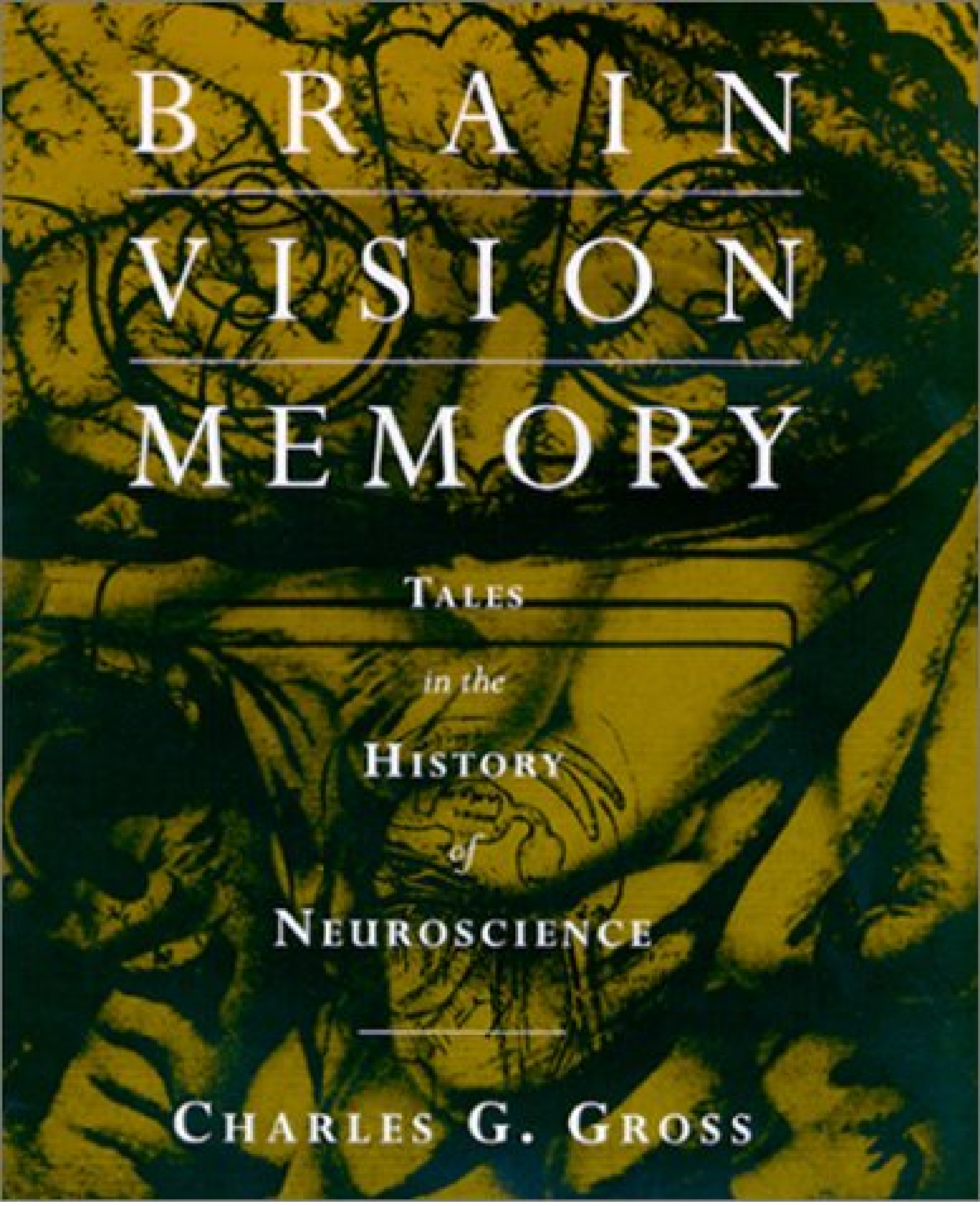
BRAIN
VISION
MEMORY
TALES
in the
HISTORY
of
NEUROSCIENCE
CHARLES G. GROSS

Introduction

I am an experimental neuroscientist specializing in brain mechanisms in vision, and a teacher of neuroscience. This introduction explains what led me temporarily to put aside my experiments and neglect my students to write the five tales on the history of neuroscience.

The first essay began in 1960. I had just completed the experimental work for my Ph.D. thesis, "Some Alterations in Behavior after Frontal Lesions in Monkeys," at Cambridge University and sat down to write the requisite review of the literature. Six months later I had reached Galen and the second century. At that point, my advisor, Larry Weiskrantz, suggested that, actually, it might be better if I got on with the write-up of my experiments, even though, as I explained to him, Galen had carried out experiments on frontal lobe damage in piglets. So I never included this historical survey in my thesis, and ultimately its review of previous work began with studies in the 1930s.

I did show my "up to Galen" manuscript to Joseph Needham. He wrote me an encouraging note, resplendent with Chinese characters, comparing Greek pneuma with Chinese chi. After graduate school I went to the Massachusetts Institute of Technology as a postdoctoral fellow to work with Hans-Lukas Teuber, the charismatic founder of the Department of Psychology, now the Department of Brain and Cognitive Sciences (Gross, 1994a). I showed him my history manuscript and proposed to continue working on it on the side. Teuber was deeply knowledgeable about the history of biology, almost as deeply as he pretended to be; however, he assured me that I had no time "on the side" and should save history for my retirement days.

Despite this advice, when I began to teach what became my perennial undergraduate course on physiological psychology (later renamed cognitive neuroscience), first at Harvard and then at Princeton, I increasingly inserted historical interludes on Vesalius, Willis, and Gall, and other "high points in man's understanding of his brain." When some of the premedical students in the course started getting restless at the length of these interludes, I began occasionally teaching a separate course entitled "Ideas on Brain Function from Antiquity to the Twentieth Century."

After the (perceived) success, described below, of my paper on the hippocampus minor, I reached into my "up to Galen" draft and my history of neuroscience lecture notes and began revising and updating them for publication. So when I was asked a few years ago to write an article on visual cortex for the multivolume handbook *Cerebral Cortex* I seized the opportunity to achieve my thwarted ambition to write a historical introduction starting at the beginning. I began with the first written mention of the brain from the pyramid age, went on to investigations and theories of brain function among Greek physician-philosopher-scientists, and continued through the coma of European science between Galen and the Renaissance. At that point in the article, for obvious practical reasons (my word limit and, certainly, my time were not infinite), I began to narrow my subject, first to the cerebral cortex and then, by the end of the article, to striate cortex. Chapter 1, "From Imhotep to Hubel and Wiesel: The Story of Visual Cortex" is a combination of that article (Gross, 1997c) and one I wrote entitled "Aristotle and the Brain" for the *Neuroscientist* (Gross, 1995).

The second essay was inspired by a visit to an exhibit of Leonardo's anatomical drawings at the Metropolitan Museum of Art in New York. The rooms were dimly lit and the hushed crowd slowly and reverentially shifted from drawing to drawing of bones, muscles, and viscera, all borrowed from the

Queen's collection at Windsor Castle. No pamphlets were available nor were there explanations on the walls, not even labels or dates of the drawings. What were we looking at? The drawings of the superficial musculature seemed accurate enough and certainly beautiful. But the viscera often seemed rather strange, the organs not looking quite right or in the correct places. Of course, I had previously seen his two drawings of brain ventricles, one a purely medieval three circles in the head and the other a realistic, but not quite human ventricular system. I became intrigued as to what Leonardo was illustrating in these famous drawings: the body observed? the body remembered? the body read about? the body rumored? the human body, or animals in human form? Was he illustrating medieval theory, as in the drawing of circular ventricles? Or was he drawing from his own dissection, as in the later ventricular drawing? Hence, eventually, the article on Leonardo's anatomy. Although it is restricted to a detailed discussion of only a few of Leonardo's neuroanatomical drawings, I think my comments are applicable to his other biological work. Chapter 2, "Leonardo da Vinci on the Eye and Brain," was first published in the *Neuroscientist* (Gross, 1997b).

The third essay derived from the question of whether there can be a theoretical biology or a theoretical biologist. Certainly I see no sign yet of anyone who made significant and lasting theoretical contributions while remaining only a theorist. All the great theoretical work was done by individuals buried up to their necks if not their eyebrows with empirical data all their busy lives, such as Darwin, Mendel, Bernard, Sherrington, and even Freud. In contrast, those individuals who were only theorists and did little empirical slogging, such as Lotka, Reshevsky, and D'arcy Thompson, have disappeared except as antiquarian curios.

Was Emmanuel Swedenborg, the eighteenth-century Swedish mystic, an exception? Solely on the basis of reading the literature of the day, he proposed theories of the functions of the cerebral cortex, of the organization of motor cortex, and of the functions of the pituitary gland that were at least 200 years ahead of everyone else. On the other hand, perhaps he was no exception since, although he often got it right, he never had any impact on biology. Indeed, his work was published and republished in many volumes, but his ideas on the brain continued to go unnoticed until after those that were actually correct were rediscovered independently. Chapter 3, "Emanual Swedenborg: A Neuroscientist Before His Time," first published in the *Neuroscientist,* tells his story (Gross, 1997a).

The fourth essay originated when my wife, Greta Berman, bought me a copy of Desmond and Moore's biography of Darwin soon after it appeared. She had been attracted by a very enthusiastic blurb on the back cover written by a friend of ours. At first I was skeptical, as the book had been rather negatively reviewed in the *New York Times Book Review* by my old history of science teacher, I. B. Cohen. But as soon as I began to read, I realized what an absolutely splendid book it was, a truly exciting page turner placing Darwin in his social, economic, and scientific world.

Right in the middle of the book I encountered several references to a lobe of the brain called the hippocampus minor. I do sometimes come across names of unfamiliar brain structures, but never a whole lobe, particularly one that was supposed to be unique to humans. As I looked into more accounts of Victorian biology and the battles over evolution, I realized that although the hippocampus minor was repeatedly mentioned by historians of evolution, it was clear that none of them had any idea of what or where it was. Apparently they had never read or even looked at the pictures in the many articles about the hippocampus minor in midnineteenth-century scientific and popular journals. Furthermore, I could find no mention of such a structure in any of my neuroanatomy textbooks (until later when I looked at outdated ones). When I called several of my friends around the country who were among the leading students of the anatomy and physiology of the hippocampus, they too had never heard of the hippocampus minor. Clearly, there was or should have been a ready audience for a paper on this mysterious structure. Hence I researched and wrote "The Hippocampus Minor and Man's Place in Nature: A Case Study in the Social Construction of Neuroanatomy," a version of which constitutes chapter 4. It tells what the hippocampus minor is, why it was so important in 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.

Several of the essays were improved by the detailed comments of David Czuchlewski, George Krauthamer, Larry Squire, Derek Gross, Phil Johnson-Laird, Mort Mishkin, Maz Fallah, and Robert Young. Maggie Berkowitz and John Cooper were particularly helpful with the classical material. George Krauthamer was kind enough to dissect the hippocampus minor of a human and several species of primates for my benefit, as well as translate from the German, Dutch, and French. Steve Waxman, founding editor of the *Neuroscientist,* encouraged the entire project by publishing two of the essays and signing me up for lots more in the future. Linda Chamberlin of the Princeton University Library was tireless in getting me old books and journals from everywhere. Mairi Benson, librarian of the Sherrington Collection in the History of Neuroscience in the Physiological Laboratories, Oxford University, was also very helpful, as was the Wellcome Institute Library in London. I thank Michael Rutter and Katherine Arnoldi, editors at The MIT Press, for their assistance and tolerance, Sarah Jeffries for copy editing the manuscript, and Shalani Alisharan for proofreading and making the index.

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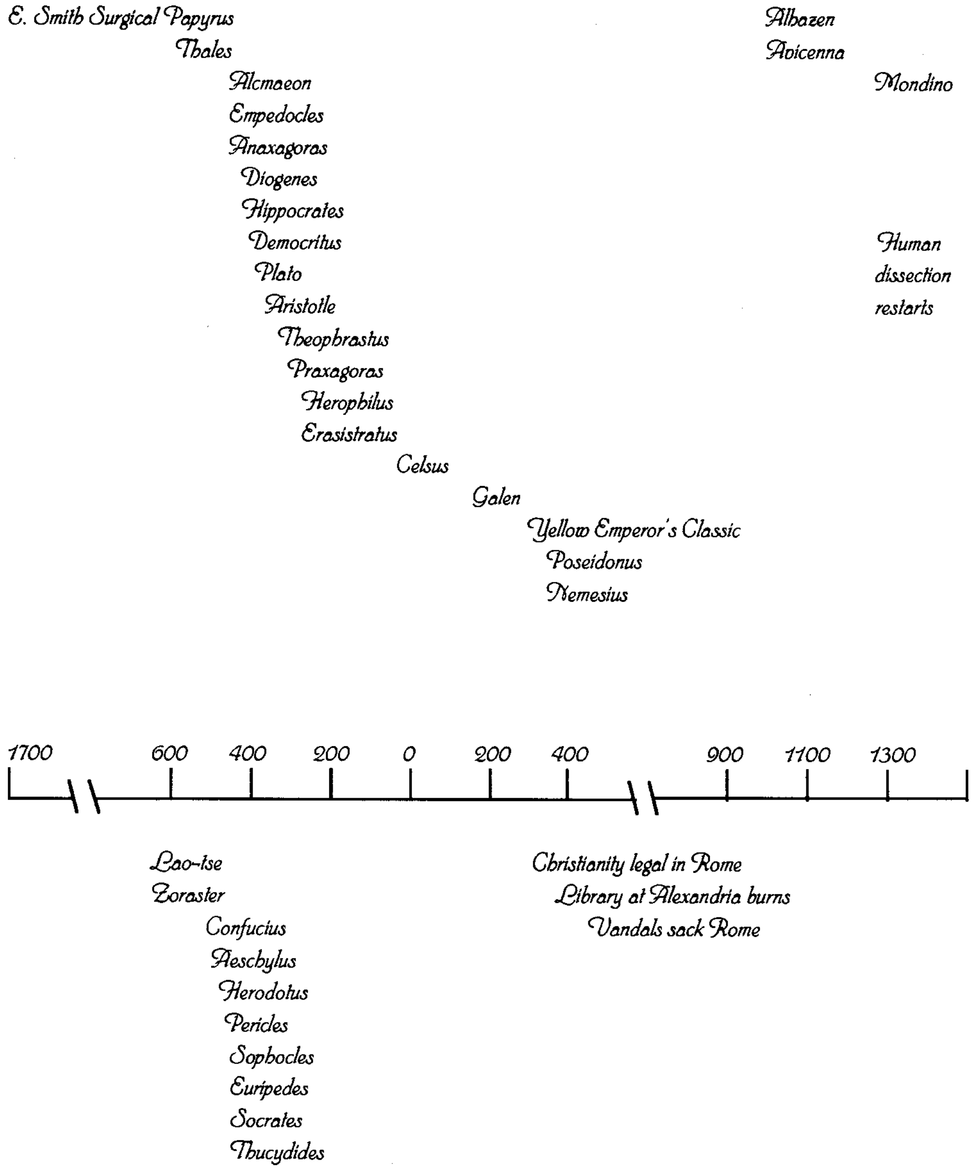
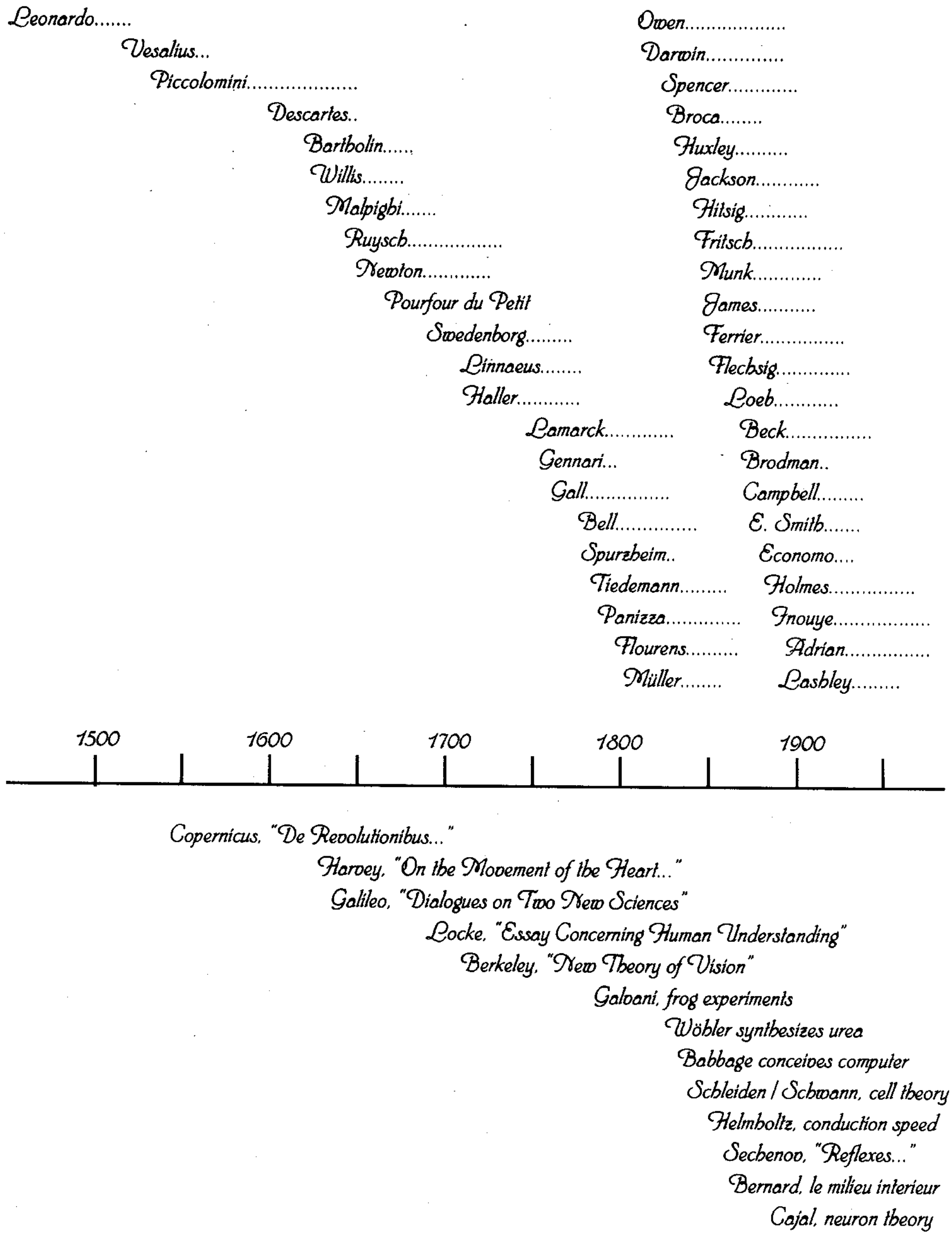
Brain, Vision, Memory



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.



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.

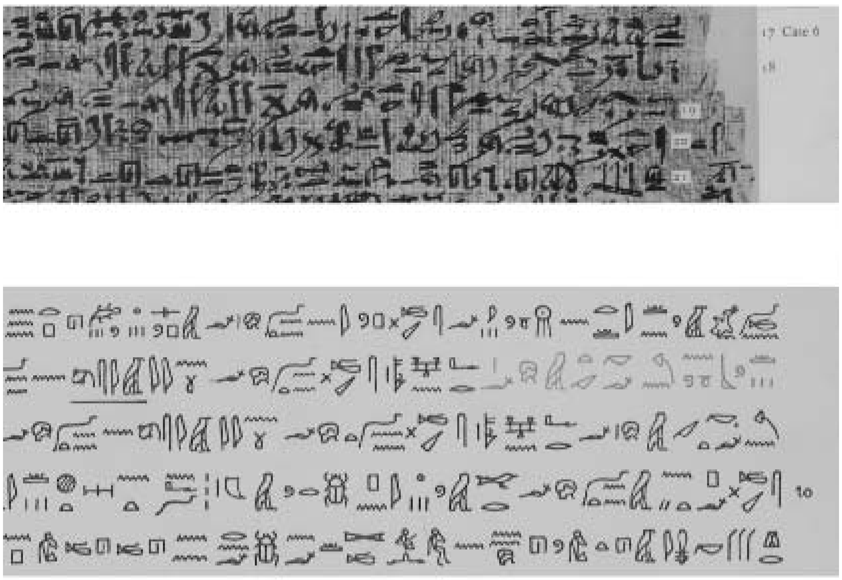


Figure 1.1 A portion of the Edwin Smith surgical papyrus, case six, concerning a skull fracture that exposed the cortex (Breasted, 1930). Upper, the actual papyrus, written in a hieratic script. Lower, the hieroglyphic transliteration. The word for brain is underlined. Writing is left to right in both figures. (Princeton University Library)

1

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, penetrating 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

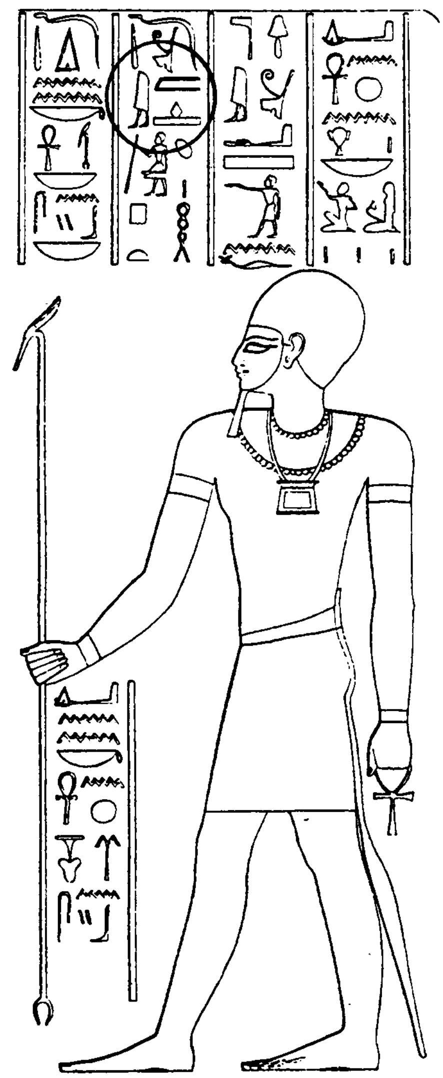
Figure 1.2 A statuette of Imhotep as a demigod, a person of human origin who after his death was viewed as superhuman and worshipped. He achieved this status within 100 years of his death. As a demigod, Imhotep was typically represented with an open scroll on his lap. Statuettes like this one, from the 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).

Chapter 1

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