the controversies that swirled around Darwin, and why it is now so completely forgotten.

I could not resist publishing it in a journal called *Hippocampus,* which is devoted to studies on the anatomy, physiology, and functions of that structure (Gross, 1993a). I liked my article so much that I published a shorter version entitled "Huxley versus Owen: The Hippocampus Minor and Evolution" in the less specialized, more widely read journal, *Trends in Neuroscience* (Gross, 1993b). Both versions were well received. Indeed, I received more letters of praise for them than I had in response to the over 200 straight science papers I had previously written. I was so reinforced by this reception, as we used to say in B. F. Skinner's heyday, that over the next few years I submitted for publication several other history of neuroscience articles: versions of them make up the rest of this book.
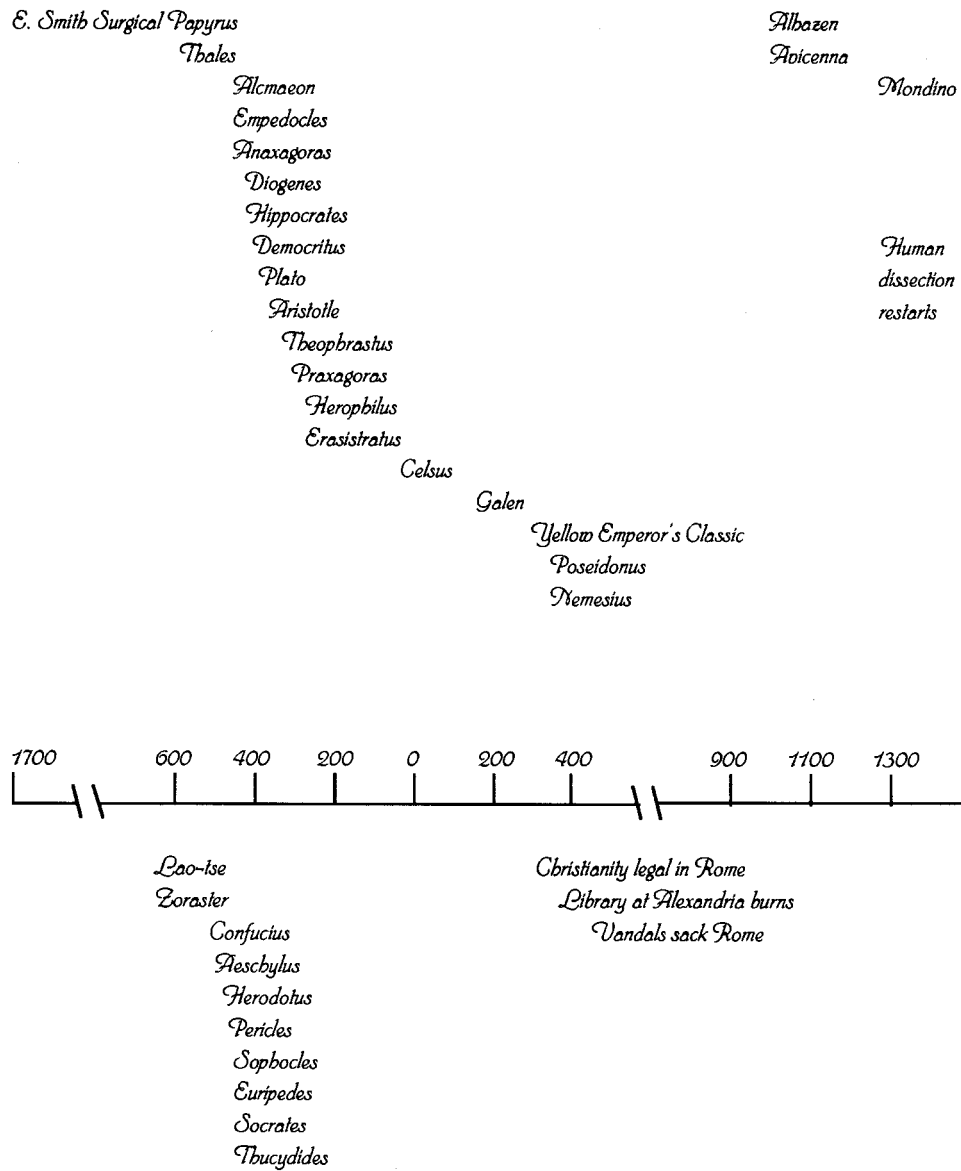
The fifth essay arose when I was asked to organize a conference on object recognition and the temporal lobes at the Massachusetts Institute of Technology in honor of Hans-Lukas Teuber in 1993. After the conference, Pat Goldman-Rakic, the editor of the journal *Cerebral Cortex,* asked me to edit a special issue based on the meeting. I decided to add a history article of my own to introduce the issue. The article, entitled "How Inferior Temporal Cortex Became a Visual Area," traced how the visual functions of the temporal cortex were discovered (Gross, 1994b). My colleagues and I had been the first to record from neurons in the temporal cortex (we did so at MIT, under Teuber's sponsorship), so I made the account of this work at the end of the article very personal and autobiographical. Chapter 5, "Beyond the Striate Cortex: How Large Portions of the Temporal and Parietal Cortex Became Visual Areas," is derived in part from that article. I expanded its scope to include not only the temporal lobe but also how the parietal lobe became a visual area. Both developments followed from nineteenth-century observations on the effect of temporal and parietal lesions in monkeys that were forgotten and had to be subsequently rediscovered.

Greta Berman, Michael Graziano, and Hillary Rodman read all the essays at least once and gave many helpful comments and much encouragement.
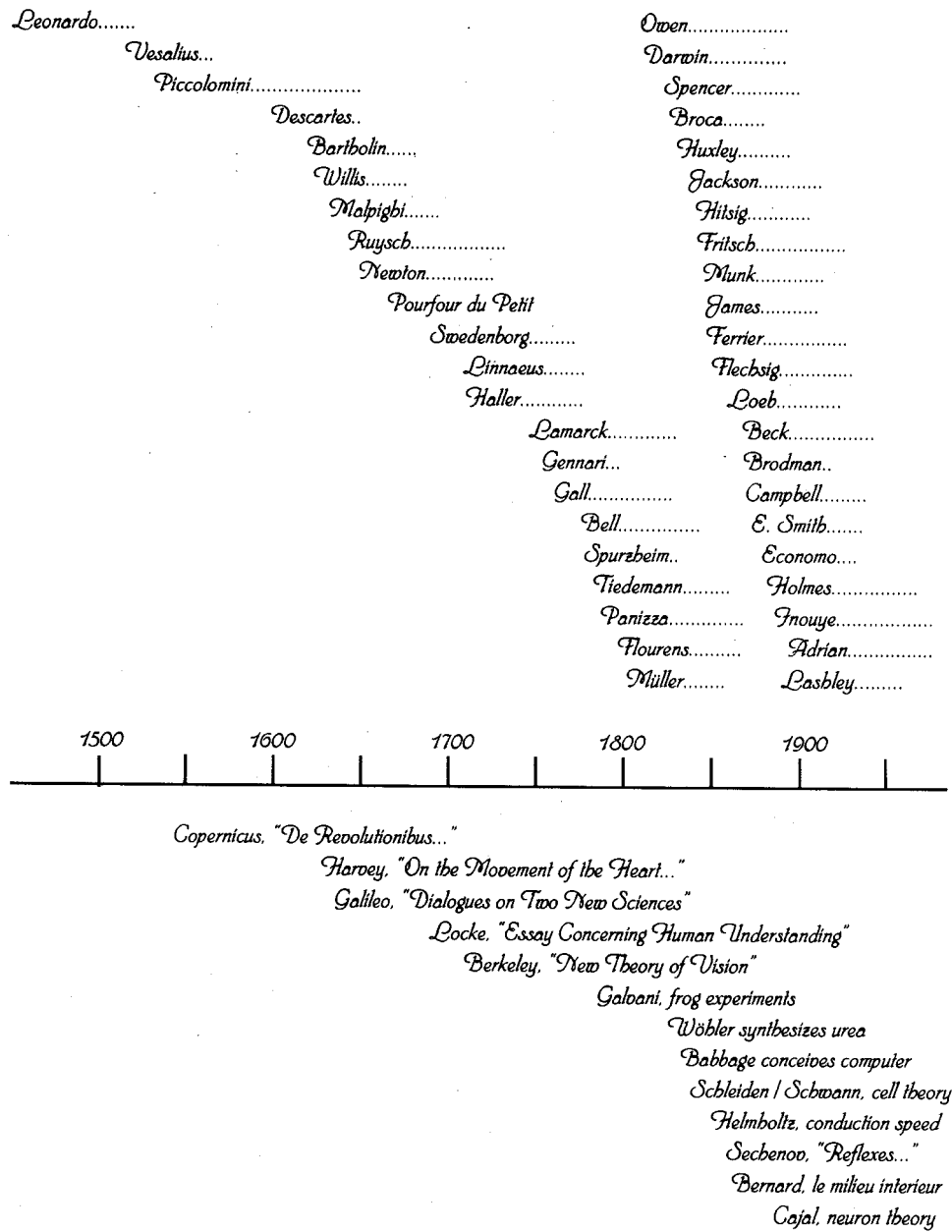
B R A I N ,   V I S I O N ,   M E M O R Y

E. Smith Surgical Papyrus
Thales
Alcmaeon
Empedocles
Anaxagoras
Diogenes
Hippocrates
Democritus
Plato
Aristotle
Theophrastus
Praxagoras
Herophilus
Erasistratus
Celsus
Galen
Yellow Emperor's Classic
Poseidonus
Nemesius

Albazen
Avicenna
Mondino

Human
dissection
restarts

1700   600   400   200   0   200   400   900   1100   1300

Lao-tse
Zoraster
Confucius
Aeschylus
Herodotus
Pericles
Sophocles
Euripedes
Socrates
Thucydides

Christianity legal in Rome
Library at Alexandria burns
Vandals sack Rome

The upper time line shows when each of the major Pre-Renaissance figures discussed in this book flourished. The lower one indicates some contemporaneous figures and events.

Leonardo....... Owen..................

Vesalius... Darwin.............

Piccolomini.................... Spencer............

Descartes.. Broca........

Bartholin...... Huxley..........

Willis........ Jackson............

Malpighi....... Hitsig............

Ruysch................. Fritsch.................

Newton............ Munk............

Pourfour du Petit James..........

Swedenborg......... Ferrier...............

Linnaeus........ Flechsig.............

Haller............ Loeb............

Lamarck............ Beck...............

Gennari... Brodman..

Gall............... Campbell........

Bell.............. E. Smith.......

Spurzheim.. Economo....

Tiedemann......... Holmes...............

Panizza.............. Inouye..................

Flourens.......... Adrian................

Müller........ Lashley.........

1500	1600	1700	1800	1900

Copernicus, "De Revolutionibus..."

Harvey, "On the Movement of the Heart..."

Galileo, "Dialogues on Two New Sciences"

Locke, "Essay Concerning Human Understanding"

Berkeley, "New Theory of Vision"

Galvani, frog experiments

Wöhler synthesizes urea

Babbage conceives computer

Schleiden / Schwann, cell theory

Helmholtz, conduction speed

Sechenov, "Reflexes..."

Bernard, le milieu interieur

Cajal, neuron theory

The upper time line shows the birth (initial letter) and death (final dot) of the major Post-Renaissance figures discussed in this book. The lower gives the year of major events relevant to the development of modern neuroscience.
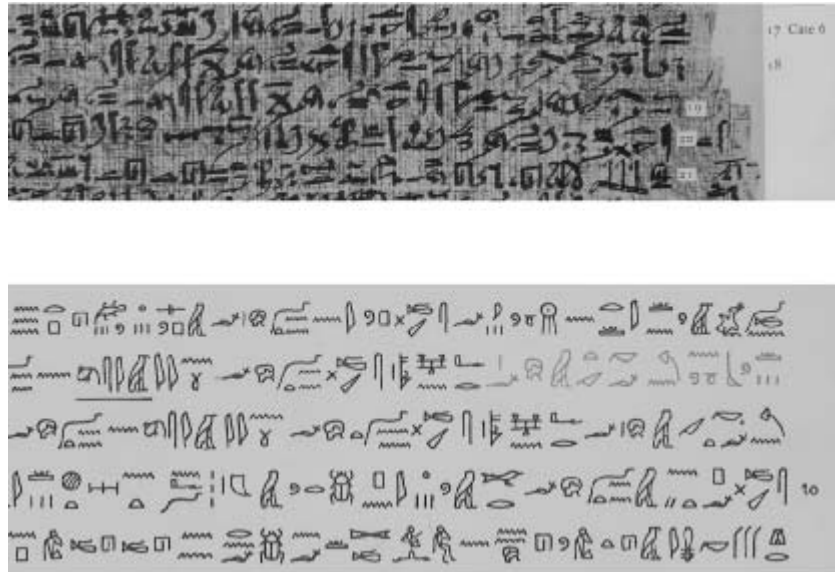
Figure 1.1 A portion of the Edwin Smith surgical papyrus, case six, concerning a skull fracture that exposed the cortex (Breasted, 1930). Upper, the actual papyrus, written in a hieratic script. Lower, the hieroglyphic transliteration. The word for brain is underlined. Writing is left to right in both figures. (Princeton University Library)

From Imhotep to Hubel and Wiesel: The Story of Visual Cortex

This chapter traces the origins of our current ideas about visual cortex. I begin in the thirtieth century BCE with the earliest description of the cerebral cortex. In the second part I consider the views of Greek philosopher–scientists on the functions of the brain. The third part concerns the long period in which there were virtually no advances in Europe in understanding the brain or any other aspect of the natural world. In the fourth part I describe how even after brain research was again well under way, the cerebral cortex tended to be ignored. The fifth section considers the beginning of the modern study of the cerebral cortex and the localization therein of psychological functions. Our focus narrows in the sixth section, and I address how a specifically visual area of the cortex was delineated. The chapter ends with the award of the Nobel prize to David Hubel and Thorsten Wiesel in 1981 for their discoveries about visual cortex.

Ancient Egyptian Surgery and Medicine

The First Written Mention of the Brain

The first written reference to the cortex, indeed to any part of the brain, occurs in the Edwin Smith surgical papyrus (figure 1.1). Although written about

1700 BCE, this papyrus is a copy of a much older surgical treatise dating back to the pyramid age of the Old Kingdom (about thirtieth century BCE). The papyrus was bought in 1862 by an American Egyptologist, Edwin Smith, from a local in Luxor, probably one of the "hereditary" tomb robbers who inhabit a nearby village. It eventually found its way to the great American Egyptologist James H. Breasted.[1]

The publication of Breasted's translation in 1930 made an enormous impact on medical historians and Egyptologists.[2] Previously, Egyptian medicine had been thought to be a jumble of incantations, amulets, and superstitions. Rational medicine was supposed to begin only with the Greeks. Yet, the Edwin Smith papyrus is clear evidence of a scientific observer attempting to understand the human body and to treat, rationally, its injury.

The papyrus consists of a coolly empirical description of forty-eight cases, starting from the head and working down to the shoulders, where the copyist stops in midsentence. For each case, the author systematically describes the examination, diagnosis, and feasibility of treatment. Each diagnosis comes to one of three conclusions: that the patient should be told that it is "an ailment that I will treat," "an ailment that I will try to treat," or "an ailment that I will not treat."

The word for brain first comes up in case six, a person with a skull fracture:

> (*Title*) Instructions concerning a gaping wound in his head, pene-
> trating to the bone, smashing his skull, (and) rending open the brain
> of his skull.
> (*Examination*) If thou examinest a man having a gaping wound in
> his head, penetrating to the bone, smashing his skull, and rending
> open the brain of his skull, thou shouldst palpate his wound.
> Shouldst thou find that smash which is in his skull [like] those
> corrugations which form in molten copper, (and) something
> therein throbbing (and) fluttering under thy fingers, like the weak
> place of an infant's crown before it becomes whole . . . (and) he

---

> [the patient] discharges blood from both his nostrils, (and) he suffers
> with stiffness in his neck.
> *(Diagnosis)* [you say] an ailment not to be treated.[3]

And indeed, the "corrugations" that form in molten copper during the smelting process such as that of early Egypt really do look like cerebral cortex.

In several cases, the author notes the relation of the laterality of the injury to the laterality of the symptom. For example, in case five, the patient "walks shuffling with his sole on the side of him having that injury which is in his skull." (Presumably, a contracoup injury; that is, a blow to one side of the head that causes the brain to shift within the cranium and make impact on the inside of the contralateral skull, thereby causing damage contralateral to the site of the blow.)

The author was clearly aware that the site of injury determines the locus and nature of the symptoms. Thus, in case thirty-one, "It is a dislocation of a vertebra of the neck extending to this backbone which causes him to be unconscious of his two arms and legs." Elsewhere, the author mentions the meninges and the cerebrospinal fluid, and describes aphasia ("he speaks not to thee") and seizures ("he shudders exceedingly").

Although the document is startling in its rationality and empiricism and in the virtual absence of superstition and magic, Breasted did tend to overinterpret the papyrus; he wrote, for example, "this recognition of the localization of function in the brain . . . shows an astonishing early discernment which has been more fully developed by modern surgeons only within the present generations."[4] Perhaps Breasted's greatest flight of fancy was the suggestion that the papyrus was written by Imhotep, a famous physician who flourished about the time the original of the papyrus was written. There is absolutely no evidence that he wrote it, however; in fact, he is very unlikely to have done so, since the papyrus deals largely with battle wounds, and in the rigidly hierarchical world of Egyptian medicine, Imhotep was certainly not a battlefield surgeon.

He certainly was, however, an interesting figure in his own right.[5] He was the grand vizier of the third dynasty Pharaoh Zoser (2700–2650 BCE). A


Figure 1.2   A statuette of Imhotep as a demigod, a person of human origin who after his death was viewed as superhuman and worshipped. He achieved this status within 100 years of his death. As a demigod, Imhotep was typically represented with an open scroll on his lap. Statuettes like this one, from the Civica Raccolta Egizia in Milan, must have been common, as there are, for example, forty-eight in the Wellcome Historical Medical Museum, twenty-one in the Cairo Museum, about fifty in the Louvre, and ten in the Hermitage (Hurray, 1928).

contemporary inscription describes him as "chancellor of the king of Lower Egypt, the first after the King of Upper Egypt, administrator of the great palace, hereditary noble, high priest of Heliopolis, the builder, the sculptor." He is credited with designing the step pyramid of Sakkara, which was the tomb of Zoser, the first pyramid, and the first example of large-scale dressed stone architecture. He was also a priest, astrologer, and magician. Yet his fame as a physician seems to have impressed his contemporaries and later generations most of all. Miniature statues of him were used as amulets to ward off disease (figure 1.2), and eventually, he was deified as the Egyptian god of medicine (figure 1.3), an unusual honor even for a successful physician.[6, 7]

The Legacy of Egyptian Medicine

The period of the Middle Kingdom (starting about 2000 BCE) saw a gradual decline in the artistic, architectural, and intellectual creativity and vibrancy that characterized the earlier dynasties. The society became more rigid and hierarchical, intellectual life more dominated by priests, sculptures were largely copies of earlier works, and buildings more gigantic and grandiose. The rational and empirical spirit of medical practice that suffuses the Edwin Smith papyrus largely gave way to mysticism, religion, and elaborate speculations on the next world.[8] Yet, the fame of ancient Egyptian medicine lived on, in the *Odyssey,* in the Old Testament, among the presocratic physicians, in Galen, in the Cabala, and today, in any New Age boutique or "health food" store.

It is important to view the correlations between brain injury and symptom in the Smith papyrus in the context of ancient Egyptian medical theory and practice. We know that the Egyptians thought that the heart was the most important organ in the body, the seat of the mind, and the center of intellectual activities. This is clear from their philosophical and religious writings, and emphasized by their practice of mummification. Both Herodotus's descriptions[9] of the process of embalming and later examination of mummies show the contrast between the importance of the heart and brain in Egyptian thought. The first step in mummification was to scoop out the brain through the nostrils
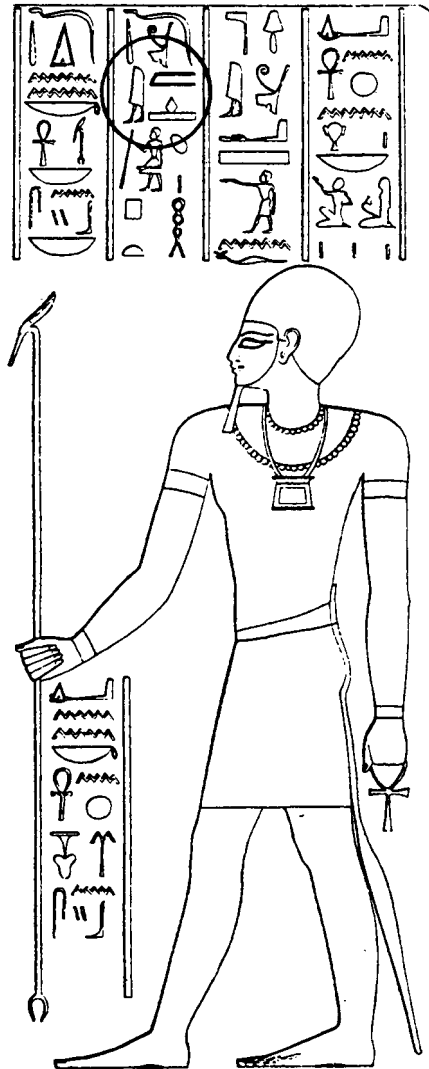
with an iron bar. In contrast, the heart (and most other internal organs) was either elaborately wrapped and replaced in the body or carefully stored in canopic jars near the body. As indicated in the *Book of the Dead,* ancient Egyptians considered it essential that the body be preserved and all the important organs be retained so that in the afterlife the body would be in a suitable condition for resurrection when the soul returned to it. Dead Pharaohs were prepared for their next life with everything but a brain.

The idea of the heart as the sensory and intellectual center of the body seems to have been universal, as it occurs also in other ancient civilizations such as Mesopotamia, Babylonia, and India.[10, 11] It is reported to be common among preliterature cultures,[12] as well, as illustrated by the oft-quoted remark of a Pueblo chief to C.G. Jung,[13] "I know you white men think with the brain. That accounts for your shortcomings. We red men think with the heart." Ancient Chinese medicine held rather more complicated views than the relatively simple heart-centered ones, but it also seems to have largely ignored the brain.[14] In fact, the role of the brain in perception and cognition does not appear to enter Chinese thought until the Jesuit Matteo Ricci's treatise (1595, in Chinese) on the art of memory, which he wrote as part of his campaign to convert the scholar class.[15]

As we will see, the view that the heart was the seat of sensation and thought was even held by the greatest of all savants, Aristotle. It persisted for over a millennium, together with the more prevalent theory that the brain, not the heart, was crucial for these functions.

Figure 1.3   Imhotep as the Egyptian god of medicine. The earliest known divine representation of Imhoptep dates from about 525 BCE, about twenty-five centuries his death. This painting is from the temple of Ptah at Karnak. Typical for a god, he wears a ceremonial beard and carries a scepter in his right hand and an ankh in his left, and a lion's tail is attached to his belt. The hieroglyphs representing an abbreviated version of his name are circled. The most famous temple devoted to Imhotep was at Memphis, and became a hospital and school of medicine and magic. By Ptolemaic times Imhotep was assimilated into the Greek god of medicine, Asclepias (Hurray, 1928).

Greek Philosopher-Scientists and
the Beginning of Brain Science

The approach to head injury of the Edwin Smith surgical papyrus stands out as a rock of empiricism in the sea of mysticism and superstition in which biological and medical writings in the Near East swam for about the next twenty-four centuries. Even so, one could hardly call the papyrus scientific. Science is not just craft or knowledge. Medical science is not just description of symptoms or treatment, and it is not just the absence of superstition or magic. Rather, science, or perhaps we should say formal, self-conscious science, is the assumption that the world can be understood by human reason, a mechanism that works in some consistent way with a regularity governed by a limited set of rules. In this scientific world view, the universe is not the playground of gods and ghosts acting in a capricious fashion, moved by passion and whim. Science is public: it demands rational, critical debate; it involves observation, description, and measurement; it carries the assumption that underlying principles or laws are potentially accessible by these methods.

This idea of formal science begins, at least in the West, with a group of Greek thinkers known as presocratic philosophers.[16] They used the term *physiologia* to describe themselves, which is perhaps best translated as "natural philosophers," rather than physiologists, physicists, or just philosophers.

Miletus, Cradle of Science

The earliest presocratics came from Miletus, one of a set of Greek city-states in Ionia, located on the west shore of modern Turkey (figure 1.4). What was special about this time and place that made it the cradle of science? The Ionians were a Greek people deriving from Crete. They were pioneers living in a new land and creating a new set of political institutions. The Bronze Age was becoming the Iron Age, enabling the cheap production of tools and weapons, and thus these city-states could maintain themselves, at least for a while, in the face of the empires to their East. By the sixth century BCE, Miletus was a great

Figure 1.4   Some of the important centers of classical medicine and biology.

port city that had established trading colonies throughout the Mediterranean and Black seas. It was a meeting of the sea lanes of Greek, Phoenician, and Egyptian traders and the overland caravans from the East as far as India and China. Its wealth derived both from its merchant ships and from local industries such as textiles and pottery. With its rich ferment of races, cultures, and ideas, Miletus was an interface between East and West.

At about this time, the rule of the landed aristocracy was breaking up and power was going to the merchant classes. They had the wealth to support speculation on the nature of the universe, and they had the desire for new techniques, particularly in math and astronomy. In addition, the development of alphabetic writing broke the monopoly held by the class of scribe-priests that characterized the cuneiform and hieroglyphic civilizations. The Ionian philosophers were neither prophets nor priests, but usually inventors, engineers, traders, or politicians, and often several of these at once. Slavery was not yet so pervasive that the ruling classes regarded manual labor with contempt.

Finally, in these new city-states there was debate about the nature of society and about the best form of government. These freedoms to question the nature of social institutions seem to have been part of the spirit of inquiry into the physical and biological world. All this ferment bubbled up into the beginning of the systematic examination of the universe that we call science.

Thales (ca. 583) was the first of the presocratic philosophers and thus is traditionally named the first (Western) scientist. He visited Egypt, returned with a number of geometric facts, and applied them to practical problems such as measuring the height of a building and the distance of a ship at sea. He seems to have been the first to conceive of the value of a general proposition or theorem in geometry. He is credited with such proofs as that the base angles of an isosceles triangle are equal and a circle is bisected by its diameter.[17]

Thales is most famous, however, for his idea that water was the basic and original substance. He thought that the earth was a flat disk floating on water, that water was all around the world, and that the heavenly bodies were water vapor. What is new or scientific about this? After all, the Egyptians, the Babylonians, and indeed all peoples have cosmologies about how things began, and water cosmologies are particularly common. For example, in one Babylonian legend[18] the creator is Marduk and "All the lands were sea . . . Marduk bound a rush mat upon the face of the waters, he made dirt and piled it on the rush mat." Thales's cosmology was fundamentally different from the Babylonian and other prescientific ones for two reasons. First, he left gods such as Marduk out of his scheme. Second, he sought a common element underlying all phenomena.

Alcmaeon of Croton, the First Neuroscientist

By the middle of the fifth century BCE there were three major centers of Greek medical science: Croton, in what is now southern Italy, Agrigentum on the south coast of modern Sicily, and Cos, an island off modern Turkey. The oldest was in Croton, and its most famous member was Alcmaeon.

Alcmaeon (ca. 450) was the first writer to champion the brain as the site of sensation and cognition.[19] He also seems to have been the first practitioner

of anatomic dissection as a tool of intellectual inquiry. His most detailed dissections and theories were on the senses, particularly vision. Alcmaeon described the optic nerves and noted that they came together "behind the forehead" (which is why, he opined, the eyes move together) and suggested that they were "light-bearing paths" to the brain. He removed and dissected the eye and observed that it contained water. Observations of what are now called phosphenes occurring after a blow to the eye led him to conclude that the eye also contained light (fire) and that this light was necessary for vision. This became the basis of theories of vision that persisted beyond the Renaissance. Indeed, Alcmaeon's idea of light in the eye was only disproved in the middle of the eighteenth century.[20]

Among the other presocratic philosopher-scientists who adopted and expanded on Alcmaeon's view of the functions of the brain were Democritus, Anaxagoras, and Diogenes[21] (all ca. 425). Democritus developed a version that became especially influential because of its impact on Plato. Specifically, Democritus taught that everything in the universe is made up of atoms of different sizes and shapes. The psyche (soul, mind, vital principle) is made up of the lightest, most spherical, and fastest-moving atoms. Although the psychic atoms are dispersed among other atoms throughout the body, they are especially numerous in the brain. Slightly cruder atoms are concentrated in the heart, making it the center of emotion, and still cruder ones are located in the liver, which consequently is the seat of lust and appetite. As discussed in the next section, this trichotomy developed into Plato's hierarchy of the parts of the soul. Then, much later, in Galen's medical theorizing, these three parts became the three pneumas of humoral physiology that dominated medical thought for centuries.[22]

Alcmaeon's view of the hegemony of the brain was not universal among the presocratic philosopher-scientists. For example, Empedocles (ca. 445), the leading member of the medical center at Agrigentum, the second great center of Greek medicine, taught that the blood was the medium of thought, and the degree of intelligence depended on the composition of the blood.[23] Thus, for him, the heart was the central organ of intellect and the seat of mental disorder, as it had been among Near Eastern civilizations.

———

The Hippocratic Doctors

The third great center for the teaching and practice of medicine in the fifth century BCE was the island of Cos, and its most famous member was Hippocrates (ca. 425). The first large body of Western scientific writings that have survived is the Hippocratic corpus. Although there is no question that Hippocrates was a real historical figure, it is not clear which of the works called Hippocratic he actually wrote. The corpus consists of over sixty treatises that vary enormously in style and technical level, and that were not written by one author or even in one period. It may have been the remaining part of the medical library at Cos or, alternatively, it may have been assembled some time later in Alexandria.[24]

Unlike Alcmaeon and the Croton School, the Hippocratic doctors did not practice dissection and their knowledge of anatomy was slight. Like presocratic thinkers in general, however, they rejected supernatural causes of disease and sought natural explanations through observation and extended case studies. Such detailed studies of disease processes were rare until after the Renaissance, and even then they tended to be advertisements for the skill of the physician rather than empirical studies.

The Hippocratic work of greatest relevance to brain function is the famed essay "On the Sacred Disease," that is, epilepsy. Probably designed as a lecture for laymen, it opens with an homage to reason and a rejection of superstition[25]:

> I do not believe that the "Sacred Disease" is any more divine or sacred than any other disease, but, on the contrary, has specific characteristics and a definite cause. . .
>
> It is my opinion that those who first called this disease "sacred" were the sort of people we now call witch-doctors, faith-healers, quacks, and charlatans. These are exactly the people who pretend to be very pious and to be particularly wise. By invoking a divine element they were able to screen their own failure to give suitable treatment and so called this a "sacred" malady to conceal their ignorance of its nature.

The author has no doubt that the brain is the seat of this disease. As to the general functions of the brain, he is equally clear:

> It ought to be generally known that the source of our pleasure, merriment, laughter, and amusement, as of our grief, pain, anxiety, and tears, is none other than the brain. It is specially the organ which enables us to think, see, and hear, and to distinguish the ugly and the beautiful, the bad and the good, pleasant and unpleasant . . . It is the brain too which is the seat of madness and delirium, of the fears and frights which assail us, often by night, but sometimes even by day; it is there where lies the cause of insomnia and sleep-walking, of thoughts that will not come, forgotten duties, and eccentricities.

Furthermore, he states that neither the diaphragm nor the heart has any mental functions, as some claimed: "Neither of these organs takes any part in mental operations, which are completely undertaken by the brain."

What then is the cause of epilepsy, the so-called sacred disease? It attacks only the phlegmatic, those with an excess of phlegm or mucus.

> Should . . . [the] . . . routes for the passage of phlegm from the brain be blocked, the discharge enters the blood-vessels . . . this causes aphonia, choking, foaming at the mouth, clenching of the teeth and convulsive movements of the hands; the eyes are fixed, the patient becomes unconscious and, in some cases, passes a stool . . . All these symptoms are produced when cold phlegm is discharged into the blood which is warm, so chilling the blood and obstructing its flow.

These extracts typify Hippocratic medicine: absence of superstition, accurate clinical description, ignorance of anatomy, and physiology that is largely a mixture of false analogy, speculation, and humoral theory. Perhaps the entire history of medicine can be viewed as the narrowing of the gap between the

medical empiricism characteristic of the School of Cos and the knowledge of structure and mechanism sought by the School of Croton.

Finally, it should be noted that the Hippocratic oath not only had no connection with the Hippocratic School but is quite deviant from mainstream Greek medical and social practice in several ways.[26] In its original form it forbids both suicide and abortion, but, in fact, neither was censured or illegal in Hippocratic times, or more generally, in classical Greece and Rome. The oath also forbids surgery. Although surgical intervention was not common, it was definitely carried out by Hippocratic doctors to drain pus, set fractures, and reduce dislocations. Finally, Hippocratic doctors, like most others before and after, taught for a fee, despite the oath's injunctions against such practices. The so-called Hippocratic oath seems to have derived from a later secret neopythagorean sect that was antisuicide, antiabortion, and antisurgery. It may then have become popular with the rise of Christianity, since the Church was opposed to suicide and abortion, and with the separation of medicine from the "lower craft" of surgery.

Plato: Antiscientist

Plato (427–347 BCE) was unsympathetic to what we and the presocratics meant by science: the empirical investigation of the universe. Indeed, because of the beauty and subtlety of his dialogues, and his towering reputation outside of science, particularly in ethics and politics, Plato can be considered one of the most important ideological opponents of natural science of all time. Furthermore, he dominated European philosophy until about the twelfth century, when Aristotle began to filter into Europe through Muslim civilization. As we will see later, Aristotle, unlike Plato, was very heavily involved in and enthusiastic about scientific investigation.

Plato was born in Athens at a time when that city was the center of the Greek intellectual world. He came from an aristocratic background and was Socrates's most famous student. After Socrates was executed for subversion by the Athenian democracy, Plato left Athens and traveled widely for about a dozen years. He then returned to Athens at the age of forty and founded a

school, the Academy, where he taught primarily politics and ethics for another four decades until his death.

Whereas the presocratic philosophers sought laws independent of the supernatural, Plato made "natural laws subordinate to the authority of divine principle," as Plutarch put it. Furthermore, whereas, most of the earlier natural philosophers stressed observation over reason alone, Plato took the opposite view[27]:

> [The universe is] to be apprehended by reason and intelligence, but not by sight (*Republic,* 529).

> . . . If we are to know anything absolutely we must be free from the body and behold actual realities with the eye of the soul alone (*Phaedo,* 66).

In the *Republic* (529–30) Plato ridicules the observational approach of the astronomer:

> The starry heavens . . . are to be apprehended by reason and intelligence, but not by sight . . . a true astronomer will never imagine that the proportions of night, day or both to the month, or of the month to the year . . . and any other things that are material and visible can also be external and subject to no deviation—that would be absurd; and it is equally absurd to take so much pains in establishing their exact truth.

He is similarly opposed to the experimental acoustics of the Pythagoreans, as in this exchange between Glaucon and Socrates (*Rep.,* 531):

> *Socrates:* The teachers of harmony compare the sounds and consonances which are heard only, and their labor, like that of the astronomers is in vain.

Glaucon: Yes, by heaven! And it is as good as a play to hear them talking about their condensed notes, as they call them; they put their ears close alongside of the strings like persons catching a sound from their neighbor's wall—one set of them declaring that they distinguish an intermediate note and have found the least interval which should be the unit of measurement; the others insisting that the two sounds have passed into the same—either party setting their ears before their understanding.

Socrates: You mean those gentlemen who tease and torture the strings and rack them on the pegs of the instrument . . . they too are in error, like the astronomers; they investigate the num- bers of the harmonies which are heard, but they never attain to problems.

Plato's rejection of the possibility of a biology of behavior is similarly total, as in this ridicule of Anaxagoras by the now condemned Socrates in *Phaedo* (97–99):

Then I heard someone reading, as he said, from a book of Anaxagoras, that mind was the disposer and cause of all . . . What expectations I had formed, and how grievously was I disappointed! As I proceeded, I found my philosopher altogether forsaking mind or any other principle of order, but having recourse to air, and ether, water, and other eccentricities. I might compare him to a person who began by maintaining generally that mind is the cause of the actions of Socrates, but who, when he endeavored to explain the causes of my several actions in detail, went on to show that I sit here because my body is made up of bones and muscles; and the bones, he would say, are hard and have joints which divide them, and the muscles are elastic, and they cover the bones, which have also a covering or environment of flesh and skin which contains them; and as the bones are lifted at their joints by the

contraction or relaxation of the muscles, I am able to bend my limbs, and this is why I am sitting here in a curved posture—that is what he would say; and he would have a similar explanation of my talking to you, which he would attribute to sound, and air, and hearing and he would assign ten thousand other causes of the same sort, forgetting to mention the true cause, which is, that the Athenians have thought fit to condemn me, and accordingly I have thought it better and more right to remain here and undergo my sentence; . . . to say that I do as I do because of my muscles and bones and that this is the way in which mind acts, and not from the choice of the best, is a very careless and idle mode of speaking.

Whereas Anaxagoras and the other presocratics were searching for a mechanistic cause of behavior, Plato's conception of cause was a teleological one, or, perhaps it might be better called an ethical one.

Plato did more than satirize the methods and goals of the presocratics. He offered an alternative program. He taught that things we see are only superficial appearances, shadows in a cave, and hardly worth serious consideration. Corresponding to each kind of object are Ideas or Forms that are both the origin and the cause of objects that we see. For example, there are various cups in the sensory world, all of which are different, imperfect, and transient. In contrast, the Idea or Form of a cup is perfect and eternal—the archetype of all cups past, present, and future. The goal of the philosopher is to understand these ideas and especially the higher ones such as Virtue, or the highest of all, the Idea of God. The philosopher must escape the tyranny of sensory experience and empirical knowledge and climb out of the cave in order to reach the higher realities of true knowledge (*Rep.,* VII).

Plato's views on the brain were set out in most detail in the *Timaeus* (pp. 69–71), his cosmological essay that was extraordinarily influential in the Middle Ages. The soul, which is prior to the body, is divine and comes from the soul of the universe. It is divided into three parts, following Democritus's three levels of atoms. Reason or intellect is the highest and immortal part and

17

lies in the brain, which controls the rest of the body. In his words "It is the divinest part of us and lords over all the rest." The higher division of the mortal soul lies in the heart. To avoid it polluting the divine soul a neck was built between the two. Appetite, the lowest division, was placed in the liver, "tethered like a beast . . . as far as possible from the seat of counsel" in the head. In the *Republic* (435–442) the three parts of the soul are compared with the three classes of Plato's Utopia. Just as the divine soul or reason must be kept separate from base sensation and appetite, so must rulers be protected from contamination by the masses.

The *Timaeus* did convey presocratic and Hippocratic ideas about the brain, body and, more generally, the universe to the Middle Ages It was particularly successful in spreading Plato's teleology and his rejection of sensation and observation in favor of reason. Thus, modern historians of science have referred to its role in the history of science as "nefarious," "essentially evil," and "an aberration."[28]

Aristotle on Brain and Heart

Aristotle's name is invariably linked to philosophy; indeed, for centuries he was known as "The Philosopher." He was also the leading biologist of classical antiquity and one of the greatest biologists of all times.[29] He is usually considered the founder of comparative anatomy, the first embryologist, the first taxonomist, the first evolutionist, the first biogeographer, and the first systematic student of animal behavior. Not only was he important to the development of biology, but his experience in biological research played an essential role in his own development as a thinker. Over a quarter of his writings were on biology, and his biological work was crucial in distancing him from his teacher, Plato.[30] Beyond biology, he was a true universal genius, writing with permanent impact on such subjects as logic, metaphysics, art, theater, psychology, economics, and politics. His dominating influence on the physical and biological sciences, however, largely disappeared in the last several centuries. Perhaps Aristotle's most egregious scientific error fell in the domain we now call neuroscience: he

systematically denied the controlling role of the brain in sensation and movement, giving this function instead to the heart.

Aristotle was born in 384 BCE in Stageira to a medical family. His father, who had been personal physician to Amyntas II, King of Macedonia (father of Philip II), died at a young age, and Aristotle's early education was probably provided by his father's fellow physicians. In those days, as now, a well-educated physician needed some general culture, so at the age of seventeen he was sent off to Plato's Academy in Athens. He stayed there for twenty years and never did begin his medical training.

When Plato died in 347, his nephew took over the Academy, and Aristotle left Athens with some friends for the island of Lesbos and the adjacent mainland where he apparently spent much time studying marine biology. Philip then appointed him private tutor to his son, Alexander, until, at age sixteen, Alexander became regent of Macedonia and had little time for further academic studies. Aristotle returned to Athens in 335 and founded a new school and research center, the lyceum. It received financial support from Alexander who, according to Pliny, also sent it biological specimens as he proceeded to conquer the known world. Thirteen years later and a few months before his death, Aristotle was driven from Athens by the ascent of anti-Alexandrian factions. Aristotle, or so Diogenes Laertius and other ancient authorities tell us, was small, lisping, sarcastic, arrogant, elegant, and happily married.[31]

Now let us turn to Aristotle's views on the brain, which have embarrassed and puzzled historians and scientists since Galen of Pergamum, who "blushed to quote" them.[32] Aristotle believed that the heart, not the brain, was the center of sensation and movement[33]:

> And of course, the brain is not responsible for any of the sensations at all. The correct view [is] that the seat and source of sensation is the region of the heart. (PA656a)

> . . . the motions of pleasure and pain, and generally all sensation plainly have their source in the heart. (PA666a)

> . . . all sanguineous animals possess a heart, and both movement and the dominant sense perception originate there. (SW456a)

> . . . in all sanguineous animals the supreme organ of the sense-faculties lies in the heart. (YO469a)

Table 1.1 summarizes Aristotle's arguments.

Aristotle was well aware of the earlier claims for the dominance of the brain as opposed to the heart, such as those of Alcmaeon, Plato, and Hippocrates, and repeatedly argues against these "fallacious" views (PA656a, b). For example, he claims his predecessors say that there is a scarcity of flesh around the brain so that sensation can get through. But, Aristotle answers, the fleshlessness is in accordance with the cooling function of the brain; furthermore, the back of the head is also fleshless, but it has no sense organs. The earlier theorists observed that the sense organs are placed near the brain, but Aristotle gives a number of alternative reasons for that. For example, the eyes face forward so that we can see along the line we are moving, and ". . . it is reasonable enough that the eyes should always be located near the brain, for the brain is fluid and cold, and the sense organ of sight is identical in its nature with water." The ears are located on the sides of the head to hear sounds from all directions. In any case, some animals hear and smell but do not have these organs in their head. Furthermore, sense organs are in the head because the blood is especially pure in the head region, which makes for more precise sensation.

Galen and many subsequent historians of medicine were somewhat unfair in maintaining that Aristotle simply dismissed the brain as cold and wet. Rather, for Aristotle the brain was second only to the heart in importance and was essential to the functioning of the heart. In fact, the two formed a unit that controlled the body. The heart, which is naturally hot, he determined, must be counterbalanced, in order to attain the mean, the true and the rational position. Thus, the brain, which is naturally cold, "tempers the heat and seething of the heart" (PA652b):

Table 1.1   Aristotle's Arguments for the Heart and Against the Brain as the Center for Sensation and Movement

Heart	Brain
1. Affected by emotion (PA669a)	1. Not affected (PA652b,656a)
2. All animals have a heart or similar organ (GA771a, PA665b)	2. Only vertebrates and cephalopods have one, and yet other animals have sensations (PA652b)
3. Source of blood which is necessary for sensation (PA667b)	3. Bloodless and therefore without sensation (HA494a, 514a, PA765a)
4. Warm, characteristic of higher life (SS439a)	4. Cold (PA652, HA495a5)
5. Connected with all the sense organs and muscles, via the blood vessels (GA744a, HA492a, 469a, GA781a)	5. Not connected with the sense organs or the connection is irrelevant (PA652b, HA503b)
6. Essential for life (YO469a, PA647a)	6. Not so (HA532a, GA741b)
7. Formed first, and last to stop working (GA741b)	7. Formed second (GA674b)
8. Sensitive (SS439a, PA669a)	8. Insensitive: if the brain of a living animal be laid bare, it may be cut without any signs of pain or struggling (PA652b, 656a)
9. In a central location, appropriate for its central role (PA670a)	9. Not so

For if the brain be either too fluid or too solid, it will not perform its office, but in the one case will freeze the blood and in the other will not cool it at all, and thus, cause disease, madness and death. For the cardiac heart and the center of life is most delicate in its sympathies and is immediately sensitive to the slightest change or affection of the blood or the outer surface of the brain. (PA653b)

Aristotle gave the following explanations for the cold nature of the brain: (a) the blood it contains in its vessels is thin, pure, and easily cooled (SS444a); (b) the vessels on and in the brain are very thin and permit evaporation, cooling

the brain (SW458a); and (c) when the brain is boiled and the water in it evaporates, hard earth is left, indicating that the brain is made of water and earth, both of which are intrinsically cold (PA653a). So that the brain does not become completely cold, it receives a moderate amount of heat from branches of the aorta and the vena cava that end in the membrane that surrounds the brain (PA652b). When the brain cools the hot vapor reaching it from the heart, phlegm is produced. This idea that the brain produces phlegm is also found in "On the Sacred Disease," as noted above, and is fossilized in our own word "pituitary," coming from the Latin *pituita,* which means phlegm.

Man's brain, according to Aristotle, is the largest and moistest brain for its size (HA494b, PA653a). This is because man's heart is hottest and richest and must be counterbalanced, for man's superior intelligence depends on the fact that his larger brain is capable of keeping the heart cool enough for optimal mental activity (PA648a, 650b–51a). [Woman's brain is smaller than man's (PA653b), a view of Aristotle's that persisted much longer than his view of the mental functions of the heart.] Thus, Aristotle did not merely dismiss the brain as cold and wet. Indeed, it would have been unlike him to dismiss any organ, as he thought none was made without a function to perform. Rather, he believed the brain played an essential, although subordinate, role in a heart-brain system that was responsible for sensation; indeed, man's superior intelligence is credited to his large brain.

Although Aristotle may have not ignored the brain quite as much as is often claimed, it remains puzzling why he made such a startling error and took such a different view from Alcmaeon and the Hippocratic doctors, and above all from his teacher Plato. Aristotle had adduced anatomical, physiological, comparative, embryological, and introspective evidence for his notion of brain function. But an essential approach was absent, namely, the clinical approach, the study of the brain-injured human. The two champions of the hegemony of the brain, Alcmaeon and Hippocrates, were both practicing physicians. The evidence that both gave in support of their opinions was strictly clinical. Since no evidence of systematic experiments on the brain and nervous system appears until Galen in the second century, the accidents of nature were the only sources of information about the function of the brain. It is hard to conceive of

Aristotle, in the course of his strictly zoological observations and dissections, coming across evidence strongly contradicting his theory of the brain and heart.

It seems clear that he never dissected a human, and of the forty-nine animals he did dissect, from elephant to snail, the majority were cold blooded,[34] as were the two, chameleon and turtle, that he obviously vivisected (HA503b, YO486b). These did indeed have cold and wet brains, and the connections of the sense organs with the heart (blood vessels) might have seemed more prominent than those with the brain (nerves). On the other hand, he dissected enough vertebrate brains to describe the two covering membranes (HA494b, 495a), the two symmetrical halves (PA669b), and a "small hollow" in the middle (HA495a), perhaps the lateral ventricles. Finally, it should be noted that Aristotle never localized such psychological faculties as imagination, reasoning or memory in the heart or any place else, but instead viewed them as activities of the whole organism.

Despite (or perhaps because of) his father's profession, Aristotle at no time seemed interested in medicine or medical writing. Indeed, medicine appears to be one of the few things that did not concern this polymath. And, in the fourth century BCE, the study of the effects of damage to the human brain was the most likely way of reaching a "more correct" conception of the brain than Aristotle had. In fact, one of the few places where he approaches a correct view of brain function is in the rare "clinical" passage quoted above (PA653b), in which he suggests that mental disease follows from a malfunctioning of the brain's cooling functions. As discussed in detail below, 600 years later, Galen's observations of human head injuries led him to perform the first recorded experiments on the brain (using piglets), and his observations of spinal injuries to gladiators led directly to his brilliant series of experiments on the effects of spinal cord transection. Even today, it is often primarily clinical data that inspire experiments on animal brains. Aristotle was a pure biologist, not an applied one, and in his day the methodology of academic biology was incapable of defining the brain's actual role.

Alcmaeon and the Hippocratic doctors' theory of the dominance of the brain in mental life soon prevailed. It was transmitted through Plato's *Timaeus* to the Arab world and then to medieval and Renaissance Europe.[35] Yet,

Aristotle's advocacy of the hegemony of the heart persisted alongside. A common resolution was to combine the two views. For example, the great Arab Aristotelian and physician Ibn Sina (Avicenna) did this by placing sensation, cognition, and movement in the brain, which in turn he believed was controlled by the heart.[36] Similarly, according to the thirteenth-century Hebrew encyclopedist Rabbi Gershon ben Schlomoh d'Arles,[37] the brain and heart share functions, so "when one . . . is missing, the other alone continues its activities . . . by virtue of their partnership." As Scheherazade[38] tells it on the 439th night, when the Caliph's savant asks the brilliant girl Tawaddud, "where is the seat of understanding," she answers, "Allah casteth it in the heart whence its illustrious beams ascend to the brain and there become fixed." And Portia's song in the *Merchant of Venice* asks,

> Tell me where is fancie bred,
> Or in the heart or in the head.

Despite his fallacious understanding of brain function, Aristotle actually facilitated the subsequent development of the study of the brain. At the most general level, his stress on the importance of dissection, coupled with his prestige, encouraged others to carry out anatomical studies.[39] More specifically, he played several roles, albeit indirect ones, in the founding of the great Museum at Alexandria, and it was here that systematic human neuroanatomy started.

The Alexandrians and the Beginning of Human Neuroanatomy

Neither the presocratics nor the Hippocratic doctors referred specifically to the convolutions of the cerebral cortex. The first to do so was Praxagoras of Cos[40] (ca. 300) and his student Philotimos. Praxagoras's primary claim to fame was that he was among the first to distinguish arteries and veins clearly and to use the pulse as a major diagnostic technique. He also referred to the "long flexuosities and winding and folding of the convolutions" of the brain. How-

ever, the functions of these convolutions were not considered until the beginning of the study of human anatomy in the Museum at Alexandria.

The museum was founded at the end of the fourth century BCE by Ptolemy I, the first Greek ruler of Egypt. It was a vast state-supported institute for research, perhaps like some combination of the National Institutes of Health and the Institute for Advanced Study or All Souls College. Over 100 professors lived communally and had their salaries and expenses paid by the government. The museum contained lecture and study rooms, an astronomical observatory, a zoo, a botanical garden, and dissecting and operating rooms.[41] Its huge library was named a wonder of the ancient world.

In several ways, the museum was a continuation and expansion of Aristotle's Lyceum.[42] First, Ptolemy I had been a young pupil of Aristotle, along with Alexander. Presumably, Aristotle stressed biology in their tutorials since that was his major interest at the time. Second, Demetrius and Strato, who were both students of Theophrastus, Aristotle's long-term collaborator and his successor as head of the Lyceum, were called to Alexandria by Ptolemy to advise him on the organization of the museum. (Ptolemy tried unsuccessfully to hire Theophrastus himself.) Third, the core of the library's collection is thought to have been gathered by Demetrius, at least in part, from Aristotle's own collection. As Strabo, the first-century historian and geographer, later put it, "Aristotle taught the kings of Egypt how to organize a library."[43]

Thus, it was in the shadow of Aristotle that the great museum anatomists, Herophilus (ca. 270) and then Erasistratus (ca. 260), began the systematic study of the structure of the human body.[44] The immediate cause of this extraordinary surge in anatomy in second-century Alexandria was that it was the first time and place in which open dissection of the human body could be carried out. Previously, dissections had been done only on animals. The Greek reverence (and dread) of the dead human body had made its dissection quite impossible. What made Alexandria different? A number of factors seem to have come together.[45]

One was that Herophilus and Erasistratus had the full support of a totalitarian regime determined to glorify itself through the achievement of its

scientists. As absolute rulers in a foreign land, the Ptolemys brought few inhibitions with them. A second factor must have been that dissection of the human body for the purposes of mummification had been practiced in Egypt for centuries, and thus the general cultural background undoubtedly helped make human dissection possible. However, it is very unlikely that Greek anatomists had any contact with Egyptian embalmers, as the social gap between the Greeks in Alexandria and the natives surrounding them seems to have been enormous.[46] Another factor may have been changes in philosophical attitudes toward dying and the human corpse that were becoming common by this time: Aristotle had taught that after death the body was no more than a physical frame without feeling or rights.

The uniqueness of the Alexandria-anatomy nexus is revealed by the fact that not only was human dissection first practiced in that city, but this was the first and virtually the only place where human vivisection was systematically carried out for scientific purposes.[47] As Celsus, the Roman historian of medicine, put it[48]:

> It is therefore necessary [for medical students] to dissect the bodies of the dead and examine their viscera and intestines. Herophilus and Erasistratus, they say, did this in the best way by far when they cut open men who were alive, criminals out of prisons, received from kings. And while breath still remained in these criminals, they inspected those parts which nature previously had concealed . . . Nor is it cruel, as most people maintain, that remedies for innocent people of all times should be sought in the sacrifice of people guilty of crimes, and only a few such people at that.

Vivisection of humans for scientific research was never systematically practiced again until the Germans and Japanese did it in World War II. Even the dissection of human cadavers disappeared in the West until it was revived in the new medieval universities in the thirteenth century, and then initially only for forensic, not medical or scientific, purposes.[49]

Both Herophilus and Erasistratus were particularly interested in the brain. They provided the first detailed, accurate descriptions of the human brain including the ventricles.[50] Like Alcmaeon and the Hippocratic doctors before them, they had no question about the brain's dominant role in sensation, thought, and movement.

Herophilus claimed that the fourth ventricle was the "command center," a view later rejected by Galen,[51] who stressed the importance of brain tissue itself. Herophilus compared the cavity in the posterior floor of the fourth ventricle with the cavities in the pens that were in use in Alexandria at the time, and it is still called calamus scriptorius, "reed pen," or sometimes calamus Herophili.

Erasistratus likened the convolutions of the brain to the coils of the small intestine, a comparison that persisted into the nineteenth century, often with Erasistratus's name still attached. Indeed, in the nineteenth century the cerebral convolutions were often called the "enteroid processes," and many drawings of the cortex looked more like the small intestine than like the brain[52] (see figures 1.13 and 1.14). Erasistratus compared the brain convolutions of a number of animals, including hares and stags, with those of humans. From these comparisons, he attributed the greater intelligence of humans to their more numerous convolutions. Galen[53] later ridiculed Erasistratus's correlation between intelligence and the number of convolutions by noting that a donkey had more brain convolutions than humans. However, Galen and possibly Erasistratus may have been referring to the convolutions of the cerebellum rather than those of the cerebrum. In any case, Galen's sarcasm had an extraordinarily pervasive influence and was repeatedly quoted over the next 1500 years, by Vesalius (1543) among others. It seemed to have inhibited any serious interest in the cerebral convolutions until Willis in the seventeenth century.

Erasistratus traced both sensory and motor nerves into the brain and was reported to have made experiments on the living brain to determine its functions, but no accounts of this work survive. He certainly had a understanding of the nature of research, as reflected in this quotation from his work *On Paralysis*[54]:

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> Those who are completely unused to inquiry are in the first
> exercise of their mind, blinded and dazed and straightway leave off
> the inquiry from mental fatigue and an incapacity that is no less
> than that of those who enter races without being used to them.
> But the man who is used to inquiry tries every possible loophole
> as he conducts his research and turns in every direction and so far
> from giving up the inquiry in the space of a day, does not cease
> his search throughout his life.

After Herophilos and Erasistratus Alexandrian medicine declined rapidly into various schools that fought over arcane medical theory.[55]

Galen of Pergamon, Prince of Physicians

Galen (129–199 CE) was the most important figure in ancient medical science and is our best source of information about it. He represents its peak; it was through his eyes that the medieval world saw the human body, and that today we see the panorama of classical anatomy, physiology, and medicine.[56] His principal writings (figure 1.5) on the brain that have been translated into English are in *On the Usefulness of the Parts of the Body, On Anatomical Procedures,* and *On the Doctrines of Plato and Hippocrates.*[57]

Galen provided an accurate and detailed account of the anatomy of the brain. Indeed, quite how accurate was not appreciated until recently, when neurohistorians realized that his descriptions fit the brain of the then much more available ox than they do that of the human.[58] He described the ventricles in considerable detail because they were crucial in his physiological system. The ventricles were the site of storage of psychic pneuma (animal spirits), which was the active principle of both sensory and motor nerves and the central nervous system.

On the basis of his extensive clinical experience at the gladiatorial school in Pergamon, Galen distinguished sensory and motor nerves. He believed the

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former traveled to the anterior part of the brain and the latter came from the posterior part, a clear anticipation of Müller's doctrine of specific nerve energies (the idea that the functions of a nerve are determined by its central connections). He viewed sensation as a central process, since he knew from his clinical data as well from his animal experiments that sensation could be impaired by brain injury even when the sense organs were intact.

Although the ventricles, particularly the anterior ventricle, were important as a source of psychic pneuma, Galen located the soul not there but in the solid portions of the brain. Among the arguments for this was his demonstration that when brain lesions penetrated to the ventricles, death did not invariably result even if both sensation and movement were lost. Thus, he placed both the soul and higher cognitive functions in the solid portions. Regardless, he ridiculed Erasistratus's correlation between intelligence and the number of brain convolutions, with amazingly long-lasting effects, as mentioned above.

Galen described the optic chiasm and tract, and observed that the tract was "intimately and firmly connected . . . with a part of the brain of a peculiar kind, different in boundaries and circumference from the other parts," presumably the lateral geniculate body. He thought that the optic nerves originated in "the anterior part of the lateral ventricles" (figure 1.6) and noted that experimental pressure on this region of the anterior ventricle resulted in blindness.

A number of Galen's experiments concerned the effects on behavior of experimental lesions of both the central and the peripheral nervous system. Perhaps the most famous was his demonstration that section of the recurrent laryngeal nerve eliminates the ability of a pig to vocalize. This experiment is illustrated in the bottom panel of the frontispiece to the sixteenth-century collection of his works shown in figure 1.5.

At about the time of Galen's death in 199, Greek science and medicine died. People preferred to believe than to discuss, critical faculty gave way to dogma, interest in this world declined in favor of the world to come, and worldly remedies were replaced by prayer and exorcism.

❦ GALENI ❦

PRIMA CLASSIS HVMANI

corporis originẽ, formationem, diſſectionem,
temperaturam, facultates, facultatumq̃
cum actiones omnes, tum inſtrue
menta & loca ſingula
complectitur.

LIBRORVM TITVLOS ET DILIGEN
TIAM SEQVENS PAGINA
DEMONSTRABIT.

Τὸ φυσιλογοῦσι.

Cum Decreto Summi Pont. Senatuſq̃
Veneti per annos . X V.

Apud hæredes Luceantonij Iuntæ Florentini
VENETIIS   M. D. XLI.

The Medieval Cell Doctrine of Brain Function

The central feature of the medieval view of the brain was the localization of mental faculties in the organ's ventricles. In its basic form, the faculties of the mind (derived from Aristotle) were distributed among the spaces within the brain (the ventricles described by Galen). The lateral ventricles were collapsed into one space, the first "cell" or small room. It received input from all the sense organs and was the site of the *sensus communis,* or common sense that integrated across the modalities. The sensations yielded images, and thus, fantasy and imagination were often located here too. The second or middle cell was the site of cognitive processes: reasoning, judgment, and thought. The third cell or ventricle was the site of memory (figure 1.7).

Although the basic doctrine remained intact for about 1200 years, there were some minor developments.[59] By the tenth century the original static localization shifted to a more dynamic process analogous to digestion. Sensory inputs were made into images in the first cell and were then transferred to the second cell, whose central location made it warmer, appropriate for further processing (cf. digestion) into cognition. Leftover thoughts were then trans–

Figure 1.5   Title page of the *Omnia Opera* of Galen published in 1541 in Venice. Among the famous anatomists who edited parts of this edition were John Caius, first Master of Gonville and Caius College, Cambridge; John Linacre, founder of the Royal College of Physicians; Jacob Syvius, Vesalius's teacher in Paris and later his archrival; and Vesalius himself, who edited the centrally important *On Anatomical Procedures,* among other Galenic works in the collection.

The eight scenes clockwise from the top are Galen removing his hat and bowing to a distinguished patient; Galen predicting the crisis in a patient's illness; Galen diagnosing lovesickness, which presumably refers to a case in which he revealed sophisticated understanding of the diagnosis of this malady (Mesulam and Perry, 1972); Galen bleeding a patient; Galen's brilliant demonstration in the pig that cutting the recurrent laryngeal nerve eliminates vocalization (among the dignitaries watching is Boethus, an ex-consul who once commissioned an account of this experiment) (Gross, 1998); Galen palpating the liver; Galen and his teachers; and Aesculapius, in a dream, urging Galen's father to send him to medical school. (Courtesy of Yale University, Harvey Cushing/John Hay Whitney Medical Library.)
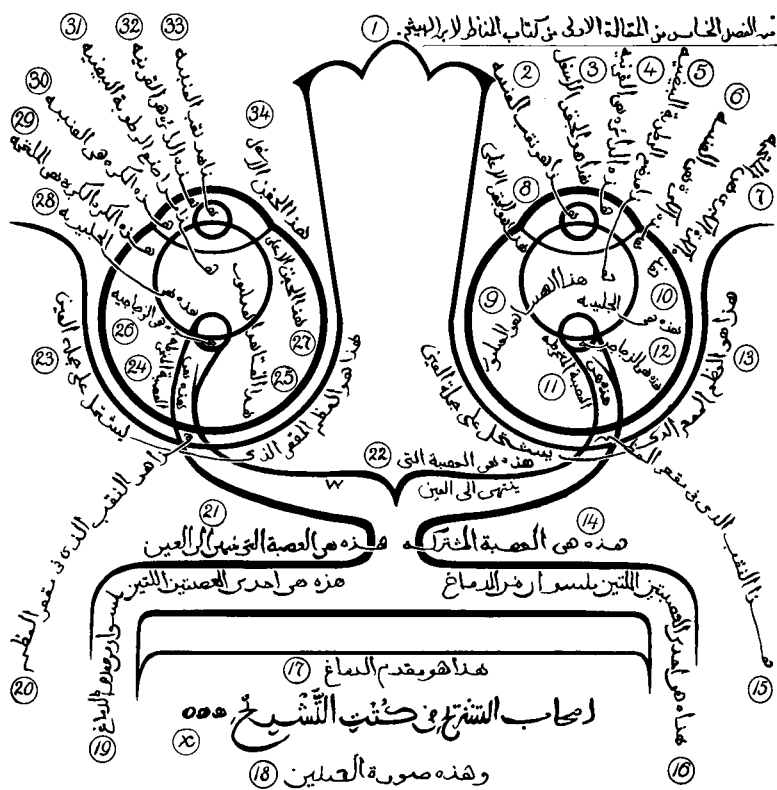
Figure 1.6   The oldest surviving illustration of the eye and visual system, from Ibn al-Haythem's (965–1039) *Book of Optics,* from a copy made in 1083, recopied and labeled by Polyak (1941). Since neither al-Haythem nor earlier Arab medical scientists practiced dissection, and since the content of this diagram is so consistent with Galen's description, Polyak suggests that it is a copy of a Greek original by or derived from Galen. Some of the keys to the numbers: 17, "the anterior portion of the brain"; 16, 19, "one of the two nerves which arise from the anterior portion of the brain"; 14, "the joining [associating] nerve" (i.e., optic chiasm); 21, 22, "the nerve which terminates in the eye." Al-Haythem was known in Europe as Alhazen and the Latin version of his *Book of Optics* (*De Aspectibus*), published in 1572, was the most influential treatise on physiological optics in Europe for at least the next 200 years (Gross, 1981).
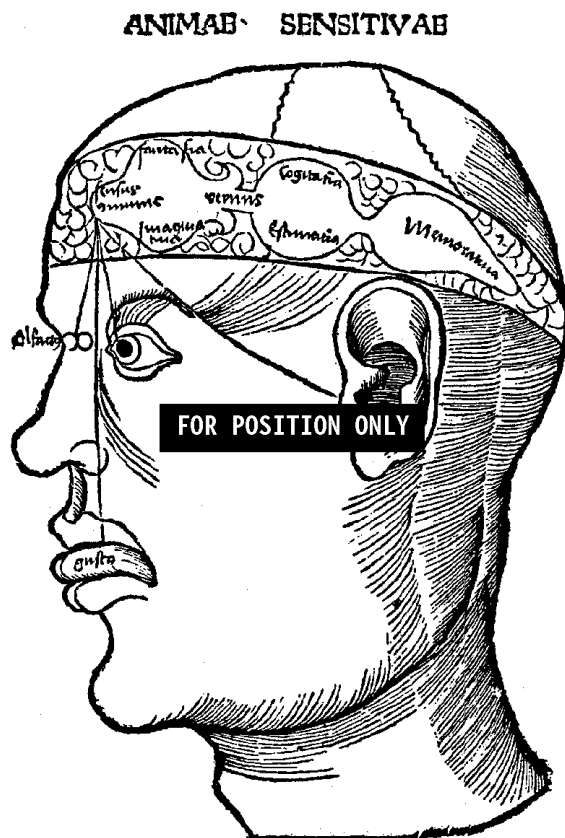
ANIMAE· SENSITIVAE

Figure 1.7   The organs of the "sensitive soul" (*anima sensitiva*) from G. Reisch (1503), *Margarita Philosophica* (*Pearls of Philosophy*), one of the first modern encyclopedias. This illustration of ventricular doctrine was copied by many subsequent illustrators as may be seen in the many versions in Clarke and Dewhurst (1996).

Messages from the organs of smelling, tasting, seeing, and hearing are united in the common sense (*sensus communis*) in the first ventricle, in which fantasy (*fantasia*) and imagination (*imaginativa*) also reside. The first ventricle communicates with the second by the vermis. Thought (*cogitativa*) and judgment (*estimativa*) are located in the second ventricle. Memory (*memoria*) is in the third ventricle. The curlicues around the ventricles may represent cerebral convolutions. As described in the text, Vesalius ridiculed this particular figure.

ferred to the third cell for storage. These transfers of information occurred through passages between the ventricles that had been described by Galen. Another shift was in the quality of the drawings of the heads in which the ventricles lay, from the crude medieval conceptual representations to the sophisticated pictorial representations of the Renaissance by such masters as Durer and Leonardo (see chapter 2).

How did the cell doctrine arise and why was it so attractive to the medieval and early Renaissance mind? It developed out of a curious amalgam of Greek medical theory and practice and ideological concerns of the early church fathers. Although Galen had described the ventricles in great detail, he localized the mental faculties in the solid portions of the cerebrum. The fourth-century Byzantine Poseidonus developed this idea further.[60] He seems to have been the first to report in detail on the effects of localized brain damage in humans. He said that lesions of the anterior brain substance impaired imagination and lesions of the posterior brain impaired memory, but damage to the middle ventricle produced deficits in reasoning.

The early church fathers were very much concerned with the nonmaterial nature of the soul. Therefore, rather than localize the soul, they localized Aristotle's classification of its functions, namely, those of the mind such as sensation and memory. Furthermore, they believed that brain tissue was too earthy, too dirty to act as an intermediary between the body and soul, so they located mental faculties in the ventricles, empty spaces of the brain. Thus, Nemesius, Bishop of Emesia (ca. 390), put all the faculties of the soul into the ventricles, following the same anteroposterior pattern as his contemporary Poseidonus, but making the site of mental faculties entirely ventricular.[61] Besides the desire for a suitable intermediary between the body and noncorporeal soul, another contribution to the doctrine of three brain cells may have been a parallel with the Trinity.

The three stages of processing postulated for the three cells were also influenced, or at least rationalized, by a comparison with the spatial division of function in classical law courts, as in the following quotation from the *Anatomia*

Nicolai Physici, a twelfth-century text derived from an Islamic synthesis of Nemesius and Poseidonus with Greek humoral and pneumatic physiology[62]:

> On the account of the three divisions of the brain the ancient philosophers called it the temple of the spirit, for the ancients had three chambers in their temples: first the vestibulum, then the consistorium, finally the apotheca. In the first, the declarations were made in law-cases; in the second, the statements were sifted; in the third, final sentence was laid down. The ancients said that the same processes occur in the temple of the spirit, that is, the brain. First, we gather ideas into the cellular phantisca, in the second cell, we think them over, in the third, we lay down our thought, that is, we commit to memory.

The specific placement in the anterior and posterior cells clearly derives from Galen. As noted above, Galen had put sensory processing in the soft and impressionable anterior regions. He thought the posterior portions were motor in function and therefore hard, in order to be able to move muscles. The early church fathers choose this hard region as a good one for the safe storage of valuable brain goods, that is, memories.

Empirical support for the cell doctrine was not lacking, as shown in this quotation from Andre du Laurens (ca. 1597), professor of medicine and chancellor of Montpellier University and physician to Henry IV[63]:

> If we will (saith Aristotle in his Problemes) enter into any serious and deepe conceit we knit the browes and draw them up: if we will call to mind and remember anything, wee hang downe the head, and rub the hinder part, which sheweth very well that the imagination lieth before and the memorie behinde . . . in the diverse pettie chambers in the braine, which the Anatomists call ventricles . . .

ANDREAE VESALII
BRVXELLENSIS, SCHOLAE
medicorum Patauinæ professoris, de
Humani corporis fabrica
Libri septem.

CVM CAESAREAE
Maiest. Galliarum Regis, ac Senatus Veneti gra-
tia & priuilegio, ut in diplomatis eorundem continetur.

B A S I L E AE.

The Rebirth of Brain Science

Vesalius Resurrects Neuroanatomy

Andreas Vesalius of Padua (1514–1564) was the greatest of the Renaissance anatomists: he rekindled anatomical science and virtually broke Galen's stranglehold on the field. He is often paired with Copernicus as an initiator of the scientific revolution. In his *De Humani Corporis Fabrica* (1543), the study

Figure 1.8   Title page of Andreas Vesalius's *De Humani Corporis Fabrica* (1543) and one of the most striking and famous woodcuts of the fourteenth century. Until the nineteenth century, the artist was usually thought to be Titian, but modern scholarship suggests that he was a member of Titian's workshop. In any case the engraver of this and the other plates must have been closely supervised by Vesalius. This very busy scene contains many symbols and details of Vesalius's times and work (O'Malley, 1964; Saunders and O'Malley, 1950).

It is a public dissection conducted by Vesalius, recognizable in the center from his portrait. Unlike the custom of the time (see figure 1.9), Vesalius is dissecting with his own hands. His assistant, shown below the table, is relegated to sharpening his knives. Such dissections were required by the statutes of the University of Padua. The bodies, usually male, were obtained from executions, which the courts often spaced out for the convenience of the dissections. This woman tried to escape the hangman by claiming pregnancy, but midwives denied her claim. The dissection is being held outdoors in front of an imaginary Palladian building, with a temporary wooden structure for the spectators that was customary until 1584 when dissections were moved indoors. Ten years later, a permanent dissecting theater was built, which can still be visited in Padua.

Vesalius is surrounded by representatives of the university, the city, the church, and the nobility, as well as by other doctors and students. The toga-clad symbols of classical medicine are shown on the same level as Vesalius. Galen's use of animals is symbolized by the monkey on the left and the dog on the right. The central skeleton represents the importance Vesalius gave skeletal anatomy. Such articulated skeletons, including ones of animals and of humans on horseback, were common fixtures of the anatomical theaters of the time. The bearded figure to the right of the skeleton is wearing Jewish clothing and perhaps is Lazarus de Frieis, a Jewish physician and friend of Vesalius.[64] The nude on the left reflects the importance of surface anatomy for Vesalius. The decorations at the top include the lion of Venice (of which Padua was a part), the ox head of the University of Padua, Vesalius's crest, three sables courant, and the monogram of the publisher, Johannes Oporinus.[65]

of nature, particularly the nature of humanness, begins again in the West and, by implication, dependence on church-sanctified authority for knowledge is rejected. The teaching of anatomy by Vesalius is illustrated in figure 1.8 and before Vesalius in figure 1.9.

Figure 1.10 shows one of Vesalius's famous and beautiful drawings of a horizontal dissection of the human brain. Vesalius ridiculed the ventricular doctrine of brain function, writing with regard to Reisch's representation, "Such are the inventions of those who never look into our maker's ingenuity in the building of the human body."[66] His principal argument against placing the functions of the soul in the ventricles was that many animals have ventricles similar to those in humans and yet they are denied a reigning soul. Indeed, he so equated human and animal brains that he was opposed to vivisection of the brain in animals because "it would be guilty of depriving brute creatures of memory, reason and thought as their structure is the same as that of man."

As to the true functions of the ventricles, he commented[67]:

I believe nothing ought to be said of the locations of the faculties . . . of the principle soul in the brain—even though they are so assigned by those who today rejoice in the name of theologians.

Despite this skepticism about the importance of the ventricles, note that Vesalius drew and labeled the ventricular structures in much more detail and with much more care than he depicted the cerebral cortex.

Ventricular localizations continued among both scientific and lay writers. Perhaps the most recent attribution of important cognitive function to the ventricles by a major scientist was Sir Richard Owen's attempt, in the middle of the nineteenth century, to find the uniqueness of humans in their supposed unique ventricular structures, particularly the hippocampus minor. (See chapter 4.) The most famous lay mention of ventricles is certainly Shakespeare's in *Love's Labours Lost* (IV, ii, 68):
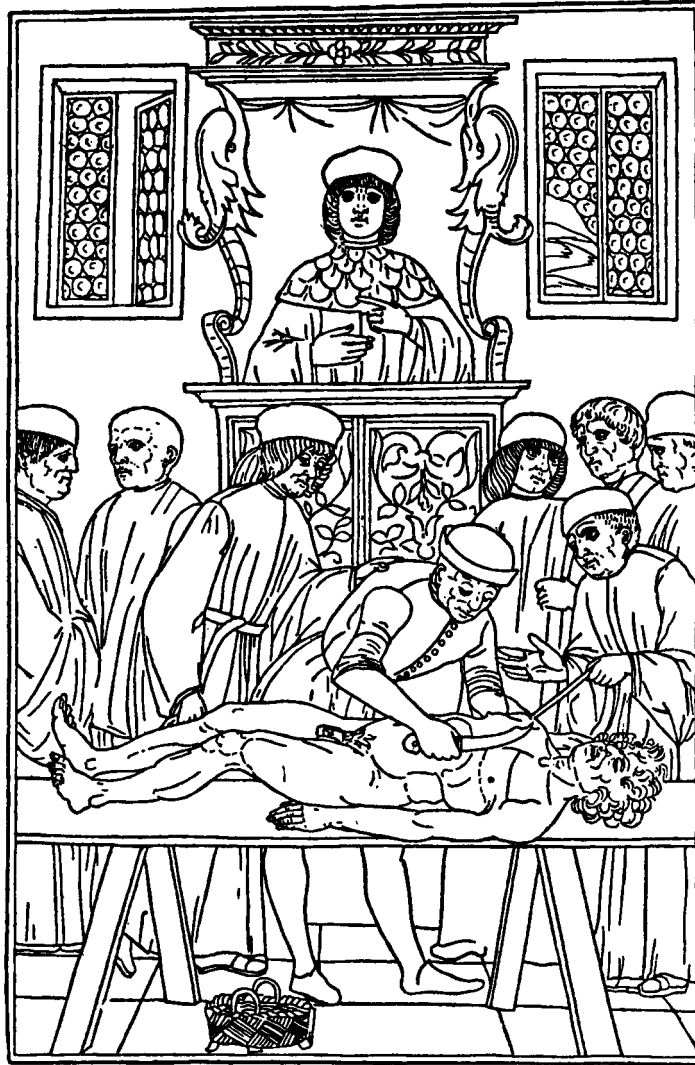

Figure 1.9 Frontispiece of Mondino de Luzzi's *Anothmia* (1493) showing the
teaching of anatomy in the fifteenth century. The professor in his academic robes
and in his academic chair reads from Galen, or perhaps in this case from Mondino,
an *ostensor* or teaching assistant directs with a pointer, and the menial *demonstrator*
actually dissects. The students standing around in academic dress are supposed to be
observing but not dissecting. This work was the first European anatomy textbook;
its first edition was unillustrated, written in 1316. It was essentially a guide for
learning Arabic accounts of Galen rather than for actual dissection of the human
body.
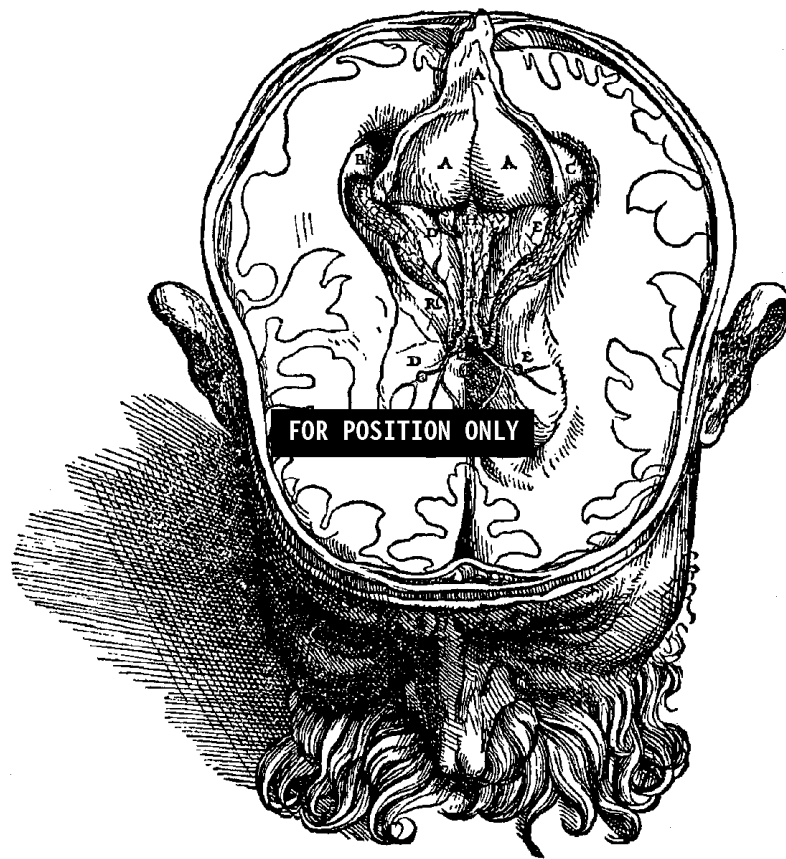
Figure 1.10   One of the series of horizontal dissections of the brain from Vesalius (1543). The fornix (A) has been retracted. Note how the various ventricular structures have been drawn and labeled in detail, but the cortex is drawn in a rudimentary fashion.

A foolish extravagant spirit, full of forms, figures, shapes, objects, ideas, apprehensions, motions, revolutions. They are begat in the ventricle of memory, nourished in the womb of pia mater.

Turning to the convolutions, Vesalius pointed out, you "may learn the shape of these twistings by observing the brain of some animals [on your plate] at breakfast or at dinner." He agreed that Galen was correct in rejecting Erasistratus's correlation of their number with intelligence; he believed their true function was to allow the blood vessels to bring nutriment to the deeper parts of the brain.[68]

Cerebral Cortex: Gland or Rind?

The first clear distinction between the cerebral cortex and white matter was made by Archiangelo Piccolomini (1526–1586), professor of anatomy in Rome, who succeeded in separating the two in gross dissection. He called the former cerebrum and the latter medulla, and noticed "certain lines" in the cerebrum.[69] The terms cortex (or rind), substantia cineretia (or brown substance), convolutions, and cerebrum continued to be used interchangeably into the nineteenth century. Medullary substance also continued to be a synonym for white matter. As reflected in the word "rind," most workers attributed little importance to the cortex.

Marcello Malpighi (1628–1694), professor in Bologna, the founder of microscopic anatomy and discoverer of capillaries, was the first to examine the cortex microscopically. He saw it as made up of little glands with attached ducts (figure 1.11). Similar globules were reported by Leeuwenhoek and many subsequent microscopists.[70] Perhaps they were observing pyramidal cells.[71] At least in Malpighi's case, artifact is a more likely possibility, since his globules were more prominent in boiled than fresh tissues.[72] Malpighi's theory of the brain as a glandular organ was commonly held in the seventeenth and eighteenth centuries, perhaps because it fit with the much earlier, but still persisting,
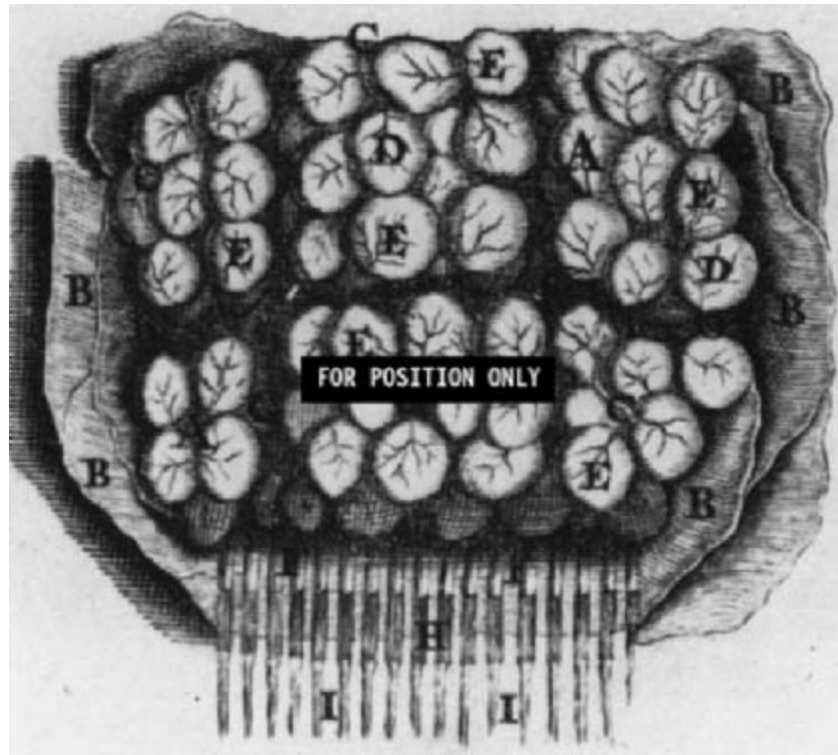
Figure 1.11 Malpighi's cortical glands from his *De Cerebri Cortice* (1666) with their at-
tached fibers. Although he may have seen brain cells, these drawings are likely to be of ar-
tifacts as explained in the text. Swedish mystic Swedenborg used these supposed cortical
elements to build an elaborate theory of brain function that has close similarities with the
neuron doctrine. (See chapter 3.)

Aristotelian concept of the brain as a cooling organ, and the Hippocratic theory that it was the source of phlegm.[73]

The other common view was that the cortex is largely made up of blood vessels. One of the earliest advocates of this was Frederik Ruysch (1628–1731), professor of anatomy in Amsterdam, who noted, "the cortical substance of the cerebrum is not glandular, as many anatomists have described it, nay have positively asserted, but wholly vascular."[74] Here the convolutions were considered mechanisms for protecting the delicate blood vessels of the cortex. Representative of this notion was Thomas Bartholin (1660–1680), professor of anatomy in Copenhagen and discoverer of the lymphatic system. After yet again rejecting Erasistratus's association of the convolutions with intelligence, Bartholin indicated that their true purpose was[75]:

> . . . to make the cerebral vessels safe by guiding them through these tortuosities and so protect them against danger of rupture from violent movements, especially during full moon when the brain swells in the skull.

Thomas Willis Turns Toward Cortex

Before Gall and the development of his phrenological system at the beginning of the nineteenth century, only a very few isolated figures advocated significant functions for the cerebral cortex. The first was Thomas Willis (1621–1675), one of the most important figures in brain science since Galen.[76] Willis was educated at Oxford, quite early gained the Chair of Natural Philosophy there as well as a very lucrative private practice, and was one of the founders of the Royal Society. His *Cerebri Anatomie*[77] was the first monograph on the brain and dealt with physiology, chemistry, and clinical neurology as well as anatomy. Many of its illustrations were by the great architect Sir Christopher Wren, then professor of astronomy at Oxford.

Willis implicated the "cortical and grey part of the cerebrum" in the functions of memory and will. In his scheme, sensory signals came along sensory
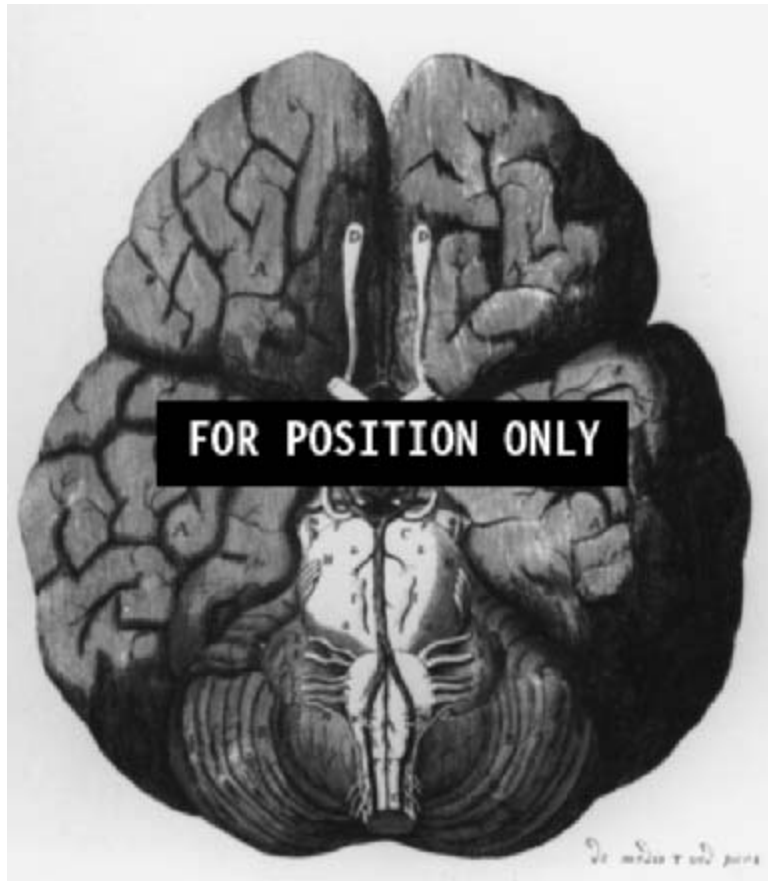
Figure 1.12 Ventral view of the brain from Willis, *Cerebri Anatomie* (1664), drawn by Christopher Wren. Note the detailed drawing and labeling of the cranial nerves and basal brain structures (including the circle of Willis) in contrast to the vague and partially obscured representation of the cerebral cortex, all of which has the single designation A. This schematic and stylized treatment of the cortex was characteristic of all of Willis's illustrations, although he took relatively more interest in the cortex than most others in the surrounding centuries.

pathways into the corpus striatum, where common sense was located. They were then elaborated into perceptions and imagination in the overlying white matter (then called the corpus callosum or hard body since it was harder than the cortex) and passed to the cerebral cortex where they were stored as memories. In his words[78]:

> As often as a sensible impression, such as a visual stimulus, arrives from the periphery it turns inwards like an undulation of water and is transferred to the corpora striata where the sensation received from outside becomes a perception of internal sense. If, however, this impression is carried further and penetrates the corpus callosum, imagination takes the place of sensation. If after this the same undulation of the spirits strikes against the cortex, as it were the outermost banks, it imprints there a picture or character of the object which, when it is later reflected from there revives the memory of the same thing.

The cortex initiates voluntary movement whereas the cerebellum is involved only in involuntary movement.

Willis's ideas on brain function came not only from his dissections but also from his experiments on animals and correlation of symptoms and pathology in humans. Willis noticed that whereas the cerebellum was similar in a variety of different mammals, the complexity of the cerebral convolutions varied greatly among animals; this variation was correlated with intellectual capacity:

> Hence, these folds or convolutions are far more numerous and rarer in man than in any other animal because of the variety and number of acts of the higher Faculties, but they are varied by a disordered and almost haphazard arrangement so that the operations of the animal function might be free, changeable and not limited to one. Those gyri are fewer in quadrupeds, and in such as the cat, they

are found to have a particular shape and arrangement so that this beast considers or recalls scarcely anything except what the instincts and demands of nature suggest. In the smaller quadrupeds, and also in birds and fish, the surface of the brain is flat . . . Hence it is that animals of this sort understand or learn few things.

Despite the importance of the cerebral cortex in Willis's schema, his work contains no adequate drawing of the cortex; he apparently never asked Wren or anybody else to produce one (figure 1.12). In fact, for another 150 years the cortex continued to be drawn as Erasistratus first suggested: as coils of the small intestine (figures 1.13 and 1.14).

Although Willis was a major figure of his time and beyond, his ideas on the importance of the cerebral cortex fell out of favor, and theories of the cortex as a glandular, vascular, or protective rind returned to their original dominance. Two men, however, did challenge the earlier beliefs. The first was Francois Pourfour du Petit (1644–1741), a French army surgeon.[79] He carried out a series of systematic experiments on the effects of cortical lesions in dogs and related them to his clinicopathological observations in wounded soldiers. From these studies he realized that the cerebral cortex plays a critical role in normal movement and that this influence is a contralateral one. However, his observations were totally ignored until they were rediscovered much later. Perhaps this was because du Petit did not hold an academic post and he published his account in a very limited edition. Yet, his conclusion that the cortex was insensitive to touch was repeatedly cited to support the theories of von Haller who, as discussed below, was the dominant physiologist of the day. Thus, du Petit's work demonstrating motor functions of cortex was probably ignored largely because of the anticortex ideology of the time, not because it was published in a minor journal.

The second major figure advocating the importance of the cortex between Willis and Gall was Emanuel Swedenborg (1688–1772), founder and mystical prophet of the New Jerusalem or Swedenborgian Church, which is still active in United States and Great Britain. On the basis of reviewing the
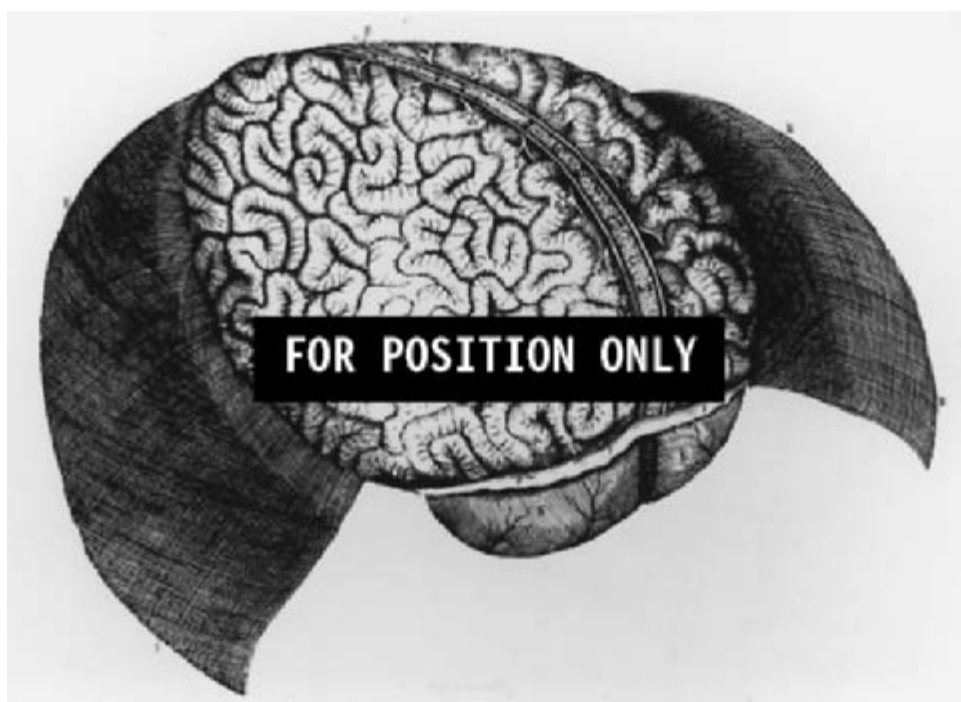
Figure 1.13   The depiction of the cerebral convolutions by Raymond de Viessens of Montpellier, a leading neuroanatomist of the late seventeenth century, in *Neurographia Universalis* (1685). The convolutions are not differentiated in any way and, following Erasistratus, look like intestines.

contemporary literature, Swedenborg arrived at an amazing set of prescient ideas on the importance of the cerebral cortex in sensation, cognition, and movement. The nature of these ideas and why they remained essentially unknown until the twentieth century are discussed in chapter 3.

Von Haller and the Insensitivity of Cortex

The space we have given to Willis, du Petit, and Swedenborg, men who thought the cortex was a crucial brain structure, is somewhat misleading since
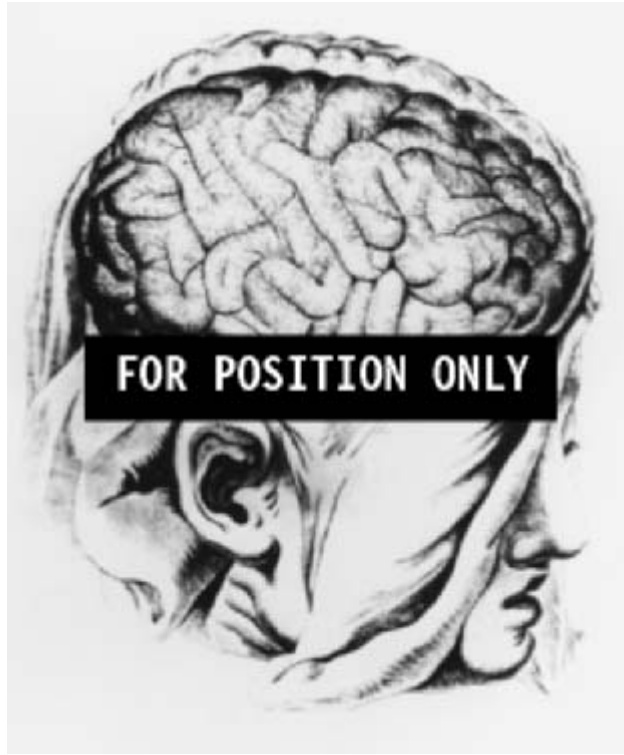
Figure 1.14   In Vicq d'Azyr's *Traite d'Anatomie et Physiologie* (1786)
the convolutions still are drawn looking like intestines, but now
bear some relation to the actual morphology of the brian.

the opposite view prevailed heavily throughout the 2000 years between Erasis-
tratus and Gall (figure 1.15). Much more representative and influential was
Albrecht von Haller (1708–1777), professor at Tubingen and later Bern, who
dominated physiology in the middle of the eighteenth century.[80] In his monu-
mental *Elementa Physiologiae Corporis Humani* (1757–1765, in eight volumes)
and his *Icones Anatomicae* (1743–1756) he divided the organs of the body, as
well as parts of the nervous system, into those "irritable" (e.g., muscle) and
those "sensible" (e.g., sense organs and nerves). He tested sensibility with

mechanical and chemical stimuli and found the cortex to be completely insensitive. In contrast, he reported that stimulation of the white matter and subcortical structures in experimental animals produced expressions of pain, attempts to escape, or convulsions, thereby demonstrating the sensibility of these structures.

From observations such as these Haller concluded that all parts of the cortex were equivalent because stimulation had the same negative effect, and that all subcortical regions were also equivalent because their stimulation had similar positive effects. Thanks to his prestige and many students and followers, Haller's concept of the insensitivity and equipotentiality of cortex superceded the observations of Willis, Swedenborg, and du Petit, and persisted well into the next century.[81, 82] As to the cortex itself, Haller was of the cortex-as-blood-vessels school[83]:

> . . . the greater part of it consists of mere vessels . . . as to glandules
> making the fabric . . . that notion has been discarded; nor has there
> been any opinion received with less probability than this.

Gennari and His Stripe

A few years after Swedenborg died, an event occurred that was particularly central to the theme of this discussion: the discovery of the stripe of Gennari, which we now know marks, in primates, the location of striate cortex—the primary visual cortex. Francisco Gennari (1752–1797), then a medical student, in the course of examining frozen sections of an unstained human brain, observed and reported on a white line in the cortex that was especially prominent and sometimes double in the posterior part of the brain[84] (figure 1.16). This was the first evidence that the cerebral cortex was not uniform in structure. The more famous Vicq d'Azyr[85] rediscovered the stripe and for a while it was known as the stripe of Vicq d'Azyr, until priority was sorted out and the name reverted to Gennari.[86] As to its function, Gennari commented, "Just as the use of so many other things is as yet concealed from us, so I do not know the purpose for which this substance was created."[87]

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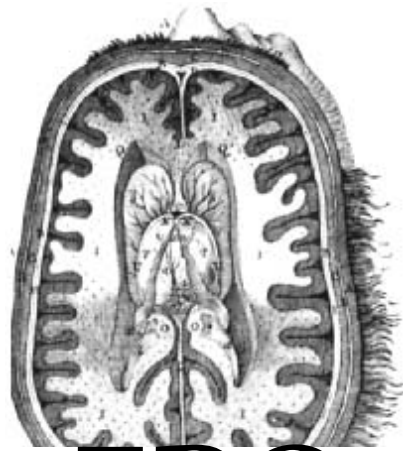
Figure 1.15   In this drawing from the article on anatomy in Diderot's *Encyclopedia,* note how the ventricular structures are drawn and labeled in detail, whereas the cortical convolutions are represented schematically and hardly labeled, reminiscent of Vesalius's drawing (figure 1.10) 200 years earlier (Diderot and D'Alembert, 1751).
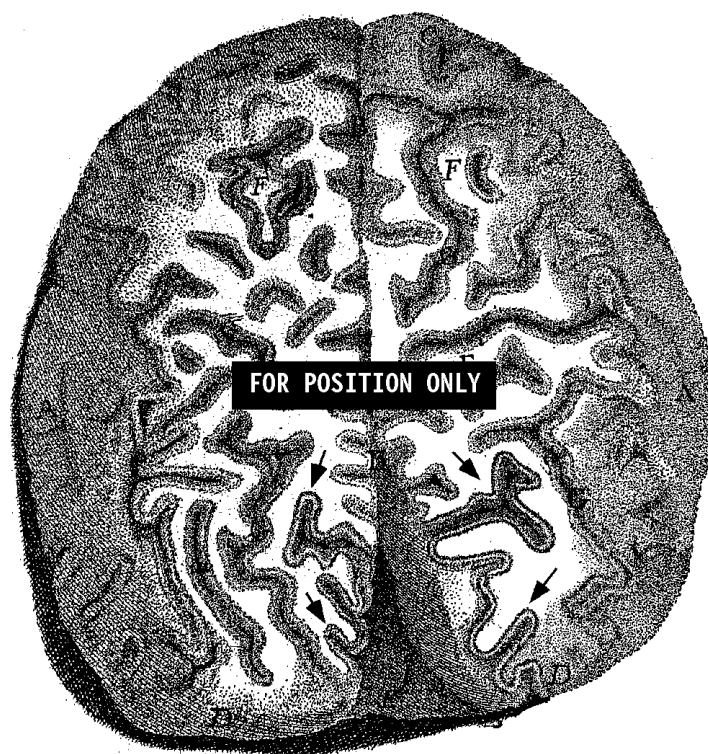
Figure 1.16   In *De Peculiari Structura Cerebri Nonnullisque Eius Morbis* (1782), Gennari was the first to describe regional variations in the structure of the cerebral cortex. Specifically, he noticed a white line in the cortex that is more prominent in the medial and posterior portions of a frozen human brain (arrows added by me). It is now known as the stripe of Gennari.

Gennari never published again, and died a young, penniless compulsive gambler.[88]

Gall and Phrenology

The localization of different psychological functions in different regions of the cerebral cortex begins with Franz Joseph Gall (1758–1828) and his collaborator J. C. Spurzheim (1776–1832), the founders of phrenology.[89] Before they developed their phrenological system, the two men made a number of major neuroanatomical discoveries that would have fixed them in the history of neuroscience even if they had never begun their project of correlating the morphology of the cranium with psychological faculties (figure 1.17). Among Gall's significant anatomical contributions were the recognition that the grey matter is functioning neural tissue connected to the underlying white matter (to which he attributed a conductive function), the first description of postembryonic myelinization, proof of the decussation of the pyramids, the first clear description of the commissures, demonstration that the cranial nerves originate below the cerebrum, and the realization that the brain is folded to conserve space.[90]

The central ideas of their phrenological system were that the brain was an elaborately wired machine for producing behavior, thought, and emotion, and that the cerebral cortex was a set of organs with different functions.[91] They postulated about "thirty-five affective and intellectual faculties" and assumed that (a) these were localized in specific organs of the cerebral cortex; (b) the development or prominence of these faculties was a function of their activity, and the amount of activity would be reflected in the size of the cortical organ; and (c) the size of each cortical organ was indicated by the prominence of the overlying skull, that is, in cranial bumps.

The primary method of data collection used by Gall and Spurzheim was examining the skulls of a great variety of people from lunatics and criminals to
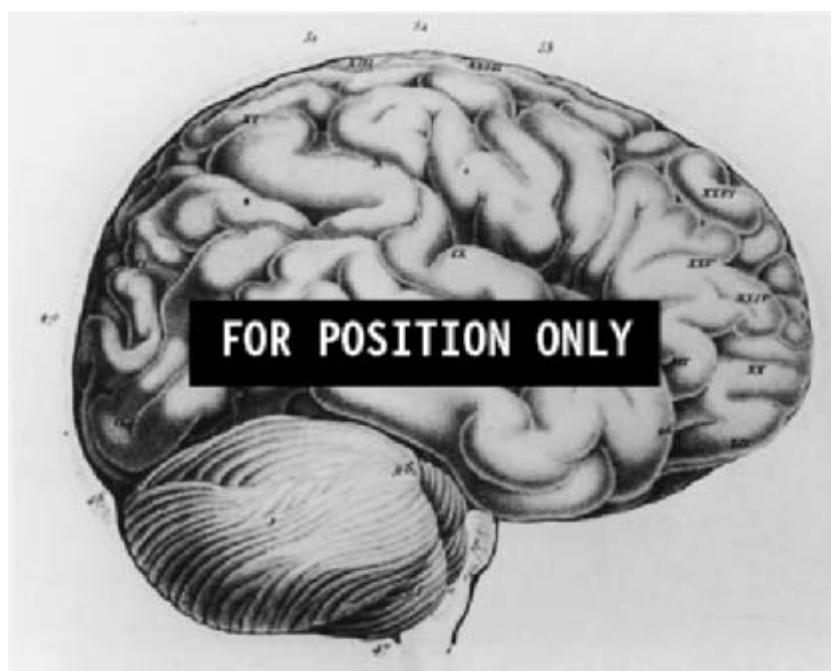
Figure 1.17   This drawing of the cortical convolutions in Gall and Spurzheim's *Anatomie et Physiologie du Systeme Nerveux* (1810) is quite accurate, one of the first to be so. The numbers refer to different phrenological organs.

the eminent and accomplished (figure 1.18). Neuropsychological and animal experimental data, even those gathered by themselves, they considered only minor and ancillary evidence.[92]

Phrenology had wide popular appeal, particularly in England and the United States, and among many leading intellectuals, such as Honoré de Balzac, A. R. Wallace, Horace Mann, and George Eliot.[93] However, it met considerable opposition from the religious, political, and scientific establishments of the day. For example, Gall's public lectures were banned in Austria because they led to materialism and opposed religion and morality. His works were

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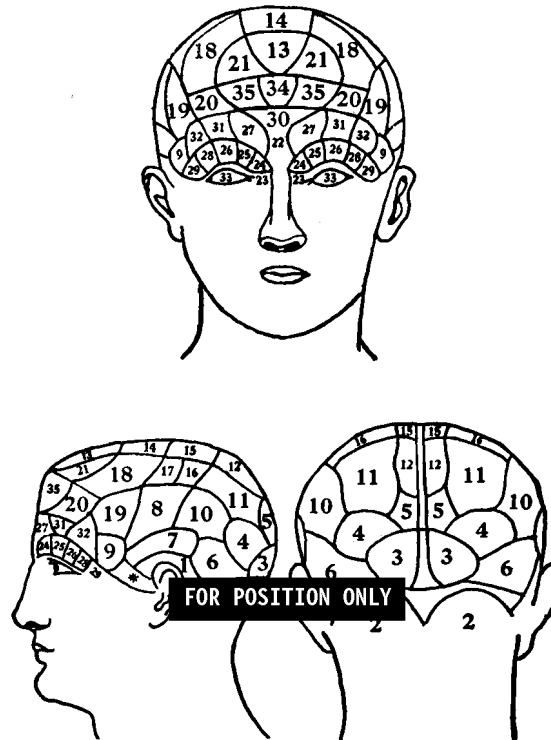
AFFECTIVE FACULTIES

PROPENSITIES	SENTIMENTS
? Desire to live	10 Cautiousness
* Alimentiveness	11 Approbativeness
1 Destructiveness	12 Self-Esteem
2 Amativeness	13 Benevolence
3 Philoprogenitiveness	14 Reverence
4 Adhesiveness	15 Firmness
5 Inhabitiveness	16 Conscientiousness
6 Combativeness	17 Hope
7 Secretiveness	18 Marvelousness
8 Acquisitiveness	19 Ideality
9 Constructiveness	20 Mirthfulness
	21 Imitation

INTELLECTUAL FACULTIES

PERCEPTIVE	REFLECTIVE
22 Individuality	34 Comparison
23 Configuration	35 Causality
24 Size	
25 Weight and Resistance	
26 Coloring	
27 Locality	
28 Order	
29 Calculation	
30 Eventuality	
31 Time	
32 Tune	
33 Language	

placed on the Index of the Catholic Church for similar reasons. In 1908 the French Institute, later the Academy of Science, under the leadership of the great Cuvier, totally rejected even the anatomical parts of a paper that Gall submitted.

Flourens Attacks Gall, but the Cortex (Re)emerges as a Higher Structure

In the scientific world the most important and influential critique of Gall came from Pierre Flourens (1794–1867), later professor of natural history at the Sorbonne.[94] A technically brilliant experimenter, Flourens quickly rose in the French scientific establishment and at the age of thirty-five was elected to the Academy that had rejected Gall. Starting in the 1820s and continuing for over twenty years, he carried out a series of experiments on the behavioral effects of brain lesions, particularly with pigeons. Flourens reported that lesions of the cerebral hemispheres had devastating effects on willing, judging, remembering, and perceiving. However, the site of a lesion was irrelevant: all regions of the hemispheres contributed to these functions. The only exception was vision, in that a unilateral lesion produced only contralateral blindness, but again there was no localization within the hemisphere. These holistic results tended to eclipse Gall's ideas of punctate localization, but only in scientific circles and only temporarily.

Flourens's finding of cognitive losses after hemispheric lesions was actually a confirmation of Gall's emphasis on the cognitive role of the cortex, a concept that had been virtually absent before Gall. This change in attitude toward the cortex was reflected in mid-nineteenth-century textbooks that now routinely attributed intellectual function to the cortex. William Carpenter, in his authoritative *Principles of Human Physiology,*[95] wrote that the convolutions of the cerebrum were:

Figure 1.18   Frontispiece and its legend from J. G. Spurzheim's *Phrenology or the Doctrine of the Mental Phenomenon* (1834). Note that none of the faculties were sensory or motor, but were all "higher" ones.

> . . . the centre of intellectual action . . . the site of ideas . . .
> restricted to intellectual operations . . . the sole instrument of
> intelligence . . . It is probably by them alone that ideas . . . of
> surrounding objects are acquired . . . and that these ideas are made
> the groundwork of mental operations . . . that would also seem to
> be the exclusive seat of Memory . . . and Will.

The cortex was termed a "superadded" structure lying hierarchically and physically above the highest sensory structure, the thalamus, and the highest motor structure, the corpus striatum (figure 1.19). The general idea that the thalamus had major sensory functions and the corpus striatum major motor functions was generally accepted by the middle of the nineteenth century on the basis of a number of studies that traced sensory and motor tracts from the periphery and made experimental lesions in animals.[96]

This view of the higher functions of the cortex, common for the period, combined Haller's notion of insensitivity and both Gall's and Flouren's attribution of higher faculties, but neither sensory nor motor functions, to the cortex.

Broca Confirms Gall

Despite the bitter attacks by Flourens, Gall's theory of punctate localization, and even many of his specific localizations such as language in the frontal lobes and sexuality in the cerebellum, continued to be actively debated in the middle of the nineteenth century.[97] At least in the scientific community, the supposed correlations between skull and brain morphology were quickly recognized as erroneous. Yet, Gall's ideas stimulated the search for correlations between the site of brain injury and specific psychological deficits in patients as well as in experimental animals. Reports of such correlations were published in both the phrenological and mainstream neurological literature, and the question of the localization of psychological function in the brain was hotly debated at scientific meetings.

Thus, in 1848, J. B. Bouillard (1796–1881), professor at la Charité in Paris and a powerful figure in the medical establishment,[98] offered a cash prize for a patient with major frontal lobe damage who did *not* have a language deficit. The debate about localization reached a climax at a series of meetings of the Paris Société d'Anthropologie in 1861. At the April meeting, Paul Broca (1824–1880), professor of pathology at the Sorbonne and founder of the society, announced that he had a critical case on this issue. A patient with long-standing language difficulties—nicknamed "Tan" because that was all that he could say—had just died. The next day Broca displayed his brain at the meeting, and indeed it had widespread damage in the left frontal lobe. Over the next few months he presented several similar cases. Not only did these cases finally establish the principle of discrete localization of psychological function in the brain, but the discovery was hailed as a vindication of Gall. Broca himself regarded Gall's work as "the starting point for every discovery in cerebral physiology in our century."[99]

Evolution and Brain Function

Contributing to the growing interest in the cerebral cortex were ideas about organic evolution that were in the air in the decades before the publication of Darwin's *Origin of Species* (1861). In J.B. Lamarck's (1809) theory of evolution, the first coherent one, evolution involved continuous upward progress, the inevitable transformation of lower into upper forms. The anonymous and widely influential best-seller *Vestiges of the Natural History of Creation* (1844) took a similar progressive view of evolution. (See chapter 4.)

Herbert Spencer (1820–1903) was the first and most important figure to apply evolutionary ideas to the nervous system and psychology.[100] Spencer had virtually no formal education, but read widely in the sciences as a boy. A seminal experience at age 11 was hearing a lecture on phrenology by Spurzheim, and it was decades before he decisively parted from a phrenological position. Before he did so he published in phrenological journals and invented a more accurate device for measuring skull bumps. After a few years as a railway
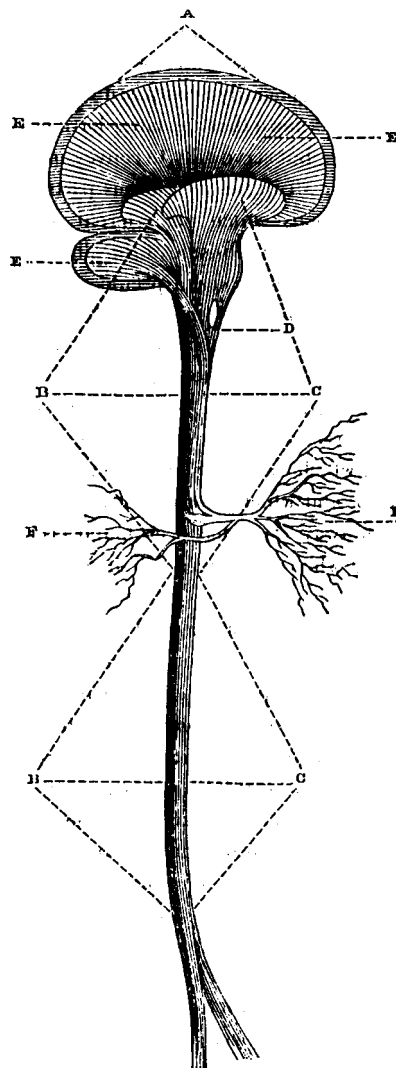
A. The cortical substance or mental portion.
B. B. The sensitive column.   C. C. The motor column.
D. The passage of motor fibres to the cerebellum.
E. E. E. Fibres of volition and consciousness.
F. F. Sensitive and motor fibres.

engineer he drifted into political journalism, where he came into contact with T. H. Huxley, Thomas Carlyle, and George Henry Lewis (and, to use a modern but particularly apt expression, Lewis's partner, George Eliot), and was exposed to the scientific and political issues of the day.

In his first book, *Social Statics* (1851), Spencer set out a quasi-Lamarckian progressive theory of evolution. He argued that it justified survival of the fittest (a phrase Darwin later adopted) in human society. This led him to oppose such things as government help for the poor, public health, and public education. These views were the theoretical bases of the ultraindividualist and conservative ideology that later became known as social Darwinism, although Spencerism would have been a more appropriate designation.[101] Spencer's social theories were particularly welcome among the elites in postbellum America. As John D. Rockefeller put it in a Sunday school address[102]:

> The growth of a large business is merely survival of the fittest. . . . The American beauty rose can be produced in the splendor and fragrance which bring cheer to its beholder only by sacrificing the early buds which grow up around it. This is not an evil tendency in business. It is merely the working-out of a law of nature and a law of God.

In his next work, *Principles of Psychology* (1855), Spencer combined association psychology with evolutionary theory to produce "evolutionary associationism." From evolution he took the idea of a progressive increase in the complexity of the nervous system both phylogenetically and ontogenetically. This led to the conception of the cortex as the newest, highest, and most important level of the nervous system. Furthermore Spencer posited that

Figure 1.19   This figure from a 1837 dissertation illustrates the prevailing view at this time that the highest sensory and motor structures were subcortical (the thalamus and the striatum, respectively, although not so labeled here), and only the cortex had mental functions (Bennett, 1837).

function must be localized in the cortex just as it clearly is in lower nervous structures[103]:

> But no physiologist who calmly considers the question . . . can long resist the conviction that different parts of the cerebrum subserve different kinds of mental action. Localization of function is the law of all organization whatever: separateness of duty is universally accompanied with separateness of structure: and it would be marvellous were an exception to exist in the cerebral hemispheres. Let it be granted that the cerebral hemispheres are the seat of higher psychical activities; let it be granted that among these higher psychical activities there are distinctions of kind . . . more or less distinct kinds of psychical activity must be carried out in more or less distinct parts of the cerebral hemispheres. . . . It is proved experimentally, that every bundle of nerve fibers and every ganglion, has a special duty; and that each part of every bundle of nerve fibers and every such ganglion, has a duty still more special. Can it be, then, that in the great hemispherical ganglia alone, this specialization of duty does not hold?

When the *Origin of Species* was published in 1859, Spencer became a enthusiastic follower of Darwin. He set out to unify all knowledge along the principles of Darwinian evolution and attempted to do so in his massive, multivolume *Principles of Synthetic Philosophy.* Today, his synthetic philosophy is all but forgotten, whereas the disastrous consequences of his social views are still reverberating. However, Spencer did make one permanent and major contribution to modern neuroscience. That was the profound influence of his views of the evolution of the nervous system on John Hughlings Jackson.

John Hughlings Jackson (1835–1911) is the perennial holder of the title, "father of English neurology." As a medical student in Yorkshire, he was so enthralled with Spencer's writings that he almost abandoned medicine to pursue their study full time. Instead, he spent forty-five years as a clinical neurologist

at the National Hospital, Queen Square, London, applying Spencer's ideas on the evolution and dissolution of the nervous system. Many of his over 300 papers began with such sentiments as "I should say that a very great part of this paper is nothing more than the application of certain of Herbert Spencer's principles."

Spencer taught that evolution implied a continuity of nervous organization from spinal cord to cerebral cortex. Therefore, as Jackson put it, "If the doctrine of evolution be true, all nervous centers [including the cortex] must be of sensory-motor constitution," that is, they must have both sensory and motor functions.[104] It was the combination of Spencer's theory of cortex as a sensorimotor structure and his insistence on cerebral localization of function, and Jackson's many observations of seizures (including his wife's) that led him to the brilliant clinical inference that the seizures we now call Jacksonian reflect a somototopically organized cortical motor mechanism.

Jackson's ideas on the motor mechanisms of the cerebral cortex were dramatically confirmed in 1870 by Fritsch and Hitsig's demonstration of specific movements from electrical stimulation of the cortex of the dog.[105] These authors were not reticent about the more general implications of their results, as shown by the final lines of their paper:

> It further appears, from the sum of all our experiments . . . certainly some psychological functions and perhaps all of them . . . need certain circumscribed centers of the cortex.

In summary, despite their temporary eclipse under the shadow of Flourens' experiments, Gall's general ideas of punctate localization in the cortex were essentially vindicated by the third quarter of the nineteenth century. By that time, they were considered confirmed by Broca's demonstration of an association between damage to the frontal lobe and aphasia, and again by Fritsch and Hitsig's experiments on stimulation of motor cortex. Gall's ideas on the localization of mental function had a deep and lasting influence through stressing (a) that the human mind could be subdivided into specific functions,

(b) that these specific functions were mediated by discrete brain structures, and (c) that the cerebral cortex was crucially important in mental activity. It is interesting to note that one of the first accurate drawings of the cerebral cortex was by Gall and Spurzheim (figure 1.17). Before them the cortex was often portrayed as a pile of intestines (figures 1.13 and 1.14) or in a crude schematic way with no attention to detail (figure 1.15). Perhaps it is necessary to believe a structure has important functions before one goes to the trouble to portray it accurately.

The Search for Sensory Areas in the Cerebral Cortex

The last quarter of the nineteenth century saw an intense search for the localization of sensory centers in the cortex. In addition to increasing interest in the cortex from the work of Gall, Flourens, Spencer, Jackson, and Fritsch and Hitzig, a major spur to the search for sensory centers was Johannes Müller's doctrine of specific nerve energies.[106] Müller (1801–1858), professor of anatomy and physiology at Berlin, dominated midnineteenth-century physiology through his personality, his many influential students, and his massive *Handbuch der Physiologie* (1833–1840).

Müller's doctrine had three essential elements. The first and most fundamental asserted that sensation was the awareness of the states of sensory nerves, not of the outer world itself. This was a radical departure from the widespread view, derived from the presocratic philosophers Leucippus and Democritus, that images (*eidola*) from objects in the world enter the eye and travel to the brain.[107] The second element was that when a given nerve type or nerve energy was excited, the same type of experience is produced no matter what the stimulus. Thus, photic, mechanical, and electrical stimulation of the eye all produce visual sensations. Müller, following Aristotle, assumed that there were five nerve types or nerve energies; today, we would call them qualities or modalities. The third element of the doctrine was that the same physical stimulus applied to different sense organs gives rise to different sensations. Thus, a blow to the eye and one to the ear produce visual and auditory sensations, respectively.

Müller was unsure of the locus of nerve specificity. As he put it:

> It is not known whether the essential cause of the peculiar "energy" of each nerve of sense is seated in the nerve itself or in the parts of the brain and spinal cord with which it is connected.

A student of Müller, however, the great Hermann von Helmholtz, philosopher, physicist, and psychologist, located the specificity squarely in the nerve terminations. Helmholtz, who was the first to measure the speed of nerve conduction, in the original comparison of the nervous system with a telegraph system, noted that with wires[108]:

> according to the different kinds of apparatus with which we provide terminations, we can send telegraph despatches, ring bells, explode mines, decompose water, move magnets, magnetize iron, develop light and so on. So with the nerves the condition of excitement which can be produced in them and is conducted in them, is, so far as can be recognized in isolated fibres of a nerve, everywhere the same, but when it is brought to various parts of the brain, or the body, it produces motion, secretions of glands, increase and decrease of the quantity of blood, of redness and of warmth of individual organs, and also sensations of light, of hearing, and so forth.

Emil Du Bois-Reymond, another one of Müller's students,[109] his successor in the Berlin Chair, and discoverer of the action potential, went further and claimed that if it were possible to cross-connect the auditory and optic nerves, we would see with our ears and hear with our eyes.[110]

The idea that the specificity of nerves derived from their central connections was not new. On the basis of his clinical practice among gladiators in Pergamon, Galen distinguished between sensory and motor nerves, and proposed that sensory nerves were connected to the anterior part of the brain and motor nerves to the posterior. Charles Bell (1774–1842), codiscoverer of the

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law of spinal roots, or rather, the sensory half of it,[111] extended the idea of specificity inherent in that law to the five senses to yield in 1811 an account of nerve specificity essentially identical to Müller's later published one. As Bell put it[112]:

> the nerves of sense depend for their attributes on the organs of the brain to which they are severally attached . . . the properties of the nerves are derived from their connections with the parts of the brain.

It is important to note that for both Bell and Müller it was not the terminations in the cerebral cortex that conveyed specificity on the sensory nerves. Rather, for both of them, and, as noted above, more generally for almost all the physiologists and anatomists of the first half of the nineteenth century, the cortex still had no sensory (or motor) functions. The main support for this view was still Haller's that since the cortex was insensitive to touch, it could hardly be sensory. Instead, it was believed to be the site of the highest intellectual functions. This notion was often supported both by the phylogenetic correlation of cortical complexity with intelligence and reports of intellectual deficits after cortical lesions. It was clearly also heavily influenced by Gall's ideas. Note that of all the thirty-five faculties that Gall put into the cerebral cortex, none was sensory or motor. Some of Gall's faculties do have sensory sounding names, but on examination they are actually cognitive. For example as to the faculty of color, Gall notes, "I do not mean the simple faculty of seeing or perceiving colors . . . [but rather] distinguishing the relations of colors: the talent for painting."[113]

What turned Müller's doctrine and everybody else's attention toward the possible sensory functions of the cerebral cortex was Fritsch and Hitzig's discovery of motor cortex by electrical stimulation in 1870. This unambiguously demonstrated that the cerebral cortex had more than just higher functions.

Müller's doctrine of specific nerve energies now became directed toward cortex as the locus of specific energies. Thus, under its influence, in the later

part of the nineteenth century, (a) neural pathways were traced from the sense organs into the brain to find the specific regions in which they ended; (b) the cortex was divided up into separate centers or organs on the basis of the pattern of its structure, thereby yielding the techniques of cytoarchitectonics and myeloarchitectonics; (c) cortical lesions were made in animals to find the sensory centers, and (d) in close parallel, attempts were made to correlate sensory losses in humans with the site of cortical damage.

The Discovery of a Visual Center in the Cerebral Cortex

Bartolomeo Panizza: The First Claim

The first person to suggest a discrete localization of visual function in the cortex on the basis of systematic investigations was Bartolomeo Panizza (1785–1867), professor of anatomy at Pavia and a follower of Gall.[114] After examining the brains of several patients who became blind after strokes, he attributed vision to the posterior cortex. He then tested this idea by making lesions and enucleations in a number of species and concluded that the occipital region was the crucial one for vision. He also studied the anatomical and behavioral effects of monocular enucleation as a function of age, and concluded that the effects on the brain were more profound in adults than in infants. Panizza's work seems to have been totally ignored at the time. One reason for this may have been because he only published in local journals, those of the Royal Institute of Lombardy of Science, Arts, and Letters; however, these journals were exchanged with those of the Royal Society and presumably other scientific societies.

A more likely reason for the lack of impact of Panizza's work was the prevailing theoretical view of the relative role of cortex and subcortex. As we have indicated, at that time it was thought that the thalamus was the highest sensory center and the basal ganglia the highest motor center. In contrast, the cortex was believed to be concerned not with sensation or movement but with intellectual operations.[115] This view went back at least to Gall, who among his
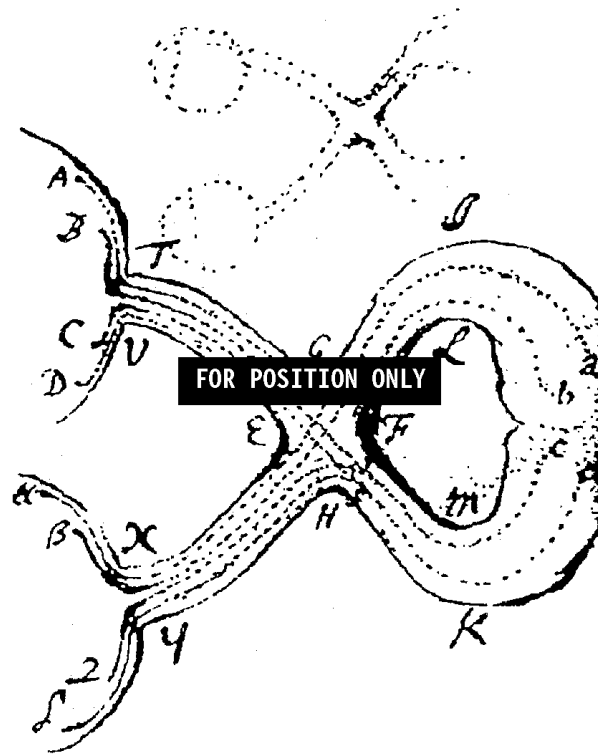
Figure 1.20   Newton (1704) was the first to suggest, in *Opticks,* that partial decussation at the optic chiasm results in binocular convergence. This is clearly and elegantly illustrated in this sketch that Grusser found in Newton's manuscript pages of the *Opticks* (Grusser and Landis, 1991). Note that Newton thought that binocular fusion occurred in the chiasm itself. There is no reason to believe that Newton had any actual anatomical evidence for his model.

thirty-five plus cerebral organs had none for any sensory or motor function. The importance of Panizza's work was realized only after the work of Ferrier, Munk, and Schafer provided convincing evidence for a cortical visual area, as described in the next section.[116]

The Battle for Visual Cortex: Ferrier versus Munk and Schäfer

Immediately after Fritsch and Hitzig's publication, the English physiologist David Ferrier (1843–1928), working at the West Riding Lunatic Asylum and at Kings College, London, confirmed their work, first in dogs and then in monkeys.[117] He then applied their electrical stimulation methods to search for the sensory cortices. He found that stimulation of the angular gyrus (area 7 in posterior parietal cortex) in the monkey produced conjugate eye movements, and he interpreted this as indicating that this area was the seat of the perception of visual impressions. In contrast, he found that stimulation of the occipital lobe or other regions did not have these effects. He further tested this theory by making angular gyrus lesions (figure 1.21) and reported that unilateral lesions produced temporary blindness in the contralateral eye and bilateral lesions produced permanent blindness in both eyes.[118] However, the animals were observed for only a few days before he sacrificed them, the operations having been done without antiseptic techniques. Summarizing the results on four animals with angular gyrus lesions, he wrote:

> The loss of visual perception is the only result of this lesion, the other senses and the powers of voluntary movement being retained so long as the lesion remains confined to the angular gyrus itself. By the term visual perception I wish to indicate the consciousness of visual impressions, and to distinguish this from mere impressions on the optical apparatus and reactions which are only of a reflex nature . . .
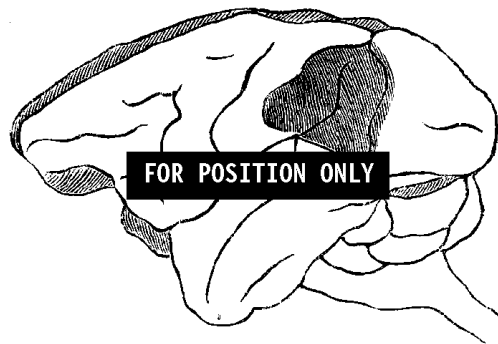
Figure 1.21 Lesions of the angular gyrus in monkeys that Ferrier first claimed produced blindness (1876) and later, only temporary blindness (1886). The lesion comes within a few millimeters of the later-discovered location of the foveal representation in striate cortex. (See figure 1.22.)

In contrast, monkeys with large occipital lesions (figure 1.22) showed no visual disturbances at all unless their lesions encroached on the angular gyrus. The only effect of occipital lesions was a temporary loss of appetite. From this he speculated that the occipital lobes were related to the "organic sensibilities and are the anatomical substrata of the correlated feelings which form a large part of our personality and subjectivity."[119]

How did Ferrier account for the finding that the visual disturbances were evident only through the contralateral eye? Isaac Newton[120] had described the partial decussation of the optic pathways and its significance for binocular vision clearly in his *Opticks* (see figure 1.20) and several other eighteenth-century figures held similar views. Indeed, homonymous hemianopia after unilateral brain damage was explained in terms of partial decussation as early as 1723.[121] Ferrier was aware of both the partial decussation and its possible relation to "hemiopia," as he called it. However, he thought that the uncrossed fibers crossed to the opposite hemisphere at some level beyond the chiasm, so that the cortex of each hemisphere received input from the entire contralateral eye.
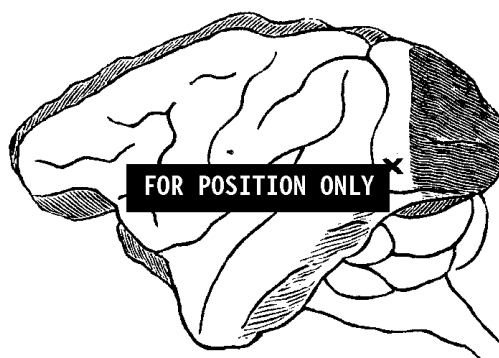
Figure 1.22 Ferrier (1886) found that these occipital lesions in monkeys do not cause any visual deficits. The lesion spares part of what we now know to be the representation of the fovea in striate cortex, the center of which is marked (by me) with an X.

Thus, he thought that only subcortical lesions produced homonymous hemianopia.[122]

Soon after these first studies by Ferrier, Hermann Munk (1839–1912), professor of physiology at the Veterinary Hochschule in Berlin, reported very different results on the effects of occipital lesions in dogs and monkeys,[123] and the battle began, a battle that was not to be resolved for more than a decade. Munk's surgical and aseptic techniques were much better than those of Ferrier, and he was able to study his animals for many months. He described two types of blindness after occipital lesions. The first type he called *Seelenblindheit* or "psychic blindness," and he reported that it occurred after limited occipital lesions in dogs. The dogs saw objects and avoided bumping into them but did not recognize their meaning:

> No abnormalities of hearing, taste, smell, motricity or sensation.
> The dog walks freely about the room without bumping into
> objects. If one blocks his path, he avoids or adroitly jumps over

obstacles. But within the psychic domain of vision a distinctive defect exists: he pays no attention to water or food, even if he is hungry and thirsty. He seems indifferent to everything he sees; threats do not frighten him. One can bring a match up to his eyes without him backing away. Seeing his master or seeing other dogs leaves him impassive . . . he no longer knows or recognizes what he sees.

Although these results were never replicated by others and Munk's interpretation was disputed, the term psychic blindness caught on, in part because the concept fit the associationist theories of the period.[124] Munk's observations on psychic blindness were brought to a wide audience by William James, who discussed them in detail in his *Principles of Psychology,* published in 1890. Thus, when Lissauer published the first detailed anatomic–clinical report of a human visual recognition deficit in the absence of sensory losses, he adopted Munk's term and went on to distinguish two types of psychic blindness, apperceptive and associative. Later, Sigmund Freud coined the term "visual agnosia" to replace psychic blindness.[125] However, "psychic blindness" continued to be used and was immediately applied by Heinrich Klüver and Paul Bucy to describe the behavior of their temporal-lobectomized monkeys. (See chapter 5.)

The second type of blindness Munk distinguished he called *Rindenblindheit,* or "cortical blindness." It was total absence of vision and he found that it followed complete removal of the occipital cortex in both dogs and monkeys. With his monkeys, Munk realized that complete unilateral occipital lesions produce blindness not in the opposite eye but in half of each retina. Presumably the fact that only half the retinal fibers cross in the monkey but about 80 percent of them cross in the dog made this phenomenon of homonymous hemianopsia much easier to detect by casual observation in the monkey than in the dog. As for Ferrier, Munk had this to say[126]:

In my first communication on the physiology of the cortex . . . I did not say anything about Ferrier's work on the monkey because

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there was nothing good to say about it . . . [Ferrier's] statements and what followed from them . . . are worthless and gratuitous constructions since the operated animals were examined by Mr. Ferrier in quite an insufficient manner . . . as the experiments show now I have said at that time rather too little than too much, Mr. Ferrier had not made one correct guess, all his statements have turned out to be wrong.

About this time, Lister described his techniques for aseptic surgery, and soon after, Ferrier and Yeo used them in a new series of cortical lesions in monkeys.[127] Now the animals could be studied for several months after operation, and Ferrier modified his previous views as to the permanence of the blindness after angular gyrus lesions[128]:

Formerly, I localized the visual centres in the angular gyrus, to the exclusion of the occipital lobes. This being a partial truth is an error. . . . Complete destruction of the angular gyri on both sides causes for a time total blindness, succeeded by a lasting visual impairment in both eyes. The only lesion which causes complete and permanent blindness is total destruction of the occipital lobes and angular gyri on both sides.

Despite this retreat, Ferrier (1886) still insisted that Munk's conclusions on the location of the visual area were "entirely erroneous" and "vitiated by the occurrence of secondary encephalitis." Ferrier's observations on angular gyrus lesions actually anticipated subsequent work implicating the parietal cortex in visual functions. (See chapter 5.)

Now Edward Albert Schäfer (1850–1935), professor of physiology at University College, London, and later at Edinburgh, entered the fray. In his first experiments, carried out with his student Victor Horsley (coinventor of the stereotaxic instrument), they obtained results opposite from those of Ferrier, namely, more eye movements from stimulation of the occipital lobe than the angular gyrus, and much greater visual deficits from occipital lesions than from

angular gyrus ones.[129] Then Schäfer carried out a series of further experiments with an American neurologist, Sanger Brown, in which the occipital lesions were more complete than anybody had made previously (figure 1.23), and they studied several of the animals in detail for several months.[130] They convincingly showed that total removal of the occipital lobe produced permanently blind animals, but only if the lesion extended on the ventral surface into the temporal lobe.

Angular gyrus involvement, however, was neither necessary nor sufficient to produce such blindness. They also failed, in several monkeys, to confirm Ferrier's claim that temporal lesions produce deafness. In explanation of this discrepancy, Schäfer suggested that Ferrier's one monkey, indisputably deaf after a temporal lesion, must have been deaf preoperatively.[131] (One of Brown and Schäfer's monkeys that retained its hearing after bilateral temporal lobectomy was a precursor to all subsequent work on the temporal lobe and vision, as discussed in chapter 5.)

Ferrier and Schäfer continued to quarrel over whether the occipital lobe or the angular gyrus was the visual area (as well as whether the temporal lobe had an auditory center), both in journals and at various national and international meetings to which they brought their critical monkeys as demonstrations and to be examined by special committees. William James in his influential *Principles of Psychology,* after complaining of all this internecine warfare, came down unambiguously for a visual area in the occipital lobes. The battle was virtually over by then.

Today, the bases for the apparent contradictions between Ferrier and Munk and Schäfer in the location of the visual area are understandable. From his descriptions and drawings (figure 1.22), it is clear that Ferrier removed the occipital lobes by an incision parallel to and about a half an inch or more posterior to the lunate sulcus. This site was chosen to make sure that the entire angular gyrus, his supposed visual center, was entirely spared. By his estimates this would remove "at least two thirds of the occipital lobes." Today we know that such a lesion would leave intact the representation of about the peripheral thirty degrees of the visual field in striate cortex and, more important, about a

Figure 1.23   The occipital lesions that Brown and Schäfer (1888) reported to cause blindness in macaques. The lesions include what we now know to be the entire representation of the visual field in striate cortex, including both the representation of the fovea on the lateral surface (left, dorsal view) and of the extreme periphery in the far anterior of the calcarine sulcus (right, ventral view).

few degrees of the entire representation of the lower half of the vertical meridian as well.[132] This is enough residual striate cortex to account for the visually guided behavior described by Ferrier after his occipital lesions.

In contrast, Schäfer's occipital lesions included not only all the striate cortex on the lateral surface by making his lobectomy through the floor of the lunate sulcus, but in the only animal totally and permanently blind, the bilateral lesion extended on the ventral surface far enough forward to have included all the buried striate cortex in the anterior calcarine fissure. Munk provided less detailed information on the sites of his lesions, but they certainly included more of striate cortex than did Ferrier's as well as at least some of the striate cortex in the calcarine sulcus on the medial surface.

Striate Cortex Is Visual Cortex

By the turn of the century, with the resolution of the Ferrier–Schäfer–Munk debate, anatomical, clinicopathological, and experimental data were converging

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as to the identity of the visual area in the cortex of humans and monkeys. French anatomist Gratiolet's (1854) identification of the optic radiation (initially called Gratiolet's radiation) proceeding from the geniculate to the posterior cortex was important as the first demonstration of a sensory pathway extending to the cortex. The terminus of this visual pathway was more accurately delimited in the developmental myeloarchitectonic studies of Paul Flechsig (1847–1929), professor at Leipzig, beginning in the 1870s. On the basis of the time of myelination, he divided human cortex into three zones: projection, myelinating at birth; intermediate, myelinating at one month; and terminal, myelinating later. The intermediate and terminal areas taken together he termed association cortex (figure 1.24). By 1896 Flechsig could identify the target of the visual radiations with the most posterior projection zone, and he realized it was the region of the stripe of Gennari. This region was soon named by G. Elliot Smith (1907) area striata.[133] (The concept of association cortex is discussed in chapter 5.)

During the 1880s, studies of human brain damage by Hermann Wilbrand in Hamburg, M. Allan Starr at Columbia University, Henry Hun in Albany, and others were identifying blindness with damage to the occipital cortex.[134] Swedish neuropathologist Salomon Henschen collected over 160 cases of blindness and hemianopia after cortical lesions, which led him to identify the center of vision or cortical retina with the calcarine cortex and later, with all of striate cortex. Final experimental proof of the identification of striate cortex with vision came with Minkowski's behavioral and anatomical studies in animals.[135]

The term "calcarine sulcus" was coined by T. H. Huxley (1825–1895) in the course of his bitter dispute with Richard Owen (1804–1992) over the hippocampus minor and man's place in nature. (See chapter 4.) Owen claimed that only humans had a hippocampus minor, also known as the calcar avis. This structure is a ridge in the floor of the posterior horn of the lateral ventricle. To prove Owen wrong, Huxley and his allies set out to demonstrate its existence in a variety of primates. In the course of his study of the brain of the spider monkey for this purpose, Huxley (1861) provided the first accurate description of the calcarine sulcus. He called it "calcarine" because its indentation into the lateral ventricle is what forms the calcar avis.

Figure 1.24   Flechsig's (1886) parcellation of the brain based on time of myelinization. The densely stippled areas are the projection zones surrounded by the marginal or intermediate zones. The terminal areas are unstippled. Association cortex is made up of the intermediate and terminal zones.

As the localization problem was being solved, the next issue was how was striate cortex was organized. The great Arab visual scientist ibn al-Haythem (965–1039), known in Europe as Alhazen, had proposed a point-to-point projection of the retinal image onto the brain.[136] This idea was well known in Europe through the translation of his work, *De Aspectibus,* the standard textbook on physiological optics until Kepler and beyond. Depictions of the visual pathways from the Renaissance onward typically show a point-to-point projection from eye to brain whether fanciful, as in Descartes (figure 1.25), or remarkably prescient, as in Newton (figure 1.20). This idea of a topographic projection seemed to have derived from the theoretical considerations of Alhazen, rather than from any empirical evidence.

Henschen, with his large number of cases, made a good start at empirically decoding the topography of striate cortex. He correctly placed the representation of the upper visual field in the lower bank of the calcarine sulcus and that of the lower one in the upper bank, but he reversed the center-periphery organization. This error was hardly surprising, given how large and diffuse many of his lesions were. As Glickstein and Whitteridge pointed out, it was the introduction of high-velocity bullets in the Russo-Japanese War that produced discrete lesions and often small entry and exit wounds, and thus made it possible to plot the locus of destroyed brain and correlate it with visual field defects. In that war, Japanese ophthalmologist Tatsuji Inouye[137] produced the first reasonably accurate scheme of how the retina is mapped on striate cortex, including magnification of the representation of the fovea, which had not been observed previously. In World War I a large number of studies reported similar results,[138] but the most widely known is that of the British neurologist Sir Gordon Holmes, perhaps because his easy-to-understand schematic diagram was reproduced in so many textbooks (figure 1.26).[139]

Neurophysiology of Striate Cortex Begins

In 1886 Adolf Beck began to work for his doctorate at the University of Kracow.[140] This was not only the period of intensive searching for sensory
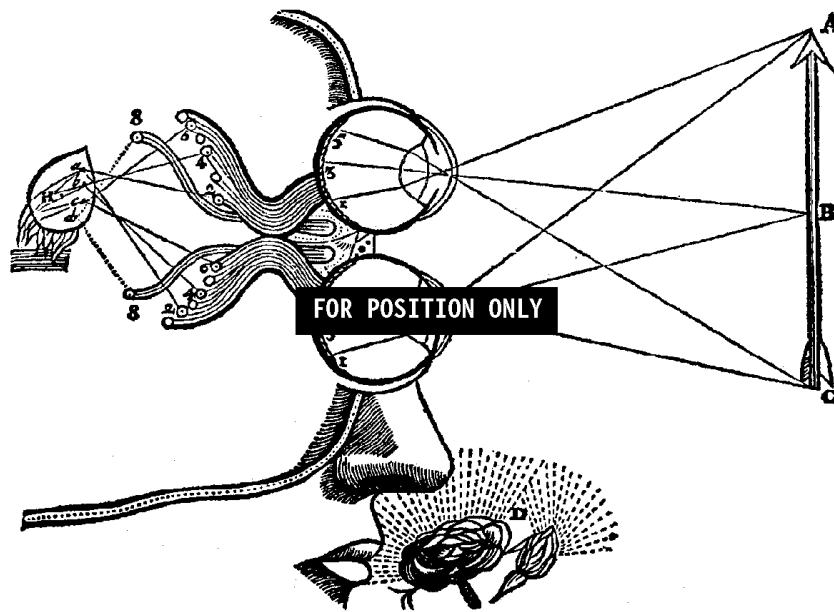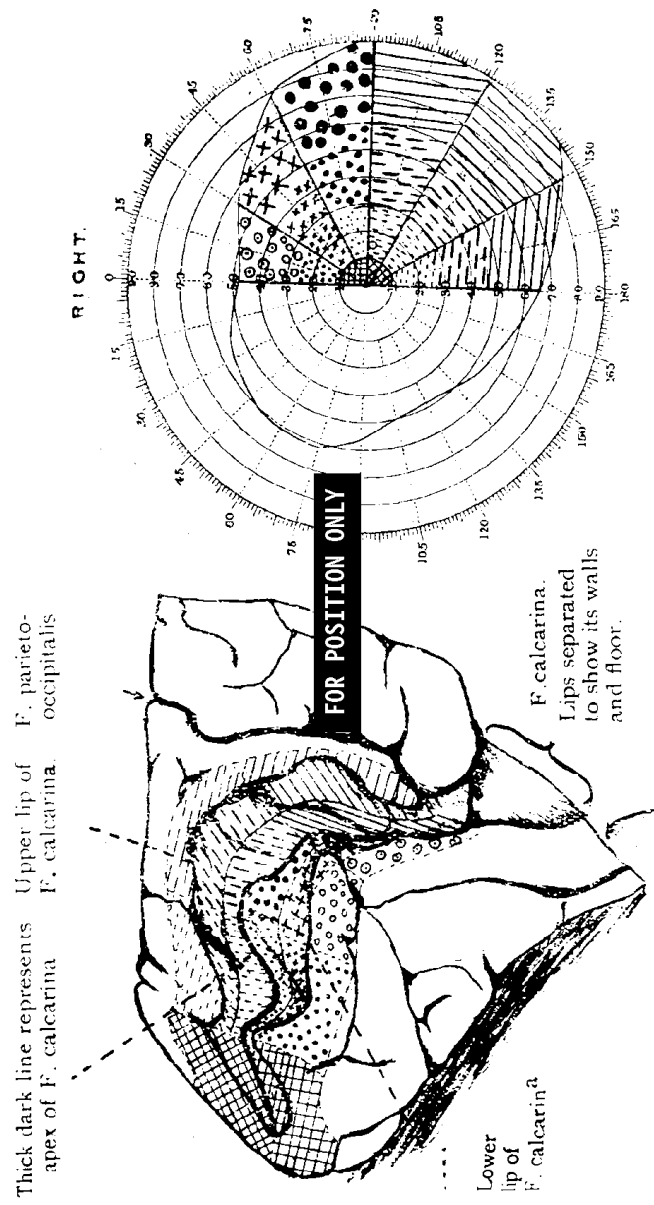
Figure 1.25 Several aspects of Descartes's theory of sensory processing are illustrated in this figure from his physiology textbook, *Treatise on Man* (1662). Light from the arrow enters the eye; the lens throws an inverted but topographically ordered image onto the retina. The message then travels in the hollow optic nerves from each eye by way of the animal spirits to the central pineal gland, where the information from the two eyes is united in a corresponding fashion to yield a single upright image. Olfactory messages from the flower also travel to the pineal body, but the strength of the visual signal (due to attention) suppresses this olfactory input.

centers in the cortex but also the beginning of electrophysiology. I. M. Sechenov and his students had recorded electrical changes in the spinal cord and brain of a frog after stimulation of its leg. Beck then set out to use this method to try to localize the different sensory systems. He wrote:

> The question arises, are there any currents in the nervous centers
> of the brain and spinal cord? If so, are there changes in these
> currents during activity? And would the localizing of such changes

Thick dark line represents   Upper lip of   F. parieto-
apex of F. calcarina.   F. calcarina.   occipitalis

FOR POSITION ONLY

F. calcarina.
Lips separated
to show its walls
and floor.

Lower
lip of
F. calcarina[a]

RIGHT.

be of any help in demonstrating a state of activity of a focal nature
in the central nervous system?

After a series of experiments on frogs in which he thought he found
spontaneous electrical activity, Beck turned to the cortex of rabbits and dogs.
He placed pairs of electrodes in various cortical regions and presented visual,
auditory, and tactile stimuli. He found an oscillating potential difference in the
occipital region in the case of visual stimuli and used it to plot the extent of
the visual cortex. As his thesis was in Polish, he published a three-page summary
in German in the leading physiology journal of the day, *Centralblatt für Physi-
ologie*. The importance of his demonstration of sensory evoked responses was
immediately recognized; indeed, it stimulated a flood of letters claiming prior-
ity. One of these was from Richard Caton of Liverpool, who had published
similar if less extensive experiments earlier.[141] However, not only had they gone
unnoticed in Poland but they were totally ignored in England. The physiology
establishment there thought Caton's "weak electric currents" quite irrelevant.

Beck went on to a distinguished academic career in Poland, including
rectorship of the University of Lvov. When he was eighty, the Germans came
to take him because he was a Jew. He swallowed the cyanide capsule supplied
by his son, a doctor, and escaped the gas chamber.[142]

In 1934, American psychologist S. Howard Bartley was the first to carry
out a systematic study of the visual evoked response of cerebral cortex and did
so in rabbits. Then in the early 1940s, at Johns Hopkins, S. A. Talbot and Wade
Marshall used visual evoked responses to carry out their pioneering studies of
the visual topography of striate cortex first in cats, then in macaques, and then,

Figure 1.26   Representation of the retina in striate cortex according to Gordon Holmes
(1918a): "A diagram of the probable representation of the different portions of the visual
fields in the calcarine cortex. On the left is a drawing of the mesial surface of the left oc-
cipital lobe with the lips of the calcarine separated so that its wall and floor are visible.
The markings on the various portions of the visual cortex which is thus exposed corre-
spond with those shown in the chart of the right half of the field of vision. This diagram
does not claim to be in any respect accurate; it is merely a scheme."

with Clinton Woolsey and others, in a variety of other mammals. Particularly in gyrocephalic animals, these maps tended to be incomplete, since the macroelectrodes used confined the recordings to the surface of the cortex. Subsequently, as described in the next section, using single-neuron recording, Daniel and Whitteridge in the monkey and Hubel and Wiesel in the cat, followed by many other studies, confirmed and extended these electrophysiological maps of the visuotopic organization of striate cortex.[143]

The Microelectrode Arrives; from Adrian to Kuffler

The analysis of visual processing by single neurons begins with the work of E. A. Adrian. Indeed, virtually all of modern neurophysiology begins with Adrian. Among his other achievements were the establishment of the all-or-none law, the first recording from single neurons, the concepts of labeled line and rate coding, the first recording of spontaneous activity from cerebral and cerebellar cortex neurons, and confirmation of the existence of brain waves, the electroencephalogram.[144] Titles and awards accrued: he was made a baron, was awarded the Order of Merit and the Nobel prize (1932), and was elected master of Trinity College and professor of physiology in the University of Cambridge, and president of the Royal Society and of the British Association for the Advancement of Science.

In 1927 he and Bryan Matthews recorded spike trains from the optic nerve of the conger eel and noted that the rate of firing increased and the latency decreased as the intensity of the light increased. Following this up, H. Keffer Hartline dissected out single optic fibers first in *Limulus,* the horseshoe crab, and then in the frog, where he distinguished on, off, and on-off responses for the first time and introduced the concept of a visual receptive field.[145] Hartline spent most of his career at the University of Pennsylvania and Rockefeller University, and shared the Nobel prize with George Wald and Ragnar Granit in 1967.

The next major development was that of Stephen Kuffler, then at the John Hopkins University. Working with cats, he developed a technique for recording from the retina without having to remove the cornea and lens, as

had been done previously. This maintained the normal optics of the eye and enabled him to focus light on the portion of the retina that he was recording from. With these techniques he discovered the center-surround, on-off antagonistic organization of the receptive fields of retinal ganglion cells.[146] Horace Barlow, who was working in Kuffler's laboratory, had made similar observations in the frog earlier. He noted that this receptive field organization made the cells much more sensitive to edges and contours than to diffuse light. (Barlow even called one of the class of cells he described a bug detector.) We now know that this receptive field structure is fundamental to the organization of the entire visual system. It was the extension of Kuffler's work from retina to cortex by Hubel and Wiesel that formed the basis of current study of visual cortex.

Hubel and Wiesel

In 1959, two physicians, David Hubel, a Canadian, and Torsten Wiesel, a Swede, came to Kuffler's laboratory in Baltimore as postdoctoral fellows. Visual physiology, and indeed all of sensory physiology and psychology, were never the same again. Through the brilliant use of single-neuron physiology they revealed the functional architecture of striate cortex. This research promised the possibility of understanding perception in terms of neurons, and became the model for subsequent explorations of visual neurons inside and outside of striate cortex and for all of contemporary neurophysiology. Subsequently, Hubel and Wiesel moved to Harvard with Kuffler, and in 1981 they shared the Nobel prize with Roger Sperry. Their remarkable achievements that extended into visual neuroanatomy and neural development have been widely reviewed and will not concern us here except for two historical notes.[147]

The first is the description of their first observation of an orientation selective neuron in a cat, perhaps the opening wedge in revealing the secrets of striate cortex[148]:

> We had been doing experiments for about a month . . . and were
> not getting very far; the cells simply would not respond to our spots
> and annuli. [The stimuli that had been used by Kuffler to reveal

the properties of retinal ganglion cells.] One day we made an especially stable recording. . . . For 3 or 4 hours we got absolutely nowhere. Then gradually we began to elicit some vague and inconsistent responses by stimulating somewhere in the mid-periphery of the retina. We were inserting [a] glass slide with a black spot into a [projecting ophthalmoscope] when suddenly over the audiomonitor the cell went off like a machine gun. After some fussing and fiddling we found out what was happening. The response had nothing to do with the black dot. As the glass slide was inserted its edge was casting onto the retina a faint but sharp shadow, a straight dark line on a light background. That was what the cell wanted, and it wanted it, moreover, in just one narrow range of orientations.

A few years later they realized that cells with similar orientation selectivity and cells with similar ocular dominance were arranged in orientation and ocular dominance columns, respectively. This discovery must have been facilitated by the proximity at Hopkins of Vernon Mountcastle, who had recently discovered columnar organization in somatosensory cortex.[149]

The second historical point is that Hubel and Wiesel were by no means the first to record from single neurons in striate cortex. In 1952 the Freiburg group starring R. Jung, G. Baumgartener, O. Creutzfeldt, and O. J. Grusser had begun a systematic program of research on the visual activity of single neurons in striate cortex of the cat.[150] Although their techniques were technically sophisticated, their central finding for about the first ten years was actually that striate neurons showed little visual responsiveness: 50 percent of the many cells sampled showed no responses, and the responses of many of the others, by subsequent standards, were rather feeble. As Jung later candidly admitted, a primary reason for their failure to activate striate cells was that their elaborate apparatus (which took two years to build) was too inflexible to vary the orientation of the visual stimulus. As he put it, "We missed the orientation specificity . . . [because of] . . . premature quantification and a too rigid methodological restriction."[151]

This completes our story of research on striate cortex. The discovery and study of visual areas outside striate cortex is recounted in chapter 5.

Notes

1. Breasted, 1930. The village was probably Qurna, which was recently bulldozed by the Egyptian government. *New York Times,* March 4, 1997.
2. Sarton, 1959; Sigerist, 1951.
3. Breasted, 1930.
4. Breasted, 1930.
5. Hurray, 1928; Sigerist, 1951; Guthrie, 1945.
6. Sarton, 1959; Sigerist, 1951.
7. Breasted, 1930.
8. Sarton, 1959; Sigerist, 1951.
9. Herodotus, 1910.
10. Sarton, 1959; Sigerist, 1951.
11. Keele, 1957.
12. Keele, 1957.
13. Zimmer, 1948. Or was the chief being metaphorical or perhaps sarcastic?
14. As in *The Yellow Emperor's Classic,* compiled from earlier sources in the third century BCE (Huang Ti, 1949; Porkert, 1974). On the other hand, in vol. 5, pt. 5 of his monumental *Science and Civilization in China,* Joseph Needham (1983) tells us ". . . the brain was always an organ of cardinal importance in Taoist anatomy and physiology," which he footnotes thus: "Exactly what its functions were considered to be is not so easy to say. We shall return to all these matters in sect. 43 on physiology in Vol. 6 . . ." Needham died in 1995 as vol. 6, pt. 3 containing sect. 42 went to press. Whether his successors will fulfill his promise to discuss the importance of the brain remains to be seen. The brain is mentioned often in the context of Taoist sexual techniques (Needham, 1983; Chang, 1977; Van Gulik, 1961; Ware, 1966). Withholding ejaculation was thought to enable the semen to be rerouted up the spinal cord to "nourish" and "repair" the brain. (The Taoist adept apparently could achieve orgasm without ejaculation.) Conserving semen was believed to lead to long life or even immortality, as in this Taoist saying provided by Needham (1983):

> who wishes life unending to attain
> must raise the essence to restore the brain.

15. Spence, 1985.

16. All the works of the presocratic philosopher–scientists are lost. All we have are quotations or fragments collected by the ancient doxographers. These were assembled by H. Diels at the beginning of the century and translated into English by Freeman (1954). This account depends on her translations, Schrodinger's (1954) appreciation, and the works of Sarton (1959), Sigerist (1961) Longrigg (1993), Farrington (1944), and others cited below.

17. Freeman, 1954; Sarton, 1959; Lloyd, 1970.

18. Farrington, 1944.

19. Lloyd, 1975; Edelstein, 1967a; Longrigg, 1993; Theophrastus, 1917.

20. Grusser and Hagner, 1990.

21. Theophrastus, 1917; Freeman, 1954; Beare, 1906.

22. Singer, 1957; Galen, 1968.

23. Freeman, 1954; Beare, 1906.

24. Smith, 1979; Lloyd, 1978.

25. Hippocrates, 1950.

26. Edelstein, 1967b.

27. The standard convention for citing Plato is the pagination used in the first Greek–Latin edition published by Henricus Stephanus (1578).

28. Lloyd, 1970; Sarton, 1959; and Farrington, 1949, respectively.

29. Sarton, 1959; Needham, 1959; Mayr, 1982; Nordenskiold, 1928. On the other hand, for ridicule by a nobelist, see Medawar and Medawar (1983).

30. Grene, 1963; Gotthelf and Lennox, 1987; Devereux and Pellegrin, 1990.

31. Sarton, 1959; Longrigg, 1993.

32. Galen, 1962, 1968.

33. Aristotle's works here, and generally, are cited by the page numbers given by I. Bekker in the nineteenth century. The abbreviations for individual works used here are GA, *Generation of Animals;* HA, *History of Animals;* PA, *Parts of Animals;* SS, "On Sense and Sensible Objects" in *Parva Naturalia;* SW, "On Sleep and Waking" in *Parva Naturalia;* and YO, "On Youth and Old Age" in *Parva Naturalia.*

34. Lones, 1912.

35. Clarke, 1963; Clarke and Stannard, 1963.

36. Avicenna, 1930.

37. Schlomoh, 1953.

38. Through Sir Richard Burton, 1885.

39. Lloyd, 1975.

40. Praxagoras's fragments were collected and translated by Steckerl (1958).

41. Farrington, 1949; Fraser, 1972.

42. Longrigg, 1993; Canfora, 1990.

43. Canfora, 1990.

44. Von Staden, 1989; Dobson, 1926–1927; Longrigg, 1988. Von Staden (1989) collected and translated the fragments of Herophilus, and Dobson (1926–1927) those of Erasistratus.

45. Fraser, 1972; Von Staden, 1989; Longrigg, 1988; Edelstein, 1967b.

46. Fraser, 1972.

47. Fraser, 1972.

48. Longrigg, 1988.

49. For German human vivisection see Lifton (1986); for Japanese see Harris (1994); for the revival of human dissection, Singer (1957).

50. Von Staden, 1989; Dobson, 1926–1927; Longrigg, 1988.

51. Galen, 1968.

52. Schiller, 1965; Clarke and Dewhurst, 1996.

53. Galen, 1968.

54. Lloyd, 1973.

55. Von Staden, 1989; Longrigg, 1988, 1993.

56. Sarton, 1954; Siegel, 1968, 1970; Lloyd, 1973.

57. Galen, 1968, 1956, 1962, and 1978–1984, respectively. Each of these relatively recent translations is the first into English. Many other works remain untranslated into English.

58. Woolam, 1958; Spillane, 1981.

59. Pagel, 1958; Clarke, 1962; Woolam, 1957.

60. Lewy, 1847.

61. Nemesius, 1955.

62. Corner, 1927.

63. Hunter and Macalpine, 1963.

64. From the Renaissance until well into the eighteenth century, Padua was by far the principal medical school accessible to Jewish students from all of Europe. Between 1617 and 1816 alone at least 350 received joint doctoral degrees in medicine and philosophy and many more attended without matriculating (Ruderman, 1995). Many of them arrived with little knowledge of Latin, Italian, or any aspect of life and culture outside of the shtetels and ghettos. The Jewish community in Padua provided boarding schools to prepare such students for entrance to the medical school while enveloping them in a Jewish support network.

65. Oporinus had been a medical secretary to Paracelsus, "the Dr. Faustus of the sixteenth century," and Professor of Greek and Latin at the University of Basel before turning to printing only a year before he published Vesalius (Le Roy Ladurie, 1997). Later he published the first Latin edition of the Koran, which got him jailed. He was released with the help of Martin Luther (Saunders and O'Malley, 1950).

66. Singer, 1952.

67. Singer, 1952.

68. Singer, 1952.

69. Meyer, 1971; Clarke and O'Malley, 1996.

70. Meyer, 1971; Clarke and O'Malley, 1996.

71. Nordenskiold, 1928.

72. Clarke and Bearn, 1968.

73. Meyer, 1971.

74. Clarke and O'Malley, 1996.

75. Bartholin, 1656 quoted in Schiller, 1965; Meyer, 1971.

76. Dow, 1940; Dewhurst, 1982; Meyer and Hierons, 1965.

77. Willis, 1664.

78. Willis, 1664.

79. Neuburger, 1981; Kruger, 1963.

80. Neuburger, 1981.

81. Neuburger, 1981.

82. Gennari, 1782, quoted in Fulton, 1937.

83. Neuburger, 1981.

84. Gennari, 1782, quoted in Fulton, 1937.

85. Although he never held an academic post, Vicq d'Azyr (1748–1794) was renowned as an anatomist (the mammillothalamic tract bears his name) and as a physician, Marie Antoinette being one of his more famous patients.

86. Glickstein and Rizzolatti, 1984.

87. Clarke and O'Malley, 1996.

88. Glickstein and Rizzolatti, 1984.

89. Gall preferred the term "organology" over Spurzheim's "phrenology." For differences between the more cautious Gall and the more popularizing Spurzheim, see Clarke and Jacyna (1987) and Zola-Morgan (1995).

90. Temkin, 1953.

91. Gall and Spurzheim, 1835.

92. Gross, 1987a; Young, 1970b.

93. Cooter, 1985.

94. Young, 1970b; Clarke and Jacyna, 1987; Clarke and O'Malley, 1996.

95. Carpenter, 1845.

96. Meyer, 1971.

97. Young, 1970b; Clarke and Jacyna, 1987; Broca, 1861.

98. Bouillard was known as the "red dean" for his participation in the Revolution of 1848. He reportedly prided himself on being the model for Balzac's Dr. Horace Bianchon (Schiller, 1979).

99. Young, 1970b; Clarke and Jacyna, 1987; Broca, 1861.

100. Young, 1970b; Boakes, 1984.

101. Hofstadter, 1955.

102. Hofstadter, 1955.

103. Spencer, 1855.

104. Jackson, 1958; Young, 1970b.

105. Fritsch and Hitzig, 1870.

106. Müller, 1838.

107. This is an example of an intromission theory of vision. Extromission holds that something streams out of the eye and interacts with the seen object (e.g., Euclid). More complicated interactive formulations (e.g., Aristotle) were also held among the Greek visual scientist-philosophers (Theophrastus, 1917; Lindberg 1976). Today, most children and many adults still hold extromission views of vision (Winer and Cottrell, 1966).

108. Von Helmholtz, 1863.

109. In 1845 Von Helmholtz, du Bois-Reymond, and two other students of Müller, Carl Ludwig and Ernst Brucke (Freud's teacher), all of whom later became famous as founders of modern physiology, got together to issue a manifesto against vitalism, the doctrine that life cannot be reduced to physics and chemistry. Perhaps not coincidentally, Müller was the last great (mainstream) biologist who was a vitalist. Their manifesto declared, "No other forces than common physical chemical ones are active within the organism," and they proceeded to support this reductionism in every branch of physiology (Coleman, 1971, particularly, the bibliography; Boring, 1950).

110. Boring, 1950; cf. Sur et al., 1988.

111. Bell's (1811) account, was in a "tiny little" pamphlet of thirty-six pages, each with 4.5 × 2.5 inches of text per page, entitled *Idea of a New Anatomy of the Brain,* 100 copies of which were privately printed for his friends. It did not seem to be noticed in Europe, although it

was published in toto in an American medical journal at the time (Bell, 1812). A long and bitter priority controversy arose between Bell and the great French physiologist Francois Magendie (1783–1855) over the discovery of the law of spinal roots (i.e., that ventral spinal roots are motor and dorsal ones sensory). In fact, (a) Bell proposed only the sensory functions of the dorsal roots, (b) there is no reason to believe that Magendie knew of Bell's claims before he carried out and published his own experiments, and (c) both halves of the law were experimentally demonstrated by Magendie, whereas Bell's consideration of the functions of the dorsal roots were largely anatomically based. See Cranefield, 1974.

112. Bell, 1811.

113. Gall and Spurzheim, 1835.

114. Panizza, 1855; Mazzarello and Della Sala, 1993.

115. Carpenter, 1845; Walshe, 1958.

116. Tamburini, 1880; Manni and Petrosini, 1994. A parallel to the neglect of Panizza's work because it was ahead of its time was the fate of Gregor Mendel's (1866) paper on inheritance in peas, which although published in an equally obscure journal, also passed into the major libraries and across the desks of the biology savants of the day, to whom it apparently had no meaning. The difference was that when Tamburini (1880) rediscovered Panizza, Munk had already gone beyond him. In contrast, when Mendel was rediscovered by De Vries in about 1900, Mendel's work was still original and important (Mayr, 1982).

117. Ferrier, 1873, 1875a. In the beginning Ferrier was very stingy in giving Fritsch and Hitzig credit for their methods and discoveries. Thus, when he submitted his paper (Ferrier, 1875b) to the prestigious *Philosophical Transactions of the Royal Society,* one of the referees, Michael Foster, objected to his failure to credit adequately Fritsch and Hitzig. T. H. Huxley was then called in as a third referee "for the purpose of ascertaining . . . whether Dr. Ferrier has or has not done sufficient justice to the labors of his predecessors" (Royal Society archives, RR.7.302). Ferrier added a more explicit recognition of their priority, but the referees still were not satisfied. In the end, Ferrier refused to make enough of the requested changes and preferred to omit all his experiments on dogs, only the ones on monkeys (which Fritsch and Hitzig had not used) making it into print (the referee reports and Ferrier's replies are in the Royal Society archives, RR.7.299–305 and MC.10.194; see also Young, 1970b).

118. Ferrier, 1875b, 1876.

119. Ferrier, 1878.

120. Newton, 1952.

121. Polyak, 1957.