as difficulty in making recency judgments (B. Milner, 1971; Petrides, 1989), and to poor recall of contextual information associated with what they may remember (impaired source memory) (Janowsky, Shimamura, and Squire, 1989). They may recall a fragment of memory but be unable to situate the memory in its appropriate context for time and place. Patients with frontal lesions tend not to order or organize what they learn, although with appropriate cueing adequate recall can be demonstrated (Jetter et al., 1986), which may account for their proportionately better performances on recognition than on recall formats where retrieval strategies are less needed (Janowsky, Shimamura, Kritchevsky, and Squire, 1989).

The frontal lobes are necessary for criterion setting and monitoring during retrieval of memories, particularly on difficult tasks (Fletcher, Shallice, Frith, et al., 1998; Incisa della Rocchetta and Milner, 1993; Schacter, Norman, and Koustaal, 1998). Failure in these functions can lead to poor recall or false memories (Schacter, 1999a, *passim;* Schacter, Norman, Koustaal, et al., 1998). Stuss and Benson (1987) showed how diminished control can affect the behavior of patients with prefrontal damage: they may be fully aware of what should be done, but in not doing it at the appropriate time, they appear to have forgotten the task (impaired prospective memory) (see also Glisky, 1996).

Patients with lesions in the medial basal region of the frontal lobes or with subcortical lesions in adjacent white matter may suffer a true amnestic condition that is pronounced and often accompanied by spontaneous and florid confabulation (M.P. Alexander and Freedman, 1984; A.R. Damasio, 2001; P. Malloy, Bihrle, et al., 1993; Rapcsak, Kaszniak, Reminger, et al., 1998; Stuss, Alexander, et al., 1978).

A 60-year-old retired teacher who had had a stroke involving the medial basal region of her left frontal lobe complained of back pain due to lifting a cow onto a barn roof. Five days later she reported having piloted a 200-passenger plane the previous day.

Prefrontal cortex and cognitive functions

Cognitive impairment associated with destruction or disconnection of frontal lobe tissue usually does not appear as a loss of specific skills, information, or even reasoning or problem-solving ability (Teuber, 1964). In fact, patients with frontal lobe lesions often do not do poorly on those formal ability tests in which another person directs the examination, sets the pace, starts and stops the activity, and makes all the discretionary decisions (Brazelli et al., 1994; Lezak, 1982a; Stuss, Benson, Kaplan, et al., 1983). The closed-ended questions of common fact and familiar situations and the well-structured puzzles with concrete solutions that make up standard tests of cognitive abilities are not likely to present special problems for many patients with frontal lobe injuries (Tranel, 2003). Perseveration or carelessness may depress a patient's scores somewhat but usually not enough to lower them significantly. Cognitive defects associated with frontal lobe damage tend to show up most clearly in the course of daily living and are more often observed by relatives and co-workers than by a medical or psychological examiner in a standard interview. Common complaints about such patients concern apathy, carelessness, poor or unreliable judgment, poor adaptability to new situations, and blunted social sensibility (Eslinger, Grattan, and Geder, 1995; Lezak, 1989; Lishman, 1997; R.S. Parker, 2001). However, these are not cognitive deficits in themselves but defects in processing one or more aspects of behavioral integration and expression.

Frontal lobe syndromes include many behavioral disorders (Grafman and Litvan, 1999; Sohlberg and Mateer, 2001; Stuss and Benson, 1986) which are differentiable both in their appearance and in their occurrence (Burgess and Shallice, 1994; Varney and Menefee, 1993). Patients with prefrontal damage show an information processing deficit that reduces their sensitivity to novel stimuli and may help explain the stimulus-bound phenomenon (Daffner et al., 2000; R.T. Knight, 1984). Difficulty with working memory and impulsivity may interfere with learning or with performing tasks requiring delayed responses (B. Milner, 1971; R.J.J. Roberts and Pennington, 1996). Defective abstract thinking and sluggish response shifts can result in impaired mental efficiency (Janowsky, Shimamura, Kritchevsky, and Squire, 1989; Sohlberg and Mateer, 2001; Stuss and Benson, 1984). Diminished capacity for behavioral or mental flexibility can greatly limit imaginative or creative thinking (Eslinger and Grattan, 1993). It can also constrain volition and adaptive decision making (E. Goldberg and Podell, 2000). These defects may be aspects of *stimulus boundedness* which, in its milder forms, appears as slowing in shifting attention from one element in the environment to another, particularly from a strong stimulus source to a weak or subtle or complex one, or from a well-defined external stimulus to an internal or psychological event. Patients who are severely stimulus-bound may have difficulty directing their gaze or manipulating objects; when the condition is extreme, they may handle or look at whatever their attention has fixed upon as if their hands or eyes were stuck to it, literally pulling themselves away with difficulty. Others, on seeing usable objects (an apple, a fork), may irresistibly respond to them: e.g., eat the apple; go through eating motions with a fork, regardless of the appropriateness of the behavior for the situation—what Lhermitte (1983) termed "utilization behavior." In describing these kinds of behavior defects as "environmental dependency syndrome" and a pathological kind of "imitation behavior," Lhermitte (1986), with his colleagues (1986), called attention to the degree to which these patients are driven by environmental stimuli (see also S. Archibald et al., 2001).

Perseveration, in which patients repeat a movement, or an act or activity involuntarily, often unwittingly, is a related phenomenon, but the stimulus to which they seem bound is one that they themselves generated (E. Goldberg, 2001; E. Goldberg and Bilder, 1987; Hauser, 1999; Na et al., 1999; Sandson and Albert, 1987). Yet

these patients often ignore environmental cues so that their actions are out of context with situational demands and incidental learning is reduced (Vilkki, 1988). They may be unable to profit from experience, perhaps due to insufficient reactivation of autonomic states that accompanied emotionally charged (pleasurable, painful) situations (A.R. Damasio, Tranel, and Damasio, 1990), and thus can only make poor, if any, use of feedback or reality testing (Le Gall, Joseph, and Truelle, 1987; Rolls, 1998; Sohlberg and Mateer, 2001).

With prefrontal damage, a tendency for a dissociation can occur between language behaviors and ongoing activity so that patients are less apt to use verbal cues (such as subvocalization) to direct, guide, or organize their ongoing behavior with resultant perseveration, fragmentation, or premature termination of a response (K.H. Goldstein, 1948; Luria and Homskaya, 1964; Shallice, 1982; Vilkki, 1988). However, fragmentation or disorganization of premorbidly intact behavioral sequences and activity patterns appears to be the underlying problem for these patients (Truelle, Le Gall, et al., 1995; M.F. Schwartz et al., 1993; see also Grafman, Sirigu, et al., 1993). Activities requiring abilities to make and use sequences or otherwise organize activity are particularly prone to being compromised by prefrontal lesions (Canavan et al., 1989; Messerli et al., 1979; Stuss and Benson, 1984; Zalla et al., 2001), possibly due to reduced ability to refocus attention to alternative response strategies (Della Malva et al., 1993; Godefroy and Rousseaux, 1997; B. Levine, Stuss, Milberg, et al., 1998; Robbins, 1998; Satish et al., 1999). For example, copying hand position sequences, especially when rapid production is required, is affected by frontal lobe lesions (Jason, 1986; Truelle, Le Gall, et al., 1995; Petrides, 1989). Thus planning—which Goel and Grafman refer to as "anticipatory sequencing"—and problem solving, which require intact sequencing and organizing abilities, are frequently impaired in these patients (D. Carlin et al., 2000; Goel, Grafman, Tajik, et al., 1997; Goel and Grafman, 2000; Koechlin et al., 1999; R.G. Morris, Miotto, Feigenbaum, et al., 1997; Pillon 1981b; Shallice and Burgess, 1991a; Vilkki, 1988). Defective self-monitoring and self-correcting are common problems with prefrontal lesions (Stuss and Benson, 1984; Walsh and Darby, 1999).

Even when simple reaction time is intact, responses to complex tasks may be slowed (Le Gall, Joseph and Truelle, 1987). The frontal lobes have also been implicated in defects of time sense including recency judgments and time-span estimations and, in patients with bilateral frontal lobe damage, orientation in time (Benton, 1968; M.A. Butters, Kasniak, et al., 1994; B. Milner, Corsi, and Leonard, 1991). These patients may make erroneous and sometimes bizarre estimates of size and number (Shallice and Evans, 1978). Practical and social judgment is frequently impaired. With all of these impediments to cognitive competency, it follows that patients with frontal lobe lesions show little of the imagination or innovative thinking essential to creativity (Zangwill, 1966).

Behavior problems associated with prefrontal damage

Practical and social judgment problems are frequently observed in patients with prefrontal damage (Dimitrov et al., 1996). In fact, social disability is often the most debilitating feature of these patients (Eslinger, Grattan, and Geder, 1995; Lezak, 1989; Lezak and O'Brien, 1988, 1990; see also Macmillan's, 2000, collection of stories, reports, and observations of Phineas Gage). Behavior disorders associated with prefrontal damage tend to be supramodal. Similar problems may occur with lesions involving other areas of the brain, but in these instances they are apt to be associated with specific cognitive, sensory, or motor disabilities. The behavioral disturbances associated with frontal lobe damage can be roughly classified into five general groups with considerable overlap.

1. *Problems of starting* appear in decreased spontaneity, decreased productivity, decreased rate at which behavior is emitted, or decreased or lost initiative. In its milder forms, patients lack initiative and ambition but may be able to carry through normal activities quite adequately, particularly if these activities are familiar, well-structured, or guided.

A 37-year-old experienced railway brakeman was slammed onto his forehead when his train suddenly lurched. After a few weeks' recuperation he returned to his job and continued to work satisfactorily. However, he had ceased to engage in activities with his family, no longer made weekend or social plans, and spent all of his leisure time playing the same computer game. His interest in food was negligible and he had ceased initiating sexual activity.

More severely affected patients are apt to do little beyond routine self-care and home activities. To a casual or naive observer, and often to their family and close associates, these patients appear to be lazy. Many can "talk a good game" about plans and projects but are actually unable to transform their words into deeds. An extreme dissociation between words and deeds has been called *pathological inertia* which can be seen when a frontal lobe patient describes the correct response to a task but never acts it out. Severe problems of starting appear as apathy, unresponsiveness, or mutism, and

often are associated with superior medial damage (Eslinger, Grattan, and Geder, 1995; Sohlberg and Mateer, 2001).

A railway crossing accident severely injured a 25-year-old schoolteacher who became totally socially dependent. She ate only when food was set before her so she could see it. The only activities she initiated were going to the bathroom and going to bed to sleep, both prompted by body needs. Yet on questioning she reported plans for Christmas, for a party for her aunt.

2. *Difficulties in making mental or behavioral shifts,* whether they are shifts in attention, changes in movement, or flexibility in attitude, come under the heading of *perseveration* or *rigidity.* Perseveration refers specifically to repetitive prolongation or continuation of an act or activity sequence, or repetition of the same or a similar response to various questions, tasks, or situations. In the latter sense it may be described as stereotypy of behavior. Perseveration may also occur with lesions of other lobes, but then it typically appears only in conjunction with the patient's specific cognitive deficits (E. Goldberg and Tucker, 1979; Walsh and Darby, 1999). In frontal lobe patients, perseveration tends to be *supramodal*—to occur in a variety of situations and on a variety of tasks. Perseveration may sometimes be seen as difficulty in suppressing ongoing activities or attention to prior stimulation. On familiar tasks it may be expressed in repetitive and uncritical perpetuation of a response that was once correct but becomes an uncorrected error under changed circumstances or in continuation of a response beyond its proper end point. Perseveration may occur as a result of lesions throughout the frontal lobes but particularly with dorsolateral lesions (Eslinger, Grattan, and Geder, 1995; Walsh, 1991). Frontal lobe patients may exhibit rigidity in their behavior and thinking without perseveration. Since behavioral and attitudinal patterns of rigidity characterize some neurologically intact people, rigidity alone does not give sufficient grounds for suspecting frontal lobe damage.

3. *Problems in stopping*—in braking or modulating ongoing behavior—show up in impulsivity, overreactivity, disinhibition, and difficulties in holding back a wrong or unwanted response, particularly when it may either have a strong association value or be part of an already ongoing response chain. They have difficulty delaying gratification of reward. These problems frequently come under the heading of "loss of control," and these patients are often described as having "control problems." The lesion is often orbital (Bechara, Damasio, and Damasio, 2000; Eslinger et al., 1995).

4. *Deficient self-awareness* results in an inability to perceive performance errors, to appreciate the impact one makes on others, to size up a social situation appropriately, and to have empathy for others (Eslinger, Grattan, and Geder, 1995; Prigatano, 1991c; Prigatano and Schacter, 1991, *passim;* Schacter, 1990b; Stuss, Gow, and Hetherington, 1992). When frontal damage occurs in childhood, the social deficits can be profound and may include impairments in acquiring social conventions and moral reasoning (S.W. Anderson, Bechara, Damasio, et al., 1999; S.W. Anderson, Damasio, Tranel, and Damasio, 2000). Defective self-criticism is associated with tendencies of some frontal lobe patients to be euphoric and self-satisfied, to experience little or no anxiety, and to be impulsive and unconcerned about social conventions. The very sense of self—which everyday experience suggests is intrinsic to human nature—turns out to be highly vulnerable to frontal lobe damage (Stuss, 1991b; Stuss and Alexander, 2000). Failure to respond normally to emotional and social reinforcers may be a fundamental deficit leading to inappropriate behavior (Rolls, Hornak, Wade, and McGrath, 1994). Impaired self-awareness and social behavior often result from lesions of the orbital cortex and related limbic areas (Sarazin et al., 1998).

A 38-year-old former truck driver and athlete sustained a frontal injury in a motor vehicle accident. Although his cognitive test scores (on Wechsler ability and memory tests) eventually improved to the *average* range, he was unable to keep a job. Repeated placements failed because he constantly talked to coworkers, disrupting their ability to work. Eventually he was tried in a warehouse job that would take advantage of his good strength and physical abilities and put limited demands on cognitive skills and social competence. However, he wanted to show his co-workers that he was the best by loading trucks faster than anyone else. His speed was at the expense of safety. When he could not be persuaded to use caution, he was fired.

5. *A concrete attitude* or loss of the abstract attitude (K. Goldstein, 1944, 1948) is also common among patients with frontal lobe damage. This appears in an inability to dissociate oneself from one's immediate surrounds in a literal attitude in which objects, experiences, and behavior are all taken at their most obvious face value. The patient becomes incapable of planning and foresight or of sustaining goal-directed behavior. This defect, which is also identified as loss or impairment of abstract attitude, is not the same as impaired ability to form or use abstract concepts. Although many patients with frontal lobe lesions do have difficulty handling abstract concepts and spontaneously generate only concrete ones, others retain high-level conceptual abilities despite a day-to-day literal-mindedness and loss of perspective.

CLINICAL LIMITATIONS OF FUNCTIONAL LOCALIZATION

> Symptoms must be viewed as expressions of disturbances in a system, not as direct expressions of focal loss of neuronal tissue.
>
> *A. L. Benton, 1981*

A well-grounded understanding of functional localization strengthens the clinician's diagnostic capabilities so long as the limitations of its applicability in the individual case are taken into account. Common patterns of behavioral impairment associated with such well-understood neurological conditions as certain kinds of cerebrovascular accidents tend to involve the same anatomical structures with predictable regularity. For example, stroke patients with right arm paralysis due to a lesion involving the left motor projection area of the frontal cortex will generally have an associated Broca's (motor or expressive) aphasia. Yet, the clinician will sometimes find behavioral disparities between patients with cortical lesions of apparently similar location and size: some ambulatory stroke victims whose right arms are paralyzed are practically mute; others have successfully returned to highly verbal occupations. On the other hand, aphasics may present with similar symptoms, but their lesions vary in site or size (De Bleser, 1988; Basso, Capitani, Laiacona, and Zanobio, 1985). In line with these clinical observations, cortical mapping by electrode stimulation (Ojemann, 1979) and neuroimaging techniques (Mazziota, Toga, et al., 1997) demonstrates a great deal of interindividual variability in cortical patterning. Examples from functional imaging studies show that many different areas of the brain may be engaged during a cognitive task (see Frackowiak, Friston, Frith, et al., 1997, *passim;* Gazzaniga, 2000a, *passim*). For even the relatively simple task of telling whether words represent a pleasant or unpleasant concept, the following areas of the brain showed increased activation: left superior frontal cortex, medial frontal cortex, left superior temporal cortex, posterior cingulate, left parahippocampal gyrus, and left inferior frontal gyrus (K.B. McDermott, Ojemann, et al., 1999).

Other apparent discontinuities between a patient's behavior and neurological status may occur when a pattern of behavioral impairment develops spontaneously and without physical evidence of neurological disease. In such cases, "hard" neurological findings (e.g., such positive physical changes on neurological examination as primitive reflexes, unilateral weakness, or spasticity) or abnormal laboratory results (e.g., protein in the spinal fluid, brain wave abnormalities, or radiological anomalies) may appear in time, for instance, as a tumor grows or as arteriosclerotic changes block more blood vessels. Occasionally a suspected brain abnormality may be demonstrated only on postmortem examination, and even then correlative tissue changes may not always be found (A. Smith, 1962a). Moreover, well-defined brain lesions have shown up on neuroimaging (Chodosh et al., 1988) or at autopsy of persons with no symptoms of brain disease (Crystal, Dickson, et al., 1988; Phadke and Best, 1983).

The uncertain relation between brain activity and human behavior obligates the clinician to exercise care in observation and caution in prediction, and to take nothing for granted when applying the principles of functional localization to diagnostic problems. However, this uncertain relation does not negate the dominant tendencies to regularity in the functional organization of brain tissue. Knowledge of the regularity with which brain–behavior correlations occur enables the clinician to determine whether a patient's behavioral symptoms make anatomical sense, to know what subtle or unobtrusive changes may accompany the more obvious ones, and to guide the neurosurgeon or neuroradiologist in further diagnostic procedures.