BRAIN AND BEHAVIOR:

A BRIEF HISTORY OF IDEAS

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If someone were to ask you what organ in the body controls blood circulation, you would immediately say, “The heart does that.” In the same way, most of us have pretty fixed ideas about what structure in the body controls behavior—the brain. Indeed, we certainly take it for granted that the brain is the “organ of the mind,” and we know, for example, that when people have brain damage, their behavior is often affected. So, there is apparently good reason to believe strongly that the brain is the seat of behavior. How we think about the brain and what it does will certainly have an impact on the kinds of medicine we would apply to the treatment of head injury and brain damage. Thus, to treat mental illness, we must have w working concept of what mental illness is and how it is caused. For example, it wouldn’t make much sense to give drugs to change the specific chemistry of nerve cells if we believed that hallucinations were really due to evil spirits invading the body. How we treat disease is very much influenced by what we believe about causality and what we take to the “good” scientific data. But what is good at one time may be considered laughable or even dangerous at another period in history. It wasn’t al that long ago that patients had holes drilled in their heads to relieve headache or to release evil spirits thought to have been causing their problems. In many cases, such treatments may have killed patients who were already weakened by disease.

Anthropologists have studied human skills from around the world and found that people living thousands of years before Christ knew that the head played an important role in determining our behavior. How canwe make such a claim when there were no writings or other documents to support this idea? Because hundreds of ancient skulls found in France, Africa the Far East, and especially South America have been found with carefully drilled holes.

Primitive peoples believed that demons and evil spirits could take possession of an individual, and that *trepanation*, combined with prayer and exorcism, could coerce the spirits to flee the body through a hole made in the head. (In fact, even up to relatively modern times, people were thought to be possessed by spirits or demons if thet behaved strangely, spoke differently, or displayed unusual body movements—think of the Salem witch trials.) Some people might argue that the holes in the skills were smply the result of accidents or battles, or that they were made as part of a religious ceremony some time after the death of the person. Yet all the evidence seems to argue in favor of a more systematic, surgical operation in the living patient. Often the holes in the skulls have smooth edges and are almost perfectly round or even square. We believe that early practitioners took very great care in performing these operations so that their “patients” could survive. Most telling of all is the fact that some of these people survived long enough after the trepanation for new bone tissue to form around the edges of the holes. And in some caes, skulls have been found with several partially “healed” holes, showing that the procedure was repeated on the same person several times, and that he or she survived each opertion long enough for scar tissue to form. Neurosurgeons even today sometimes use this drilling technique—trepanation—to reduce pressure buildup or to remove blood clots that could otherwise damage the brain. Whether medical treatment, religious ritual, or something else that we haven't uncovered yet, the trepanations performed during prehistoric times will remain somewhat cloaked in mystery. Even so, we can conclude that ancient peoples had already discovered a connection between the head and behavior.

Even during the time of the great Pharaohs of Egypt (about 3500 BCE), a papyrus taken from a tomb carefully describes a head injury and gives a fairly accurate diagnosis of its causes and symptoms. The Egyptian doctors seemed to know that the symptoms caused by damage to the head could appear in parts of the body distant from the site of the actual injury. For example, they described how certain blows to the head could change vision or the coordination of movements, and how an injury to one side of the brain caused the symptoms to appear on the opposite side of the body.

Despite the knowledge that the head had something special to do with behavior, the Egyptians (at least the people who did the embalming) did not seem to consider the brain as a particularly noble or important organ of the body. Ancient Egyptian scripts tell us that they clearly believed in an afterlife and that they developed a very sophisticated art of embalming their dead for the journey to that next life. Egyptian funeral directors took great care in embalming and conserving every part of the body, and that is why we can find almost perfect mummies in museums although they were entombed almost 5000 years ago! The only exception to this careful conservation of body parts was the brain, which was drawn out through the nose with a special tool and then thrown away. As far as we can verify, the Egyptians believed that the brain was an organ that secreted water and mucus through the nose. One the one hand, the Egyptians seemed to show some understanding of how injury to the head would produce “neurological” symptoms, yet they did not appear to recognize that the brain itself was as important as the heart, for example. This paradox suggests that even in the time of the Pharaohs there must have been competing ideas about what organs control behavior and how they work. This is not very different from the contemporary debates about brain structure and function that we discuss in this book.

For Plato, the great Greek philosopher, the substance of life—that which creates the soul and gives life itself—was located in the brain, the spinal cord, and the sperm. Yet despite his views, the dominant view for almost two thousand years was what is called the “cardiocentric doctrine,” in which *the heart* is thought to be the seat of the soul and the organ that controlled mental functions, emotions, and behavior. This view endured almost until the beginning of the seventeenth century and was shared by the other great Greek philosopher, Aristotle. Aristotle taught that the brain was primarily an organ that “cooled the passions and the spirit,” which were first fired in the heart. He believed this because when he had the opportunity to touch the exposed brain of people who had just died, it felt cool and moist to the touch, whereas the heart felt warm. Most early doctors also accepted this idea, as did the Catholic Church.

There were several reasons why the cardiocentric theory lasted for so long. First, Aristotle was such an important figure to both physicians and the Church that his teachings came to be treated as dogma. Second, except for the dissections of Herophilus and Eristratus in the city of Alexandria, there were virtually no anatomical studies done on cadavers from the time of the Greeks to the period of the Renaissance. Mostly intellectual speculation and theory, and not research and investigation, determined what was true and what was false.

Historians of ancient medicine tell us that for many Middle Eastern and Asian cultures the *liver* was considered the seat of the soul and the controller of behavior and emotion—the most important organ of the body. In some primitive cultures, victorious warriors removed the livers of their victims who fought well against them and sometimes ate the organ to gain the strength and courage of their adversaries. In New Guinea, however, cannibalism after fighting also led to eating of the brains of vanquished enemies—to gain their wisdom and strengths.

On our own continent, Friar Bernardino de Sahagun, in his “General History of the Things of New Spain,” written between 1569 and 1592, collected conversations with the Indians of the time who lived in the area of what is now Mexico City. The ideas of the Aztecs were surprisingly similar to the European and Asian perspectives. Thus, the major centers of the body were the upper portion of the head, the heart, and liver. The brain was what made people know and remember, and like the Europeans, the Aztecs believed that the heart was the vital organ necessary for consciousness. Friar Sahagun wrote that the *nahuas* (including the Aztecs) believed that the heart was the center for feelings and emotions, and that sudden loss of consciousness or convulsions was due to faintness of heart. Other diseases were thought to be the result of an “imbalance” between the head, the heart, and liver—a view that would not seem strange to many people even today.

According to Stanley Finger, who has written a wonderful new book on the origins of neuroscience, trepanation was also extensively practiced in Peru over a thousand years before Christ. He reported that almost 40 percent of the well-preserved mummies found in the area of Cuzco, the Inca Capital had trepanned skulls. Very often there was even more than one operation, with a survival rate that Finger estimates to be about 65 percent. Was the surgery for the treatment of convulsions, headaches, or mental disorders? No one can say for sure.

The debate over the seat of the passions, the soul, and the mind was still active during the time of Shakespeare. The question of whether the heart or the head was the seat of the passions was important enough for the bard to refer to the controversy in *The Merchant of Venice*. Portia, thrown into the abyss of uncertainty, ponders:

> Tell me where is fancy bred, or in
> the heart, or in the head? How
> begot, how nourished?
> Reply, reply.
> It is engender’d in the eyes, With
> gazing fed; and fancy dies
> In the cradle where it lies:
> Let us all ring fnacy’s knell;
> I’ll begin it—Ding dong, bell.
> Ding, dong, bell.
> (Act III, scene II)

Although we now know much more about the heart's functions than we did in Shakespeare's day, we still have a lot of sayings that make reference to the heart's importance in emotions. For example, we still say that an unlucky lover has a "broken heart." This is a reference to the ancient cardiocentric theory of the passions. But why do we worry ourselves over this bit of ancient history and current superstition? What difference do the beliefs of ancient philosophers and doctors make to us today?

The reason becomes clear when we realize that widely accepted ideas and conceptions of medicine and bodily functions play an important role in determining how we go about treating illness and disease. The fact that the heart was so important for behavior and for the control of the passions (the Greek word *pathologia* means the study of emotions) explains in part, at least, why leeching was a common medical practice for people suffering from profound sadness and general pessimism, a sickness which was then called "melancholy" and is now called depression. Using leeches to bleed the patient was thought to purge the bad "humors" circulating in the blood and throughout the body. If we still accepted such ideas today, just imagine what the treatments would be like for depression, for example. It is unlikely antidepressant medications would be used because these drugs were developed specifically to alter chemical imbalances that affect nerve cells in the brain, which in turn affect behavior. Then, as now, the cause of the disease determined the treatment.

When did the idea that the brain is the seat of behavior really begin to take root? No one is quite certain of that answer, but some historians of medicine believe that physicians living in Greece about 500 BCE were the first to write that the brain was the seat of the intellect. Here is the view of Philoctetes of Tarentum, a physician and the student of the philosopher Pythagoras:

> The rational living being (the human) has four vital organs: the brain, the heart, the navel and the genitals. The brain is the seat of the mind, the heart is the seat of the soul and of feelings, the navel is the site of growth of the embryo and the genitals are the seat of procreation. The brain is the principal organ of the mind, the heart, the principal organ of the animal.[1]

As far as we know, one of the first people to dissect the human brain was Alcmaeon, a contemporary of Aristotle, with whom, evidence suggests, he did not share many ideas. If Aristotle speculated, Alcmaeon examined. He dissected the brain and other organs directly, and attributed functions to them based on his direct observation. Thus, in many ways, he was a scientist in the modern sense of that word. For some historians, he is the true father of psychology and of modern experimental medicine.

One of Alcmaeon's most compelling ideas was that all of the sensory paths (e.g., taste, smell, touch, sight, etc.) in the body end up in the brain. The sensations arrive in the brain through paths that consist of hollow tubes, which contain water and fire—for the ancient Greeks, the basic elements of all life and living matter. Alcmaeon believed that all of our sensations, ideas, and memories were stored in the brain. And while he thought all living beings, including animals, could have feelings, only humans could gather the feelings to form ideas. He considered the brain to be the seat of the most noble of “faculties,” thought.

It is generally agreed that the person with the most important and lasting influence on the belief of a brain-behavior link was the Greek physician Galen, who was the “sports” doctor to the Roman gladiators. Like Alcmaeon, Galen developed his theories by dissecting animals. Through his observations and his treatment of wounded gladiators, he came to believe that there were specific chemical substances which he called *corporeal humors*[2]—the four of them being phlegm, blood, black bile, and yellow bile. These, he thought, combined in the heart with the “pneuma,” a Greek word that described breath and other more subtle and spiritual aspects of the individual, among them the mind. The four fluids entered the brain through a network of very thin tubes which he called the “*rete mirable*”—the miraculous network. The brain then distributed these fluids through the nerves to produce behavior.

This was quite an inventive theory, since nothing like the *rete* exists in humans. Perhaps even Galen saw what he wanted to see because it fit so well with this beliefs and attitudes. In any case, for Galen, behavior, and thus the “personality” of the individual, was determined by the quantity and the makeup of the fluids circulating in the nerves: Someone with “too much” blood would have a hot-headed temperament, while too much black bile resulted in depression and melancholy. Even today, the term “sanguine” (from the Latin for blood) means a quick-tempered person in many Romance languages, and “bilious” describes a peevish, ill-natured person. These views of personality types are holdovers from ideas developed almost 2000 years ago.

Galen also thought that the seat of intelligence was not in the brain tissue itself but in the “ventricles” of the brain. We know today that the ventricles are a part of the inner linings of the brain and that they are like an aqueduct that carries the cerebrospinal fluid (the fluid that is drawn in a spinal tap). For Galen, the brain itself simply gave form to the cerebral ventricles, where spirit and body humors came together to produce behavior. Galen, and later the Church Fathers, thought that they had identified three “ventricular cells” where the cerebral functions were located, and their views became known as the “cell doctrine” of localization. Intelligence was to be found in the front (or anterior) vehicle; knowledge (or mind) in the middle ventricle; and memory in the back of the head, the most posterior vehicle.

During the 1500 years that followed Galen’s ideas, there were no major changes in how physicians and academics thought about the brain. There were no changes in teaching about the cerebral functions in the universities of Europe. The debates, if they occurred at all, centered around which ventricle was responsible for which function, and how the spirit or pneuma worked together with the body’s humors. This debate was the first and longest in the history of what we call “localization of functions.” In the Middle Ages, students never wondered whether the seat of memory might be found in the frontal lobes or in the deeper structures of the brain; they argued instead about whether different aspects of intelligence (the “rational soul”) were to be found in one or another ventricle of the brain.

After the fall of the Roman Empire, and with the rise of Christianity, demons and devils took possession of the scientific spirit and quelled any further research into the brain. It was a time when debate, discussion, and the study of worldly events was viewed as the work of the devil and his disciples. The study of the human body was banned under pain of death, and the universities, which were completely under the control of the Church, ensured that most academics taught only accepted dogma. It was safer and easier to teach the dogma of the “ancients” than to risk the ire of the Church and excommunication for heresy, possible banishment, or worse. Since most teachers were members of the clergy in any case, only strictest dogma was taught. Later, during the hysteria of the Inquisition (the twelfth through the eighteenth centuries), professors were eradicated from the body of the Church on only the slightest suspicion of heresy. During that time it would have taken great courage to question established dogma, and even more courage to dissect human cadavers when severe torture and death were the penalty for such inquiry.

From the Middle Ages to the beginning of the seventeenth century, superstition, fear, and prejudice dominated even the most cultured of individuals and societies. Ghosts, demons and goblins were thought to stalk the land; women accused of being witches were tortured and burned in countries throughout Europe. In France, 134 witches were burned in Strasbourg in just four days. Special numbers, certain rocks, religious relics, plants, and “unusual” people were thought to have magical powers that could cure disease by touch. Chemistry consisted of making potions and of trying to turn common earth into silver or gold. Science, as we think of it today, could not prosper in such a hostile climate, and no real progress was made in understanding physiology or in medical treatments.

During the Renaissance (approximately 1450-1550), the medieval view of the ventricles as the seat of intellectual and rational functions began to be questioned, but not yet completely rejected. For example, the great artist of the time, Leonardo da Vinci, was able to make excellent wax mold castings of ox brain ventricles in order to reveal their exact shape. However, he still believed that memory, perception, and thought were located in different parts of the ventricular system. Even though Leonardo also carried out human dissections, he still managed to impose the *rete mirable* on the base of the brain because the teachings of Galen were still accepted in his time.

The anatomist Vesuvius (1514-1564) is thought by some historians of medicine to be the greatest anatomist of the Renaissance. As a measure of the respect in which he was held, he was appointed professor of anatomy at the University of Padua when he was only twenty-three. Some writers suggest that Vesalius was one of the first scholars to reject the cell doctrine by refusing to accept the idea that psychic functions were located in the cerebral ventricles. In fact, Vesalius argued that the ventricles were essentially the same in animals and humans and, there, had nothing to do with the ability to think and reason. He believed that the differences in intellectual abilities between animals and people resulted from the fact that people had better developed brains. Vesalius eventually came to deny the existence of *rete* in humans, although he could not quite get away from the idea that animal spirits were produced in the ventricles.

About a century later, in the mid-1600s, Thomas Willis, an English physician, published a major work on cerebral anatomy in which he suggested that the brain tissue itself controlled memory and volition. In fact, he attributed imagination to the corpus callosum—the band of nerve fibers that connects the two brain hemispheres. Willis's work was very popular at the time and he attracted many followers, thus paving the way for a more modern view of brain function and localization.

The first half of the seventeenth century saw a change, and it is now widely acknowledged that the French philosopher and mathematician Rene Descates (1596-1650) paved the way for new discoveries about the brain and its functions. Actually, Descartes left France early in his life and worked mostly in Holland, where the intellectual climate was more open and tolerant. Descartes began to influence the thinking of his time by first rejecting all previous forms of analysis in favor of reducing complex concepts into their simplest components. He actively engaged in experimental research and tried to develop quantitative explanations for the observations that he made. Descartes was clearly interested in the behavior of animals and humans. He believed that if all animals had some aspects of behavior in common, it was because, in some ways, they all behaved like machines. He thought that the laws of mechanics, as he knew them, could help to explain how we behave.

Descartes looked carefully the at the movements and behaviors of people and animals, and saw in them the kind of movements produced by the “dancing statues” in the king’s garden at Versailles. These statues were controlled by a system of valves, tubes, and chambers that varied water pressure and created the illusion of living bodies. Descartes compared this hydraulic system to the nerves in living beings. He reasoned, if one could create moving statues through the use of fluids, why would human movements not be controlled by “spirits,” Galen’s “pneumata,” circulating through the pores and tubes of the body?

Recognizing certain similarities between animals and people, Descartes still believed that there were fundamental differences between humans and animals. Humans had a soul and could think and know themselves, while animals did not, and could not think. Animals were nothing more than machines, much like those in the royal gardens which were merely animated by a network of tubes. Human beings, however, were in part machine and in part divine, because they possessed a soul. This was a very revolutionary concept for the times since the soul could remain distinct from the body but penetrate it to provide divine nature to human beings. It would then be possible for the soul to leave the body intact when death arrived. The “remains” were simply that—an empty and broken machine whose parts could be studied and analyzed, just like any other machine. This view meant that the systematic study of body functions could be made with the support of religious and moral authorities, since the soul and spirit remained intact and untouchable.

By the middle of the 1500s, physicians and professors of anatomy could make autopsies and examine the body and brain, without fear of excommunication, prison, or the stake. Despite this major advance in thinking, for Descartes one very serious problem still remained. If the soul was divine and came from God, who is the essence of perfection, it could never be divided from God because that would mean that the soul is less than perfect. To the seventeenth-century scholar, this posed an insoluble problem, for the soul would need to enter the machinery of the body as perfection and remain untainted by the body.

Descartes had enough knowledge of human anatomy to know that most structures of the body came in two or more parts—a right hand and a left hand, a right and left hemisphere of the brain, a right and left chamber of the heart, and so on. Even the highest organ, the brain itself, had distinctly visible parts, so where could the soul locate itself, and how could it control the different parts of the body while remaining "perfect and indivisible"? Descartes proposed an elegant solution to this problem: The soul penetrates the body at one point and one point only, from where it could control the physical and spiritual bases of the mind.

Descartes' point of entry was the "conarium," a small gland at the center of the brain which we now call the pineal gland. Why this small structure? Because it was the one part of the body, near all the senses, that was not divided into parts and because it was surrounded by the cerebral ventricles which he thought was a reservoir for the animal spirits. This was the first known and systematic attempt to localize function to material substance in the brain itself, and a major departure from the ventricular doctrine of the past 1500 years.

Descartes' proposition meant that, while the soul and the body interacted, they would need to remain distinct and separate. It is this idea that came to be known as the mind-body problem or "dualism," and it is still very much alive today. The soul or the mind exists on one level (the metaphysical) and the machinery of the body on another (physical). On the physical level, we can "explain" the functions of the body according to the laws and principles of nature, discovered through the application of science. The mind, as opposed to a machine, cannot be reduced to component parts and its existence can be understood only through faith and belief in God. Descartes' view, which approached that of many Church theologians, was eventually approved by the Church and marked the beginning of a new era.

It was accepted that the soul could never be affected by experimentation performed directly on the body, so doctors and anatomists could get down to their work in earnest, to study and explore all aspects of the body, including all the different parts of the brain. The ancient and long-held conceptual fiction of the cell doctrine—which "localized" mental functions in the "cells" of the ventricles—began to disappear discreetly. The science of anatomy, although primitive and often wrong, gained respect as a teaching and experimental discipline, not all that different from our approach today.

In the seventeenth century, anatomy was on its way to becoming a valued part of the university curriculum, while neurology remained trapped in its infancy. At their "professional" meetings, physicians were just beginning to present clinical cases of brain damage or tumors, and the only points that were debated were the kinds of behaviors and disturbances that resulted from disease or injury.

The fact that certain lesions and diseases of the brain could produce specific symptoms led physicians of the time to conclude that the damaged areas must, in some way, control the affected behaviors. If functions could be so localized that a small tumor could create such a radical change in behavior, all behavior must be localized—even the most minute of actions. One of the bedrock principles of neuroscience—localization—gained new footing and inspired the next generation of researchers.

With the dawning of the "age of reason" in the late seventeenth and early eighteenth centuries, it did not take long for some bold individuals to move from clinical observations of patients to real experimental research in animals. These researchers had only very crude techniques, but they tried to reproduce the same kinds of symptoms found in humans in the brains of living animals, comparing their results to those seen in brain-injured patients—and the experimental neurosciences were born.

By the eighteenth century, neuroanatomy was making great strides. New chemical dyes, first perfected for the textile industry, were now being used to stain brain tissue sections so that they could be examined in more detail with the aid of the newly developed microscope. The builder of one of the first microscopes was a Dutch textile worker, Anton Van Leeuwenhoek, who was very impressed with what he saw when he looked through his invention. It is no surprise that he was interested in staining tissue, since his main line of work was textiles! Using his new invention, he looked at the sperm cells of dogs and cats, and believed he saw miniature dogs and cats in the spermatozoa, dubbing them “animalcules.” Van Leeuwenhoek did not seem to have any problems with his vision—nor did many of his fellow scientists who reported seeing the same thing. An interesting conceptual fiction was born, which fortunately had a much shorter life span than the cell doctrine.

There is no question that without the microscope and its various improvements there would be no modern neuroanatomy. And throughout the 1700s, continuous improvements in optical lenses and microscopes allowed anatomists to examine and distinguish among cells of different size and shape. It didn’t take long for the anatomists to observe that some parts of the brain had more nerve cells than others, and that not all nerve cells had the same shapes. It was not a great leap to surmise that the different kinds of cells were arranged in layers according to some underlying structure. If parts of the brain surface looked so very different, might the different parts have distinct and unique functions? These kinds of ideas lent more support to the notion that specific functions could be “localized” according to their anatomical characteristics, or “cytoarchitecture,” meaning that different parts of the brain could be described by how the nerve cells looked.

Mapping of the brain was now well under way and mirrored the principles that governed the mapping of other complex structures, such as cities or towns. Anatomical scientists likened themselves to geographic explorers, who carefully measured and drew what they observed. To understand the brain, one needed a good map of its parts, and how these parts were related to one another.

This type of thinking, which would flower more fully in the nineteenth century, gave birth to our current variety of localization theory. It took its impetus from attempts to classify people's personalities and traits according to their brain development. The theory was fueled by the ideas of Franz Josef Gall and his colleague Johann Spurzheim, which are still with us today, though in modified form. For Gall and Spurzheim, the ~~surface~~ outer layer? of the brain (the cortex) consisted of many different "organs," each of which was a center for the control of a particular type of behavior—for example, cortical regions made a person have a well-developed "responsibility," other regions controlled the sense of "self-esteem," while still others were responsible for mathematical or artistic ability, the "gift" of poetry, and so on. Gall and Spurzheim thought that every kind of behavior imaginable was determined and controlled by a specific "locus" in the brain—a center for each behavior. This view is not all that foreign to us since many people today have very similar views—you often hear people say, "She has a real head for math." This perhaps was the major legacy of Gall and Spurzheim.

Where they went wrong was in their idea that different personality traits of an individual could be predicted and explained by the "fact" that a given brain region was particularly developed (or underdeveloped). For example, if you were particularly good at numbers, the reason was that the brain region controlling that ability was highly developed and therefore would be materially bigger in comparison to someone who was poor in math. If you were lazy or unmotivated to work, the reason was that your “cortical organ” controlling “industriousness and responsibility” was underdeveloped. Every aspect of behavior was explained according to this notion of localization. But Gall and Spurzheim went even further in their development of what they called the science of phrenology—which got them into trouble with other respectable scientists.

They proposed that by examining and measuring the bumps on a person’s head, they could exactly predict personality, sense of moral worth, and all the mental “faculties.” Since the cortical areas were more or less developed, depending on the extent to which the person had the trait, the brain tissue would shape the contours of the skull, which could then be measured for a full personality assessment. The technique was called *cranioscopy*, and special machines were developed to assist the phrenologist in assessing the distribution of the bumps. In some cases, employers insisted that prospective employees undergo cranioscopy to ensure that they had the right bumps (personality) to be trusted in sensitive jobs, as in banking or teaching. For a while, it became fashionable in the salons of high society to have a bump reading and a phrenological character assessment. Thus, by an unorthodox path, founded on a set of erroneous ideas about how human traits are defined and measured, phrenology introduced the theory of localization of function, the vestiges of which we still find, in one degree or another, in modern neurology.

Here is a recent example of localization theory taken from a study by German neurologists. Using a technique called magnetic-resonance imaging, or MRI, about which we will tell you more in the next chapter, the doctors studied a relatively rare group of musicians who had perfect pitch, the supposedly inherited ability to identify any musical note without comparison to any other reference note. By analyzing the computer-generated brain scan images, the neurologists concluded that the musicians with perfect pitch had more asymmetrical brains (this means that the two hemispheres of the brain are not equivalent) than nonmusicians. One area called the *planum temporale,* which is a brain region involved in hearing, appeared to be twice as large in perfect-pitch musicians as compared to nonmusical people. Of course, not everyone agrees with the idea that such complex musical skill is localized to a specific region of the brain, or that the size of a given brain region necessarily implies greater inherent skill or ability. We cite this study simply to show that phrenological ideas developed well over a century ago still have an impact on current thinking about brain functions.

In the long history of thinking about human structure and functions, the localization doctrine was quite new. Although the medical writings of the early Roman and Greek physicians mentioned “centers” in the brain, they were really talking about something quite different. In fact, most of the ideas we now have began to take hold only about 150 years ago. Although phrenology soon lost its popularity, the ideas of Gall and Spurzheim probably did spur physicians to perform a more careful examination of patients with stroke or injury to the brain. To determine whether such centers did indeed correspond to anatomy, postmortem examinations of patients' brains became more systematic—and more scientifically and medically respectable.

Among the most accomplished neurologists of the last century was the French physician Paul Broca. Boca, who was also interested in anthropology and personality, was one of the first to describe the case of a stroke patient. The patient seemed to understand what was said to hi, but had entirely lost his ability to speak. Broca called this symptom "aphemia," what today we call *aphasia*. When the patient, who could only utter the word "tan" in response to any question, died, Broca removed his brain, examined it carefully, and reported his findings to the French anthropological society. What he discovered was a very large lesion, probably caused by a stroke, on the left side of the patient's brain in the area called the posterior frontal cortex.

Intrigued by this case, Broca began to see if he could find other patients who had similar kinds of damage to the left frontal cortex. He was able to locate eight patients with language problems similar to his own patient, and seven of them had damage to the same brain region. Because of this linkage of language problems to injury of the left frontal cortex, Broca came to the conclusion that "we speak with the left side of the brain"—a view that is still generally accepted. Broca's contribution was considered important enough to name the "language center" of the brain in his honor, and the disorder resulting from damage to the left frontal cortex is now known as Broca's aphasia.

By the middle of the nineteenth century, physicians and scientists sought and found examples of nonlanguage functions that they could attribute to other specific regions of the brain. In America, many doctors were impressed with the report of an interesting case of very dramatic personality change that occurred after a freak accident damaged the frontal cortex of a railroad worker, a young man named Phineas Gage. Gage was employed as a track-layer for the Vermont Railway Company and was known in his community as an upstanding, religious, moral-bound family man. One day, Phineas was putting gunpowder into holes in rock that needed to be blasted away for the tracks. Phineas' job was to tamp the explosive powder into the hole and press it into place with a commonly used, three-foot-long iron rod, called a tamping iron, which was ponted on the upper end. There is quite a lot of flint in Vermont, and that rod must have struck some because the gunpowder ignited and blew that rod, just like a huge bullet, right through the front of Phineas Gage's head, taking off the top of his skull in the process.

Phineas was knocked to the ground—and survived—sitting up only a few minutes later. Although bleeding profusely, he was brought, in a sitting position, to town and treated by the local doctor who put a poultice on the open wound. Phineas seemed to make a miraculous recovery—except for the fact that he "became a totally different person"! He became abusive, lazy, passive, disinterested, and generally quite obnoxious. He eventually lost his job and made his living as a circus "curiosity," traveling around the region and showing himself and the rod that almost did him in. Gage's dramatic personality change led many physicians to believe that the development of "character" and social behavior might also be localized in the frontal cortex. That is why damage to the structure led to such a dramatic and rapid turn of personality. Thus before and for about ten years after World War II, hundreds of mental patients who were considered by medical staf as particularly aggressive were suibjected to removal or damage of the frontal cortex (the procedure known as lobotomy) in order to make them more tractable and easy to manage. Here we see how “psychosurgery,” as dramatized in the film *One Flew Over the Cuckoo’s Nest,* was based on ideas developed from phrenology, from the work of Broca, and from the early, clinical observations on people like Phineas Gage.

When we review the history of knowledge about the brain, it becomes obvious that in each period researchers believe their ideas to be the most rational and scientific, and that by using their theories or techniques, new discoveries and truths are “just around the corner.” In comparison to the science of chemistry or physics, which goes back hundreds of years to the Middle Ages, neuroscience is a youngster of only a few decades. The fact that neurology and neuroscience are so new may explain why ideas like the ill-founded brain-ventricle theory could last for fifteen centuries.

But today there are so many scientists and worldwide communication is so excellent that concepts which seem to be fundamentally important this month are rejected and forgotten a short time later. Rapid change in technology lead to exciting breakthroughs and revelations, which sometimes seem obsolete by the time the work is published. Especially in biology, new molecular techniques are allowing researchers to explore cellular events that would have been impossible a few years ago.

Modern neuroscientists can now study the chemical and electrical activity of single nerve cells while they are intact and functioning in the living brain. In this heady atmosphere there are some researchers who have been tempted to think that even the most complex of functions—like cognition, thinking, learning and memory—can one day be understood at the level of a single neuron. If we know what takes place there, we can infer from that information how the whole brain works, with its billion neurons, glial cells, and seemingly infinite connections which are always in a state of flux and change.

Other contemporary scientists believe that complex functions such as memory can be localized to discrete brain areas and have developed innovative ways to test their views. For example, Richard Thompson, at the University of Southern California, is one of the leading proponents of the local circuit model of cerebral functioning. He has sought to explain a basic form of learning called "classical conditioning"[3] as a simple response produced by modifying the activity of a few neuron circuits in the cerebellum—a posterior part of the brain implicated I the control of fine movements and balance. In his experiments Thompson first made rabbits blink in response to a puff of air to the eye. He then presented a tone just before the air puff to get the animals to blink to the sound of the tone. By carefully damaging nerve cells in a specific part of the cerebellum, Thompson was able to eliminate the rabbit's ability to learn the "conditioned" eye blink. Because of the relationship of the deficit (the inability to respond to the tone with an eye blink) to the localized brain injury, Thompson argued that the memory traces for this learning are localized in the

Purkinje cells of the cerebellum—a view that is disputed by some scientists, including ourselves. As an everyday example, let's say you were riding your bike and chain broke. You would have great difficulty in riding your bike, but would you argue that movement of the bicycle was localized to the chain? You could also disrupt "movement" by having a flat tire or even by having the bolt holding the wheel to the rim fall off. Each item may be an important link in getting the bike to roll, but none of them can be said to be the center of bike movement itself.

No contemporary researcher in neuroscience would question the idea that the physical substance of the brain plays a crucial role in behavior (when pressed, most will not admit to being dualists, in Descartes' sense). But while we have learned a great deal through the use of single-cell recordings, which measure minute changes at the level of the neuron, there are still a number of important unsolved questions about how the brain works. Should we be so certain that complex behavioral functions are so discretely localized? If scientists only use techniques and experimental strategies to prove their own views, and at the same time ignore or even suppress opposing views, they enter into the realm of dogma and away from the arena of objective science and the open debate it requires in order to flourish.

In the sciences, as in all other creative human endeavors, behavior is guided by beliefs and attitudes about how the world is really organized. These beliefs and attitudes shape our way of responding to many situations—what we consider to be edible, what type of people we would choose to speak or eat with, what situations evoke an attitude of prayer, and so on. The world of scientific research is also shaped by beliefs and attitudes that could be called “ideologies.” In science, when a group of beliefs can form our perception of the world, it is technically called a “paradigm” but it is an ideology nevertheless. The paradigms accepted by scientists will determine the methods that they employ to discover the secrets of nature. The paradigm also determines the kinds of “facts” (or data) that they will consider as valid and reliable signs of nature’s secrets. For example, an electrophysiologist[4] uses a microelectrode to record electrical potentials at the surface membrane of a neuron, at its boundary. By doing this kind of recording, the scientist implicitly accepts the idea that this tool will measure an event that is worth understanding—that is a given that does not need to be questioned by other people who use the same techniques. The electrophysiologist will examine the results of the recording and then go on to suggest that the measure of electrical activity is a reflection of the way the neuron in the brain “learns” something about the outside world. The recording of the electrical activity is said to be one measure of the cell’s ability to learn.

Localization theory is a success because so many modern techniques have been developed to provide experimental verification of the concept—and this is the way in which most science conducts its affairs. In this regard, Thomas Kuhn, the distinguished historian of science, said, “once scientists accept a paradigm, they do not need to reconstruct the entire field of investigation each time, and they do not need to justify the basic principles for each concept. They can leave all that to the people who write the basic textbooks.”

Let's put what we have said in the context of neurological research and think about the following example. If damage to the nervous system always causes a permanent loss of behavioral function, isn't it logical to suppose that the behavioral loss is caused by the destruction of the specific nerve cells that "control" the function? For example, let us consider the memory traces studied by Richard Thompson. The elimination of certain nerve cells in the cerebellum prevents the formation of a conditioned eye blink. The techniques—the anatomical ones for showing the specific loss of neurons, the electro physiological measures used to show the loss of functional activity of cells, and the behavioral measures that were used in the experiments—all support the conclusion. But what if the surgeries were done differently, so that the injury done could occur slowly over time? Would there still be a problem? What would happen if the rabbits were first conditioned extensively, for long periods, to the tone? Would lesions still disrupt their behaviors? What would it mean if the rabbits could relearn the conditioned response with special training, even though the nerve cells were no longer present? Sometimes dependence on a sophisticated scientific apparatus, combined with the use of very simple behavioral tasks designed to give quick results, can lead to an oversimplified view of how the brain really works in complex organisms such as ourselves.

Although we may disagree with Thompson's interpretations, he is a distinguished behavioral neuroscientists who has helped us focus on the critical issues in the field. But many others working on the brain take less care in performing detailed behavioral analyses in their experiments. For those of us concerned about head-injury outcome and prognosis, the failure to observe behavior as carefully as possible overlooks the most important outcome of brain injury—*changes in behavior* that make it difficult to perform the activities of everyday life.

As a physician working with patients who had received head injuries in World War II, Alexander Luria, the Russian neurologist and one of the founders of modern neuropsychology, argued against localization doctrine applied to clinical practice and insisted that neurologists pay much closer attention to the widespread and often subtle disturbances that occur following a brain injury:

> The [phrenological] idea that psychological processes are isolated faculties … which can be localized in well-defined areas of the brain (tacitly accepted by most neurologists), gave a wrong orientation to clinical practice and led neurologists to false conclusions. Without analyzing the causes of disturbances of psychological processes arising in various circumscribed brain lesions, without making a careful study of the structure of these disturbances, and without attempting to discover the physiological changes leading to these disturbances, neurologists concentrated all their attention on finding the most prominent disorders and ignored the wide range of incidental disturbance always accompanying a particular disorder. They concluded wrongly from their observations that *a disturbance of a particular complex function does not in fact arise in association with a narrowly circumscribed lesion of one part of the cortex, but is observed, as a rule, in patients with lesions of several different parts of the brain.* Disorders or writing . . . may appear in lesions of the temporal, postcentral, premotor and occipito-parietal regions of the brain, and all attempts to relate the complex act of writing to one localized cortical "center" can be dismissed at the very outset.[5]

Why do we discuss the issue of localization at such length? First, because we think that many physicians and health-care providers still hold to the view that the brain is a more or less static organ that cannot be repaired after injury. Second, we believe it is vital to understand the background of experimental and clinical findings—many of which clearly contradict the doctrine of localization as it is currently applied by people in the healthcare professions. We propose a different paradigm that has important implications not only for thinking about how the brain works, but also for designing new treatments for brain damage—treatments that would not make any sense at all in the context of strict localization theory.

From the perspective of localization theory, findings that challenge the paradigm are usually considered “exceptional” or even bizarre occurrences, the product of highly unusual individuals, with anomalous brain lesions. In the sixteenth century, for example, medical wisdom would not have accepted the idea that thinking or perception or mind could be understood by studying the anatomy of the cortex or cerebellum. The suggestion that an injury to the tissue itself could lead to a dramatic change in behavior would have been rejected or interpreted in terms of a blockage or a loss of the “pneuma” from one of the ventricular “cells” that controlled that function.

But the same kind of thinking occurs today when experimental results do not fit well with current ideas about cerebral functions. Observations that do not fit with widely held beliefs are considered anomalies or as exceptions to the rule. In this book, we consider some of these so-called anomalies of cerebral functioning. We do not focus our attention on bizarre occurrences, but simply take another look at phenomena that cannot be easily explained by currently held concepts.

One of the main reasons we need to develop new models of how the brain works is that many clinical and experimental studies show that both patients and experimental animal subjects do not always experience the functional and behavioral problems that we have come to expect with brain injury. If a specific brain structure can be destroyed without causing any deficits, what are the implications for localization of functions?

The rest of this book examines the questions of cerebral plasticity after injury or disease. By *plasticity* we mean the capacity of the brain to adapt to the "slings and arrows of outrageous fortune that the flesh is heir to," Like computers, the brain processes information about the world in which we live and control behavior "output" in response to the "inputs" it receives. Unlike computers, however, the brain is structurally and functionally modified by the information it receives, and that structural and chemical modification is what we mean when we talk about *neuroplasticity.* Injury is a form of input that certainly alters the structure of the brain and its capacity to process information. Can brain circuits be rebuilt once they have been damaged? Can the brain restore its capacity to process information and reinstate behavior to normal functioning? In this volume, we explore some of the circumstances that permit, enhance, or block recovery from brain damage. We describe the conditions that are present when brain injury does not cause the expected symptoms.

This concept of cerebral neuroplasticity starts from the assumption that most behavior is too complex to be localized to specific groups of neurons found in discrete areas of the brain. In the following chapters, we describe how behavioral and sensory functions can be shifted from one structure to another, and how neurons can be used to replace those that have been lost after injury or disease. While it is possible to believe in localization and still accept the idea of brain plasticity, it is not an easy thing to do if you want to believe that brain works like a hard-wired structure similar to a computer circuit board where there is no possibility of altering the circuits.

One of the exciting things about a new field of science is that there are many opportunities for novel ideas and concepts to challenge those that have been useful in the past. The healthy and vigorous debate that ensues from such new ideas can only advance knowledge. However, new theories do not need to explain everything. In fact, a theory that can “explain everything” cannot be tested or verified, because there are never any exceptions to it. That was the main problem with phrenology: every time a new behavioral “trait” was observed, another part of the brain was “discovered” to explain its existence.

Recent theories about neural plasticity can now explain some of the anomalous or unusual examples of brain recovery that could not be addressed from the standpoint of classical localization doctrine. And while this theoretical debate may very well be of interest only to professors and researchers, its implications have important consequences for clinical practice and the treatment of patients.

If we think about it, localization doctrine, to be consistent, has to be pessimistic about the possibilities of developing new treatments for brain and spinal cord injuries. Because once a region of the brain is lost, its function should also be irretrievably lost. For this reason, it has only been since the early 1980s or so when more evidence for plasticity became available that any research has been devoted to finding new treatments for brain damage. Even now, many physicians still believe that instances of recovery after brain damage can be explained by the fact that patients simply learn special “tricks” or new strategies to cope with losses in function. These tricks then mask or camouflage the real deficits, which would be seen if careful testing were done to reveal them.

Although we are still uncertain about all of the mechanisms involved in repairing brain damage, great strides are being made in developing new ways of examining the activity and functions of the central nervous system. One can hardly pick up a newspaper without reading about the development of some new computerized scanning device that lets us look deep into the activities of brain structures in the conscious and behaving organism. At a molecular level, some new tools are being used to alter the genetic machinery of cells, engineering new forms or programming them to make neurochemicals that they would not ordinarily be able to make. Some techniques, representing the very latest in imaging technology, are used to measure tiny changes in metabolism, blood flow, or electrical activity of nerve cells. Can these new devices help us to understand more about normal brain function as well as the processes of recovery and plasticity? In the next chapter we explore just how doctors examine the brain.

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