CONTENTS

CHAPTER ONE

BEHAVIOR AND THE BRAIN

Human behavior has an enduring appeal. Who among us has not reflected from time to time on how it is that a memory is formed, a sentence produced, or an emotion experienced? What is the origin of the thoughts and feelings that seem so distinctively to characterize the human species? Despite the enormous interest of this subject, however, our knowledge of human behavior is remarkably limited. The principle that the brain is the source of behavior has been acknowledged—with some notable exceptions—since the time of Hippocrates in ancient Greece, but the study of this relatively small organ encased in the skull presents challenges like none other in human biology. Many scientific investigators are deterred by the extraordinary complexity of brain-behavior relationships and, thus, select other areas of inquiry in which meaningful advances—and research grants—are assumed to be more easily attainable. Much of the formal study of behavior is descriptive, and even at this level there are formidable difficulties in the reliable characterization of the observed phenomena. Correlating the vast expanse of human behavior with the intricate neurobiology of the brain in health and disease is still more imposing. This state of relative ignorance is particularly regrettable since a better understanding of behavior could provide limitless benefits both in enhancing the achievements of our species and in reducing its destructiveness. Indeed, a more complete view of behavior as a function of the brain would have important implications for every realm of human activity.

By way of introduction to the core information presented in this book, it will be useful first to consider some philosophical and historical background that influences the study of behavior. Then follows a discussion of selected features of brain anatomy that pertain to neurobehavioral function in general. A brief digression into the intriguing but discredited area of phrenology is then presented as an illustration of the perils of simplistic thinking. Finally, we consider behavioral neurology and its unique viewpoint, hoping to demonstrate how knowledge of brain structure and function is critical to a comprehensive understanding of human behavior.

The Mind-Brain Problem

Traditionally, philosophers have taken a primary role in considering the phenomena of human behavior. The introspective method of thinking about one's own thoughts and feelings was the sole available technique throughout most of human history. Scientific investigation of how and why people act as they do has a rather short history. Only in recent times has there been the development of a systematic empirical approach to the study of behavior, first with the rise of psychology in the nineteenth century (James 1890), and then with the explosive growth of neuroscience in the twentieth (Corsi 1991). These two traditions can be seen as "top down" and "bottom up" to signify their different approaches, and both have made major contributions to our understanding of behavior. Yet it hardly need be stated that these empirical endeavors have not laid to rest ancient philosophical issues. Science has by no means provided answers to all questions about the nature of the mind, and some would maintain that it never can (Horgan 1994). Biology can, however, provide provocative information with which to explore these issues. Although it may seem imprudent for a clinical neuroscientist to indulge in the discussion that follows, there is good reason to suppose that old philosophical problems can be more clearly addressed in the light of new biological knowledge (Young 1987).

One of the oldest and most difficult questions in philosophy is that of the relation of mind to body, commonly known as the mind-body problem. Human beings can reasonably assume that there exists, by virtue of daily experience, a conscious mind and, because of equally evident physical realities, an entity known as the body. Of all body parts, it is also apparent that the brain very likely has the most to do with the mind, and the issue is therefore more precisely called the mind-brain problem. The difficulty arises when one realizes that mental states are clearly subjective, whereas the brain is an objective reality. Consciousness, to most people an obvious, albeit mysterious, human characteristic, does not readily appear to spring from the physical object we recognize as the brain. Many question whether a collection of nerve cells and chemicals can explain the ineffable phenomenon of consciousness, which is often equated with or regarded as akin to such concepts as the soul or spirit. As the philosopher John Searle bluntly poses the mind-brain problem: "How, for example, could this grey and white gook inside my skull be conscious?" (Searle 1984, 15). Consciousness does indeed appear to be the most mystifying feature of the human mind, and establishing it as a property of the brain is by no means straightforward.

Two fundamental solutions have dominated philosophical inquiry into this dilemma. For the sake of simplicity, these may be termed dualism and materialism. Dualism, most notably propounded by René Descartes in the seventeenth century, holds that mind and brain are independent; the famous *Cogito ergo sum* ("I think, therefore I am") asserts the primacy of mind over matter (Descartes 1637) and implies that mental activities are divorced from physical events. Descartes did imagine there to be a point of intersection between the mind and the body and suggested the unpaired pineal gland as the site where the mind receives sensory traffic and acts upon the brain. But his steadfast separation of the immaterial mind from the material brain has exerted enormous influence for hundreds of years.

Materialism, advanced in various ways by thinkers as diverse as John Locke, Bertrand Russell, and Francis Crick, contends in general that mind and body are inseparable; as a result, mental events are nothing more than the expression of the brain's physical activities. Advocates of this "identity theory" argue that the Cartesian division between mental and physical substances is no more than an assertion, in the trenchant phrase of Gilbert Ryle, that there exists a "ghost in the machine" (Ryle 1949). An extreme variant of materialism is B. F. Skinner's behaviorism, an influential movement in twentieth-century American psychology emphasizing the manipulation of behavior by environmental conditions (Skinner 1971), and which, in effect, holds the concept of mind to be irrelevant to the scientific study of behavior.

The mind-brain problem continues to be pursued with vigor. Among modern philosophers who have continued the debate are Karl Popper (Popper and Eccles 1977), an advocate of dualist interactionism, and those who reject dualism, such as Searle (1984, 2004), Patricia Churchland (1986), and Daniel Dennett (1991). In particular, Churchland and Dennett have embraced neuroscience to the extent that they employ the term "mind-brain" to express complete acceptance of the identity of mind and brain (Churchland 1986; Dennett 1991).

At first glance, the dualist position may seem untenable in view of modern conceptions of neuroscience, but difficult problems remain nonetheless.

Prominent among them is the question of free will. Do people act "freely" or under strictly determined laws of physics and chemistry? This dilemma can be more precisely posed as follows: If the mind and brain are in fact identical, and the actions of the brain can eventually be understood and predicted, then where is an escape from the determinist trap into which materialism must fall? Will not all behavior be governed by physical forces, and thus free will be impossible? Here are other questions to which science has not yet offered an answer. Arguments such as these continue to pose for some a significant obstacle to an enthusiastic acceptance of the materialist position.

Notwithstanding the lingering uncertainties raised by dualism, it is difficult to deny the practical utility of the materialist perspective. Advances in science are no less impressive if they pertain to the neural basis of behavior than if they lead to the discovery of penicillin for the treatment of bacterial pneumonia. It is undeniable that investigation of the brain has informed the understanding of a wide range of human behaviors that were previously inexplicable as physical phenomena. In clinical practice, experience with stroke, dementia, or traumatic brain injury patients leaves little doubt that activities of the mind are reliably and often dramatically affected by physical alterations in the brain. The fact that uncertain or inconsistent relationships between brain and behavior continue to challenge neuroscientists—as they clearly do—is testimony to the extraordinary complexity of the brain, not evidence that such relationships do not exist. Although occasional neuroscientists can be found who adopt a dualist position (Penfield 1975; Popper and Eccles 1977), the great majority find that physical events are providing increasingly complete and satisfying explanations for the activities of the mind. As a heuristic principle, the notion that brain events underlie and are directly correlated with mental events has been remarkably productive to date. Without necessarily presuming to answer the thorny philosophical questions introduced above, neuroscience has nevertheless assembled an impressive body of data indicating that the mind's activities are an unequivocal result of the brain's structure and function. In this sense, scientific advances shed light on old problems that, while not solved, at least seem less imposing.

The position taken in these pages derives from an unhesitating embrace of the methods and findings of neuroscience, and therefore follows in the materialist tradition. Although neuroscience cannot comment on a nonphysical reality, there seems little to gain by postulating a spiritual or mystical essence that cannot be reduced to the level of scientific analysis, especially when such complex human capacities as memory, language, and emotion are already yielding to this kind of inquiry. Indeed, as we will see in Chapter 9, a neurology of religion is a plausible approach to understanding a human experience that has traditionally been seen as representing divine influence (Saver and Rabin 1997). In this respect, the dualist tradition does remind us that many mental events have been interpreted as dissociated from any apparent physical basis. Because the task ahead requires developing an understanding of how these mental events are organized by the brain, Searle has recently proposed the idea of "biological naturalism" as a perhaps more harmonious solution to the mind-brain problem (Searle 2004). Whatever the terminology preferred, the proposition that mental events are in fact *caused* by neurobiological processes in the brain has a compelling rationale and much empirical support (Geschwind 1985; Churchland 1986; Dennett 1991; Searle 2004), and there is ample reason to expect that continuing explication of the brain's operations will also unravel the secrets of the mind.

General Features of Brain Anatomy

Neuroanatomy has been a foundation of behavioral neurology and continues to provide many insights into the neural organization of human behavior. Just as the elemental motor and sensory functions of the nervous system can be understood as emanating from the operations of brain neurons, so too can the myriad phenomena of cognition and emotion (Mesulam 2000; Kandel, Schwartz, and Jessell 2000). This book is concerned with the anatomy of higher functions, and clinically relevant regions of the brain will be covered in the chapters that follow. As an introduction, however, it will be helpful to begin with some general neuroanatomic features of the brain as they bear upon neurobehavioral concepts; complete accounts of neuroanatomy can be found elsewhere (Nauta and Fiertag 1986; Parent 1996; Nolte 2002).

The human brain is a soft, gelatinous collection of gray and white matter encased in the cranium and weighing about 1,400 grams (roughly three pounds) in the adult. Estimates vary, but there may be 100 billion or more neurons in the brain, and at least ten times this number of glial cells (Kandel, Schwartz, and Jessell 2000). As an indicator of the astonishing degree of connectivity between cerebral neurons, each one makes contact with as many as 10,000 others (Kandel, Schwartz, and Jessell 2000). Interneurons, situated between afferent and efferent neurons, constitute by far the largest class of brain neurons, so that the great majority of the brain's neuronal activity is concerned with the processing and transfer of information that occur between sensory input and motor output (Kandel, Schwartz, and Jessell 2000). In other words, a large quantity of nervous tissue lies interposed between the sensory and motor systems to elaborate the phenomena of behavior.

The brain is made up of the cerebrum, the brainstem, and the cerebellum (Figures 1.1 and 1.2). Most important for the higher functions is the cerebrum, which comprises the paired cerebral hemispheres and the diencephalon, the main components of which are the thalamus and hypothalamus. Why the hemispheres are paired, and why they have distinct functional affiliations in contrast

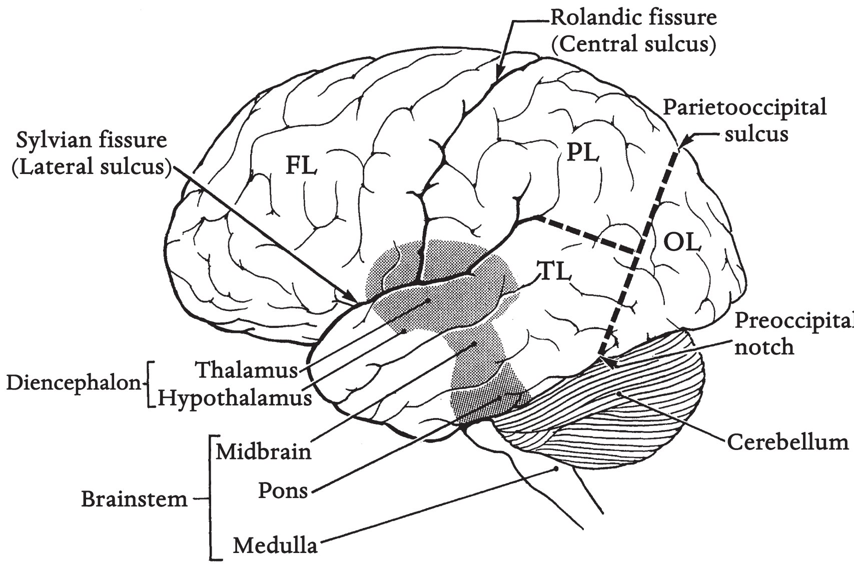

FIGURE 1.1. *Lateral view of the brain depicting lobes and major fissures (FL: frontal lobe; TL: temporal lobe; PL: parietal lobe; OL: occipital lobe).*

to other paired organs in the body such as the lungs and kidneys, are not understood, but the distinct operations of the two cerebral hemispheres will be frequently emphasized in this book. The hemispheres are folded into ridges called gyri, and the grooves between these are known as sulci or fissures. These gross neuroanatomical features form the basis for the division of the hemispheres into four lobes: frontal, temporal, parietal, and occipital.

The parcellation of the hemispheres into four lobes is somewhat arbitrary but serves to produce convenient neuroanatomical landmarks that have important functional affiliations. Table 1.1 gives a brief outline of some prominent brain-behavior relationships, which will be developed in greater detail throughout this book. The frontal lobes, largest and most anterior, provide the origin of the motor system via the corticospinal tracts, mediate the production of language and prosody, and organize the integrative capacities of motivation, comportment, and executive function. The temporal lobes receive primary auditory input, mediate comprehension of language and prosody, and, in concert with the closely connected limbic system, subserve important aspects of memory and emotion. The parietal lobes receive tactile input, mediate visuospatial competence, and subserve reading and calculation skills. The occipital lobes, smallest and most posterior, receive primary visual input and mediate perception of visual material before further processing occurs in more anterior regions.

Table 1.1. Regional functions of the human brain

Frontal Lobes	***Parietal Lobes***
Motor system	Tactile sensation
Language production (left)	Visuospatial function (right)
Motor prosody (right)	Reading (left)
Comportment	Calculation (left)
Executive function	
Motivation	
Temporal Lobes	***Occipital Lobes***
Audition	Vision
Language comprehension (left)	Visual perception
Sensory prosody (right)	
Memory	
Emotion	

The hemispheres are connected to each other primarily by the corpus callosum, a massive white matter tract containing some 300 million axons (Nolte 2002; Figure 1.2). This structure permits the continuous interhemispheric exchange of information and joins many distant but homologous cerebral areas into functionally unified networks. The diencephalon is found deep in the brain and has a major role in sensory, motor, arousal, and limbic activities. Within the diencephalon, the egg-shaped thalamus serves as a central relay station for all sensory systems with the exception of olfaction and has a critical role in wakefulness. The tiny hypothalamus exerts enormous influence through its control of the autonomic nervous system, with its sympathetic and parasympathetic divisions, and through its connections with the pituitary gland that enable the neural control of the endocrine system. In posterior and inferior regions of the brain lie the brainstem and the cerebellum. The brainstem, made up of the midbrain, pons, and medulla, plays an essential role in motor and sensory function, and the caudal brainstem contains centers for the control of respiration and cardiac function. The cerebellum acts in combination with gray matter nuclei in the hemispheres and the brainstem known as the basal ganglia (caudate, putamen, globus pallidus, and substantia nigra) to enable fine motor coordination and postural control. At the base of the brain, the medulla exits the skull through the foramen magnum, where it merges with the spinal cord, the most caudal portion of the central nervous system (CNS).

The brain is housed within and protected by the skull, and between the brain and the skull are three membranes: the dura mater, the arachnoid, and the

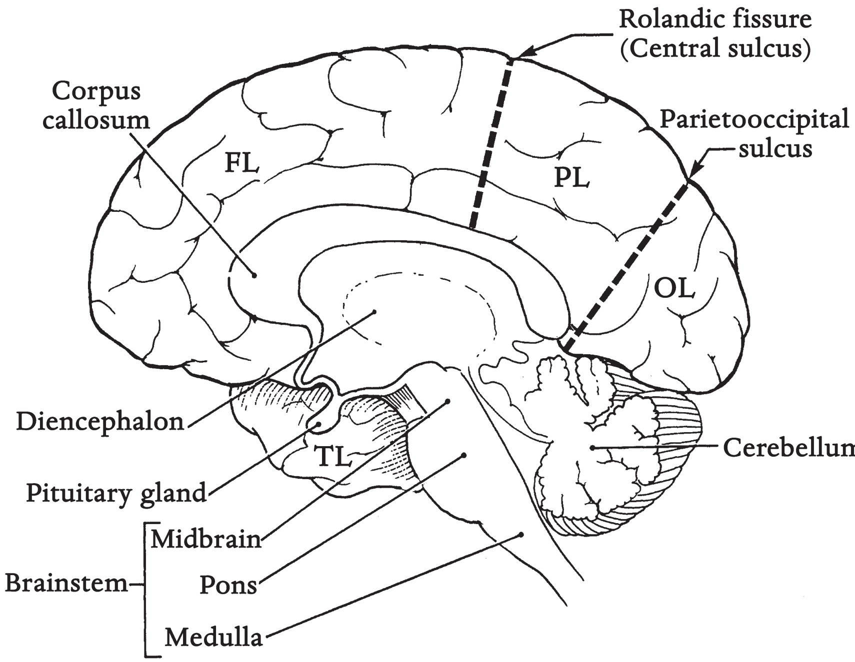

Figure 1.2. *Medial view of the brain depicting the four lobes, diencephalon, brainstem, and cerebellum (FL: frontal lobe; TL: temporal lobe; PL: parietal lobe; OL: occipital lobe).*

pia mater. Within the subarachnoid space, cerebrospinal fluid (CSF) envelops the entire CNS and provides a buoyancy that adds further protection. The CSF is continually produced within the four ventricles of the brain—the paired lateral ventricles in the hemispheres, the third ventricle situated between the two thalami, and the fourth ventricle between the cerebellum and the brainstem—and enters the subarachnoid space through apertures in the fourth ventricle. Eventually the CSF circulates to the vertex of the brain and is absorbed into the venous system through the arachnoid villi. The ventricular system and the CSF are important for the structural support of the brain and for its metabolic activity as well.

The arterial blood supply of the brain originates with two pairs of large vessels in the neck: the internal carotid and the vertebral arteries. The internal carotid arteries then bifurcate into middle and anterior cerebral arteries, which irrigate respectively the lateral hemispheric surfaces and the medial aspects of the frontal and parietal lobes. The vertebral arteries join at the junction of the medulla and the pons to form the basilar artery, which then also bifurcates at the midbrain level to form the two posterior cerebral arteries. These vessels supply the medial and inferior surfaces of the temporal and occipital lobes as well as the caudal diencephalon. Interruption of the blood supply from any of these arteries, as occurs in a stroke, leads to a wide spectrum of important neurobehavioral syndromes. A complex system of cerebral veins conveys blood away from the brain and back to the heart; venous infarction is less common than arterial but can result in similar focal syndromes.

The process of evolution has produced an impressive expansion of the human brain, relative to body weight, in comparison with other animals. There are some species, however—among them some small primates and dolphins—that have proportionately larger brains (Nolte 2002). The size of the brain, therefore, is only one factor accounting for singular human capacities. In humans, the large percentage of the brain devoted exclusively to higher functions is undoubtedly important, as is the exceedingly rich neuronal connectivity of the brain (Nolte 2002). Of all brain regions, the frontal lobes have expanded the most during evolution (Mesulam 2000), and, interestingly, it appears that the main reason for this increase in volume is expansion of frontal white matter (Schoenemann, Sheehan, and Glotzer 2005).

The surface of the brain is called the cortex, from the Latin for "bark," and its regional cytoarchitectonic variations have prompted many attempts to divide it into discrete areas. The most enduring of these cortical maps was devised by the anatomist Korbinian Brodmann (1909). In Figure 1.3, forty-seven cortical areas of Brodmann are depicted, four of which—areas 13 through 16—are not present; these areas, however, actually designate a region called the insula, which is not visible on the outer surface of the brain (Gorman and Unützer 1993). The insula is a small cortical zone buried deep in the Sylvian fissure that is overlain by portions of the frontal, parietal, and temporal lobes known as opercula (*operculum* is Latin for "lid"). Apart from its role in taste perception and some aspects of emotion, the functions of the insula are not well understood. Many of the surface parcellations of Brodmann, however, have well-established functional affiliations, and frequent reference to his schema will be made in this book.

A detailed account of the cerebral cortex is beyond the scope of this book, but selected aspects of cortical structure are relevant. The cortex is a convoluted sheet of gray matter on the outer surface of the brain, much of which is hidden from view in the depths of sulci and fissures. Its thickness ranges between 1.5 and 4.5 mm, with an average of 3 mm. More than 90 percent is made up of neocortex, the phylogenetically recent six-layered cortex that contains about 10 billion of the roughly 100 billion neurons in the brain (Popper and Eccles 1977; Kandel, Schwartz, and Jessell 2000). Other cortical areas, notably the hippocampus and certain olfactory regions linked with the limbic system, have three layers and are known as allocortex.

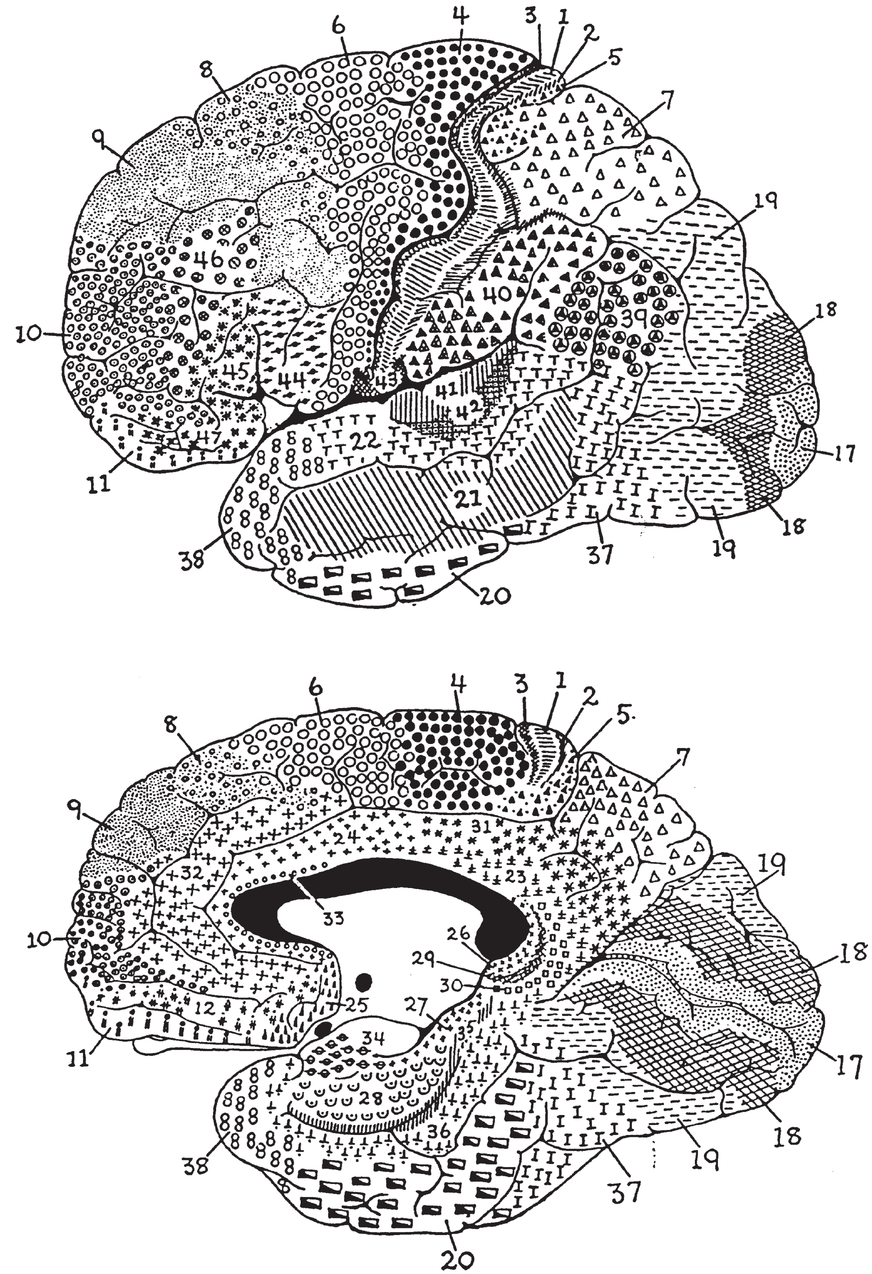

Figure 1.3. *Brodmann areas of the cerebral cortex (after Brodmann 1909).*

The neocortex has classically been divided into motor, sensory, and association areas. The last of these is so named because of a philosophical tradition, dating back to the British empiricist philosopher John Locke, holding that mentation is the result of the associations between ideas (Duffy 1984). Association areas occupy the majority of the neocortical surface and, as the presumed repository of ideas, were thus regarded as regions where the higher functions of humans take place, although a certain imprecision about the operations of these regions has always remained.

More recently, neurophysiologic studies of the neocortex have indicated that the fundamental unit of cortical function is a vertically oriented column, perpendicular to the cortical surface, that contains as few as 100 neurons and that is extensively connected with others like it throughout the neocortex (Mountcastle 1978). The most convincing evidence for these columns comes from studies of the primate visual cortex, where it is possible to show with microelectrode insertion that all cells within a column respond similarly to a given external stimulus (Hubel and Wiesel 1977). It is likely, however, that this arrangement is widespread throughout the neocortex (Mountcastle 1978).

These neocortical columns number in the hundreds of millions, and because of the massive connectivity among them, the number of potential combinations between various cortical units is vast indeed. This notion has helped develop the concept of distributed systems in the brain that are composed of large numbers of extensively interlinked modular elements (Mountcastle 1978). The general idea of distributed systems has become so popular that it has largely supplanted the concept of cortical association areas. It should be evident, however, that the two notions are in fact compatible (Duffy 1984), and the shift in terminology reflects advances in basic neuroscience more than a fundamental reconsideration of how the brain functions.

Also important in the elaboration of higher function are numerous structures below the cortical mantle. Gray matter nuclei within the diencephalon, basal ganglia, and brainstem play a special role in fundamental processes such as arousal, attention, and mood. Neurotransmitter systems arise from nuclei deep in the hemispheres or the brainstem and send projections to more rostral sites: the cholinergic system originating from the basal forebrain, the dopaminergic projections from the midbrain substantia nigra and adjacent ventral tegmental area, the noradrenergic system from the pontine locus ceruleus, and the serotonergic fibers from the raphe nuclei of the brainstem. Close structural and functional relationships between subcortical and cortical regions are also readily apparent. Thus, a number of parallel frontal-subcortical circuits have been identified that link cortical and subcortical structures—frontal cortex, basal ganglia, and thalamus—into functional ensembles subserving comportment, motivation, and executive function (Cummings 1993). Figure 1.4 depicts the general organization of these circuits.

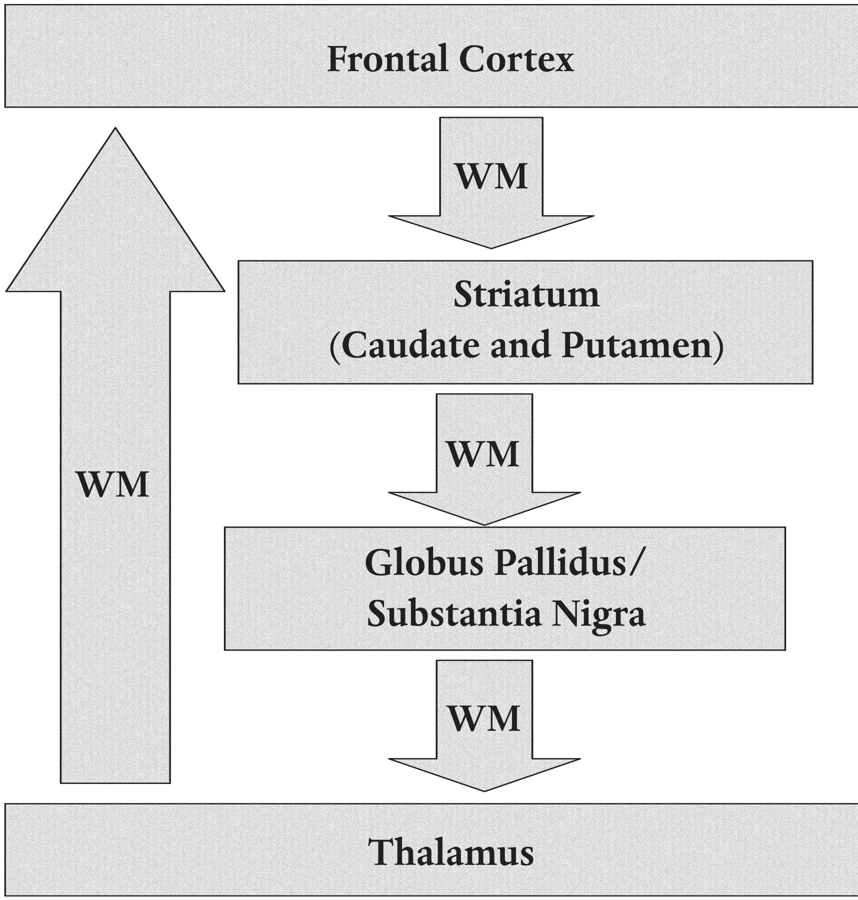

FIGURE 1.4. *General organization of frontal-subcortical circuits (WM: white matter) (after Cummings 1993).*

Not to be neglected are the many white matter tracts that serve to connect cortical and subcortical regions and facilitate rapid and efficient interregional communication (Filley 2001). Intrahemispheric association fibers and interhemispheric commissural fibers link regions within and between the hemispheres, and deeper tracts including the fornix and medial forebrain bundle connect the cerebrum to the limbic system and the brainstem. White matter makes up about one half of the brain volume, and its capacity to facilitate the transfer of information in the brain is a major foundation of normal cognition and emotion (Filley 2001). The collective function of all these subcortical gray and white matter areas thus contributes to the multifocal cerebral ensembles forming the distributed neural networks dedicated to all neurobehavioral domains (Mesulam 1990).

The complex nature of these networks has often invited comparison of the brain to the modern computer, which is increasingly capable of impressive computations that in some ways surpass the abilities of their creators. Science fiction has dealt with some of the implications of computer science, but academicians in the field of artificial intelligence have also been at work, attempting to design machines that mimic if not duplicate the abilities of the human brain (Crevier 1993). Whereas a consideration of computer science and artificial intelligence is beyond the scope of this book, it is instructive to note that the standard computer is known as a *serial* processor, whereas the brain has *parallel* as well as serial processing capacities (Dennett 1991; Mesulam 2000). Both kinds of neural operation are abundantly evident in everyday human life: parallel processing, for example, enables the simultaneous analysis of a continuous flood of sensory and interoceptive input, while serial processing assumes prominence as the most salient stimuli are selected while others are disregarded and an appropriate adaptive response is generated (Mesulam 2000). All of this mental activity features the effortless capacity of the brain to weave disparate aspects of mental experience into a seamless unity, which enables all cognitive and emotional function and culminates in the phenomenon of consciousness. These capacities of the human brain appear to be well beyond the powers of even the most powerful computer. Moreover, given that the phenomenon of consciousness likely depends on billions of living brain cells dynamically connected to each other by trillions of synapses, it is difficult to imagine that a computer will be able to simulate this central feature of the human brain.

Recognition of the imposing problems of artificial intelligence has in fact influenced a turn to more practical uses of the computer, which are in the realm of neuroprosthetics (Friehs et al. 2004). Analogous to the first neural prosthesis introduced for human use—the cochlear implant—a variety of brain-machine and brain-computer interfaces are being explored for clinical application in people with motor disability from such diverse problems as stroke, traumatic brain or spinal cord injury, the locked-in syndrome, multiple sclerosis, amyotrophic lateral sclerosis, muscular dystrophy, and cerebral palsy (Friehs et al. 2004). These laudable efforts promise to assist many people whose problems lie in the transforming of thought into action (Friehs et al. 2004).

The Excesses of Phrenology

The scientific study of localizing mental functions in the brain had an inauspicious start. One need only look to the surprisingly popular doctrine in the late eighteenth and early nineteenth centuries known as phrenology, or organology, to appreciate how a too literal approach to brain-behavior relationships can become absurd. Most strongly associated with the names of Franz Joseph Gall (1758–1828) and Johann Kaspar Spurzheim (1776–1832), phrenology claimed to allow the assessment of behavioral traits by simple palpation of the skull, the bumps and ridges thereon allegedly corresponding to anatomical features of the underlying brain that had specific implications such as amativeness, wit, and destructiveness (Gall and Spurzheim 1810–1818). It was thought that the centers for the various traits would develop and expand with regular use, and that this process would actually produce palpable protrusions in the overlying bony surface. Figure 1.5 illustrates the kind of cranial map that resulted from a phrenological interpretation of behavior.

In its heyday, phrenology was widely practiced in Europe and America, and many phrenological societies and journals appeared to advocate the doctrine. Gall, an Austrian physician and neuroanatomist who can legitimately be credited for the recognition that gray matter regions are specifically linked by white matter tracts in the brain, nevertheless assured himself a rather dubious place in medical history by the outlandish assertions of phrenology. Not only was his precise assignment of behavioral characteristics to discrete regions of the brain unsubstantiated, but his belief that cranial prominences could reveal these traits seems remarkably crude and naïve to the modern observer.

Yet the phrenologists should be recognized for mounting formal opposition to the mind-brain dualism that prevailed in their day and beginning to establish a foundation for considering the brain as the organ of behavior. Whereas this insight represented an advance over the orthodoxy of the time, Gall and Spurzheim erred, sadly, in their extremism. The radical localizationism of phrenology was excessive, but the principle of assigning behaviors to regions of the brain was not—as this book will illustrate, a reasonable view of the cerebral localization of behavior is one of the major goals of modern neuroscience, and much has been accomplished to reach this goal.

Behavioral Neurology

This book is about the anatomy of human behavior. Use of the word *behavior* will signify the activities of the mind, or, more generally, the total of all the operations ordinarily regarded as mental acts. Neurologists sometimes refer to these as "higher functions," to distinguish them from the elemental sensory and motor functions that are also found in nonhuman species. Some authorities employ the term "higher cortical function" (Luria 1980), although structures in the subcortex such as the thalamus, basal ganglia, and white matter clearly contribute to behavior and thus render this phrase misleading. As a general guideline, these higher *cerebral* functions can be usefully divided into the common-sense catego-

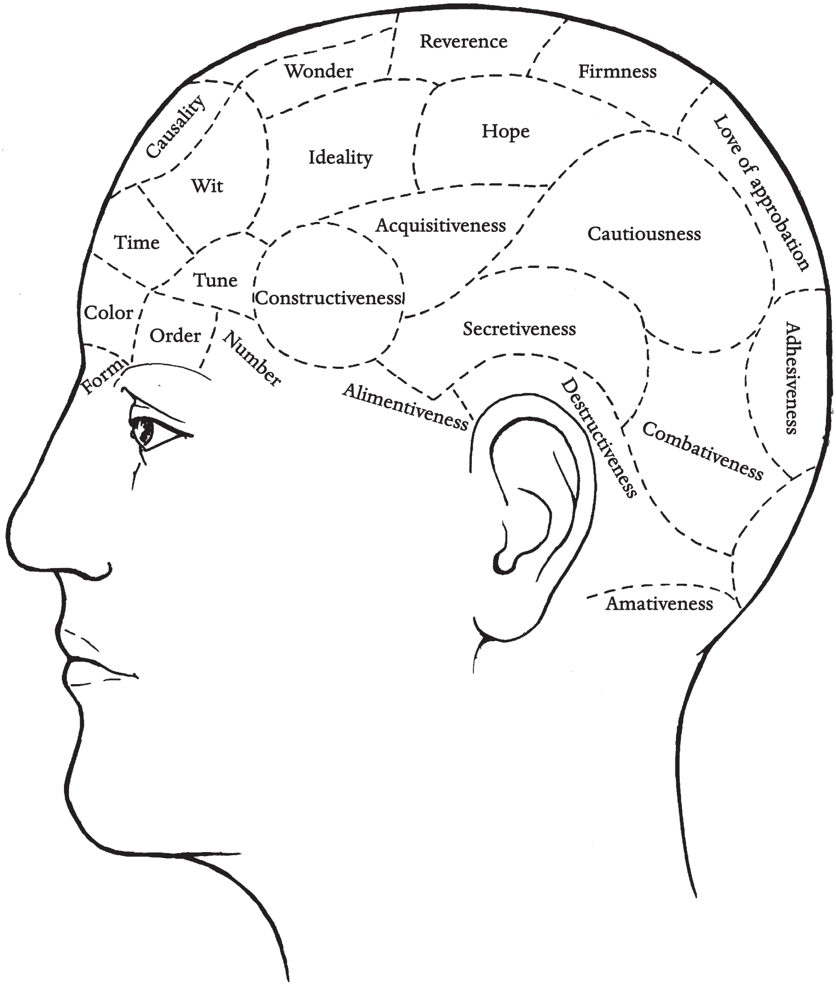

Figure 1.5. *Contemporary portrayal of a phrenological map.*

ries of thoughts (cognition) and feelings (emotion), although, in reality, human behaviors usually involve a component of both. Our aim will be to concisely summarize what is known or theorized about the localization of various behavioral capacities in the human brain. This book will concentrate on the adult brain but introduce concepts relevant to the child brain when appropriate.

Our specific approach will rely most heavily on *behavioral neurology* (Damasio 1984), the subspecialty of neurology devoted to the behavioral effects of demonstrable brain disorders, whether from disease, injury, or intoxication. Long an area of interest to neurologists, behavioral neurology has emerged in the last five decades as a subspecialty dedicated to correlating human behavior with the structure and function of the brain (Geschwind 1965; Damasio 1984; Mesulam 2000). This development has been fueled by many factors. First, the hugely influential tradition of Freudian psychoanalysis began to yield around the middle of the twentieth century to a more biological orientation in psychiatry and psychology, and thus opened the door to a more quantitative approach to the study of behavior (Kandel 1979; Price, Adams, and Coyle 2000). Second, advances in neuroscientific technology in the last several decades have kindled the hope that sensitive neuroimaging methods (see below) will help disclose more about the complexities of behavior in health as well as disease by clarifying the structure and function of the brain without the necessity for postmortem examination. Finally, the advent of behavioral neurology as a formal discipline took place largely through the efforts of Norman Geschwind, who in the 1960s established the importance of the field (Geschwind 1965) and influenced a generation of clinician-investigators. Behavioral neurology and related disciplines now stand critically poised at the intersection of modern neuroscience and the detailed clinical observation of behavior. Through study of individuals with focal and diffuse brain lesions, the understanding of contributions made by regions of the brain to various behavioral functions is increasingly complete. Thus the analysis of mind can constructively proceed by way of a clinically based examination of the brain.

A central debate in behavioral neurology has raged between localizationism, the assignment of a given neurobehavioral domain to a specific region of the brain, and holism, the view that cognitive and emotional operations are widely represented in the cerebrum without regional affiliation. We have seen an extreme example of the former in phrenology, whose dubious tradition remains something of an obstacle to a moderate localizationism. In contrast, the holistic viewpoint, also known as the organismic approach or the equipotentiality theory, assumes that the brain works as a unified whole to produce behavior, and that localization is an overly simplistic form of diagram-making. Two syndromes in which holism had vigorous support are aphasia and amnesia, where it was contended that language (Goldstein 1948) and memory (Lashley 1926) disturbances cannot be reliably related to discrete brain areas and that widespread lesions can cause similar defects. The debate is not entirely settled, and it has surely promoted a healthy scientific exchange. However, a consensus has recently been reached that might be called modified localizationism. In this paradigm, widespread interconnected networks of cerebral areas are dedicated to specific functions and not to others (Mesulam 1990, 2000; Cummings 1993); examples include the left perisylvian zone for language and the medial temporolimbic system for memory. These distributed neural networks reflect a conception of brain-behavior relationships that maintains the principle of localizationism without falling prey to its excesses. We shall deal with these networks more completely at several points in this book.

The clinical discipline known as *neuropsychiatry* also deserves comment (Arciniegas and Beresford 2001). Widely popular in nineteenth-century Europe before the ascendancy of Sigmund Freud, neuropsychiatry has recently provoked renewed interest as a discipline having much in common with behavioral neurology (Cummings and Hegarty 1994). Initially, some confusion surrounded this term, however, as the field groped for a secure definition (Caine and Joynt 1986; Yudofsky and Hales 1989; Lishman 1992; Trimble 1993). Since most behavioral neurologists began their training as neurologists and most neuropsychiatrists as psychiatrists, one understandable distinction is that the former group has been more focused on neuroanatomy and neuropathology, whereas the latter has been more concerned with neuropharmacology and psychopathology. Indeed, this book reflects an emphasis on the structural brain correlates of behavior while devoting less attention to neurotransmitter systems and their manipulation by medications. But the two fields are clearly merging. Progress has recently been made by the establishment of the subspecialty of Behavioral Neurology & Neuropsychiatry, which now combines these two traditions into a unified discipline devoted to the evaluation and care of behaviorally disturbed individuals (Arciniegas et al. 2006). This development marks an important milestone in the gradual process of neurology and psychiatry edging closer together in the effort to understand the neurobiological basis of behavior (Kandel 1989; Price, Adams, and Coyle 2000; Cummings and Mega 2003). Indeed, behavioral neurologists and neuropsychiatrists have contributed importantly to clarification of the nosology of many disorders pertinent to both fields in the fourth edition of the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders* (1994) and its planned successor. These trends are indeed welcome, both for the expanded insights that are likely to appear and for the pressing needs of many patients with disorders of the brain who have not found a comfortable position in either specialty heretofore (Geschwind 1975). Both behavioral neurology and neuropsychiatry have much to contribute to the understanding of behavior, and cooperation is clearly preferable to unproductive interdisciplinary disputes.

Although the clinical study of patients who harbor focal or diffuse brain lesions is the foundation of this book, we will also integrate information derived from the spectacular advances of neuroimaging in recent decades (Naeser and Hayward 1978; Alavi and Hirsch 1991; Posner 1993; Roland 1993; Basser, Mattiello, and LeBihan 1994; Goodkin, Rudick, and Ross 1994; Raichle 1994; Turner 1994; Wright et al. 1995; Prichard and Cummings 1997; Rudkin and Arnold 1999; D'Esposito 2000; Bandettini 2009). It is now possible to study the higher functions in normal and abnormal brains using an array of noninvasive techniques that produce elegant images of brain structure and function. The first advance in structural neuroimaging was *computed tomography* (CT), which appeared in the 1970s and quickly established its role in examining brain-behavior relationships (Naeser and Hayward 1978). Then, in the 1980s, *magnetic resonance imaging* (MRI) offered a more sensitive structural neuroimaging instrument, particularly for viewing the cerebral white matter, and had the additional advantage of avoiding radiation exposure (Goodkin, Rudick, and Ross 1994). More advanced MRI methods were then introduced in the 1990s and are applicable at this point in many areas of research (Bandettini 2009). *Voxel-based morphometry* (VBM; Wright et al. 1995) can be used for measuring gray matter volume; *diffusion tensor imaging* (DTI; Basser, Mattiello, and LeBihan 1994) is helpful in characterizing the structure and location of white matter tracts; and *magnetic resonance spectroscopy* (MRS; Rudkin and Arnold 1999) can be used to measure neurometabolite concentrations in either tissue. For behavioral neurologists, the structural images provided by CT and especially MRI remain most useful and are key components of clinical evaluation (Figures 1.6 and 1.7).

To complement these structural approaches, a variety of methods designed to image the physiology of the brain have been developed, collectively known as functional neuroimaging. *Single photon emission computed tomography* (SPECT; Alavi and Hirsch 1991) and *positron emission tomography* (PET; Roland 1993) exploit the principle that metabolic activity of the brain is coupled with blood flow, so that cerebral function during a cognitive task can be assessed by the introduction of an isotope emitting radiation into the bloodstream. These techniques are useful for identifying areas of the cerebral cortex that become selectively active when the task requires energy expenditure in the responsible neurons. Most recently, *functional MRI* (fMRI) has appeared. Based on the measurement of changes in deoxyhemoglobin concentration that arise from an increase in blood oxygenation in the vicinity of neuronal firing, fMRI has enabled another means of correlating mental operations with brain activity (Prichard and Cummings 1997). These techniques have all proven valuable, and in particular, PET and fMRI have made possible the extraordinary prospect of "seeing the mind" in action (Posner 1993; Turner 1994; Bandettini 2009). fMRI has now become the method of choice in the neuroscience community for functional neuroimaging, as it has both high spatial and temporal resolution and relatively straightforward implementation (Bandettini 2009). As a general rule, functional neuroimaging studies have largely confirmed the brain-behavior relationships discovered from the lesion method upon which behavioral neurology is founded, although methodological problems have hindered progress to some extent. The use of fMRI has enabled many insights about what cortical areas are active in association with a selected cognitive task, but explanations of the mechanisms of cognition

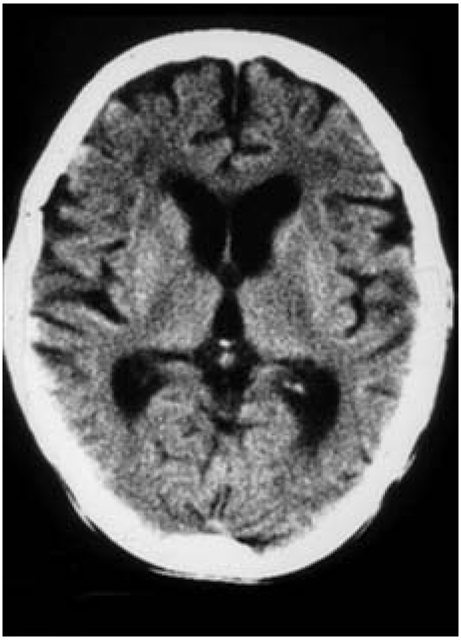

Figure 1.6. *Axial computed tomography (CT) scan of a patient with Alzheimer's disease demonstrating mild diffuse cerebral atrophy.*

and how the brain is organized are far more challenging goals that have yet to be accomplished (Bandettini 2009). Nevertheless, functional imaging has made substantial progress, and the use of these increasingly sophisticated instruments doubtless augurs well for continued progress.

Relevant information from related disciplines, including neuropsychology, cognitive science, and the basic neurosciences, will also be integrated into this account. Neuropsychology is a clinical and research discipline with major importance for the precise measurement and characterization of behavior (Lezak et al. 2004). Cognitive science promises many new insights, particularly through its emphasis on computers and theoretical models of cognition (Gardner 1987). Basic neuroscience, despite the lack of an animal model (almost by definition) for higher functions and their disorders, offers valuable information on such matters as neurotransmission and synaptic function (Kandel, Schwartz, and Jessell 2000). An air of excitement pervades the exploration of behavior as interdisciplinary work produces new advances on a daily basis. Despite the many areas of uncertainty in all areas of neuroscience, a growing body of data is providing a cogent description of the roles played by brain structures in the wondrous array of human behaviors.

The study of where and how the higher functions are represented in the human brain is clearly a formidable task. Behavioral neurology can only proceed

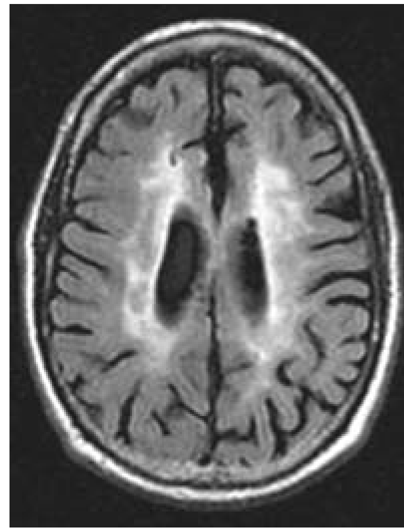

Figure 1.7. *Axial magnetic resonance imaging (MRI) scan of a patient with Binswanger's disease showing cerebral white matter ischemia.*

by analyzing abnormal behavior in the context of brain pathology and then theorizing about the normal behavior that has been disturbed (Benson 1994). Difficulties arise both in the definition of neurobehavioral functions, such as attention, memory, language, and the like, and in the precise identification of damaged brain areas, so that both sides of the brain-behavior dyad are subject to significant uncertainties. The lesion method should be used to explore the distributed networks of the brain subserving specific functions and not in an attempt to establish a strict correspondence between the location of a lesion and the site of a mental operation (Damasio and Damasio 1989). The brain is not a collection of lobes, gyri, nuclei, and tracts that each have a single and invariant functional affiliation, and the modern understanding of distributed neural networks teaches that the wide range of cognitive and emotional functions corresponds to an impressively complex neural foundation (Mesulam 2000). With this caveat in mind, it is hoped that a general portrayal of the neuroanatomy of behavior will prove useful. The study of human beings is ultimately the only way to probe their unique behaviors, even though reliance on "nature's experiments"—due to stroke, trauma, degenerative disease, and the like—restricts the scope of such investigation more than tightly controlled experiments with laboratory animals. Our goal will be to examine the domains of mental activity that have been illuminated by clinical observation, demonstrating that such an endeavor not only has great value for the care of individuals with devastating afflictions of the brain but also contributes enormously to the understanding of how human behavior is anatomically organized.

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