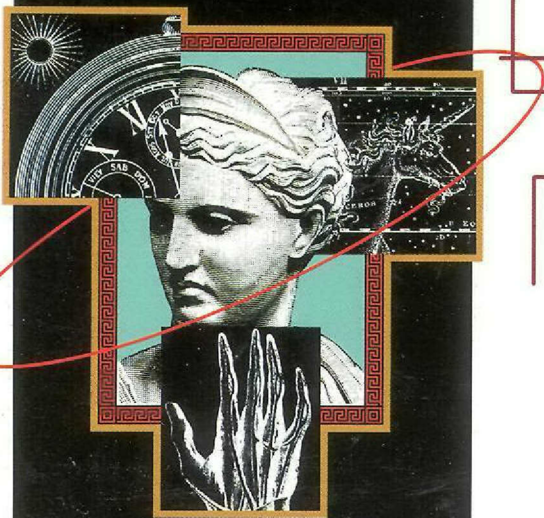
DESCARTES' ERROR



Emotion, Reason, and the Human Brain

"Antonio Damasio is a profound thinker and an elegant writer... *Descartes' Error* is a fascinating exploration of the biology of reason and its inseparable dependence on emotion."
—Oliver Sacks, author of *An Anthropologist on Mars*

ANTONIO R. DAMASIO

One

Unpleasantness in Vermont

PHINEAS P. GAGE

IT IS THE summer of 1848. We are in New England. Phineas P. Gage, twenty-five years old, construction foreman, is about to go from riches to rags. A century and a half later his downfall will still be quite meaningful.

Gage works for the Rutland & Burlington Railroad and is in charge of a large group of men, a "gang" as it is called, whose job it is to lay down the new tracks for the railroad's expansion across Vermont. Over the past two weeks the men have worked their way slowly toward the town of Cavendish; they are now at a bank of the Black River. The assignment is anything but easy because of the outcrops of hard rock. Rather than twist and turn the tracks around every escarpment, the strategy is to blast the stone and make way for a straighter and more level path. Gage oversees these tasks and is equal to them in every way. He is five-foot-six and athletic, and his movements are swift and precise. He looks like a young Jimmy Cagney, a Yankee Doodle dandy dancing his tap shoes over ties and tracks, moving with vigor and grace.

In the eyes of his bosses, however, Gage is more than just another able body. They say he is "the most efficient and capable" man in their employ.[1] This is a good thing, because the job takes as much physical prowess as keen concentration, especially when it comes to preparing the detonations. Several steps have to be followed, in orderly fashion. First, a hole must be drilled in the rock. After it is filled about halfway with explosive powder, a fuse must be inserted, and the powder covered with sand. Then the sand must be "tamped in," or pounded with a careful sequence of strokes from an iron rod. Finally, the fuse must be lit. If all goes well, the powder will explode into the rock; the sand is essential, for without its protection the explosion would be directed away from the rock. The shape of the iron and the way it is played are also important. Gage, who has had an iron manufactured to his specifications, is a virtuoso of this thing.

Now for what is going to happen. It is four-thirty on this hot afternoon. Gage has just put powder and fuse in a hole and told the man who is helping him to cover it with sand. Someone calls from behind, and Gage looks away, over his right shoulder, for only an instant. Distracted, and before his man has poured the sand in, Gage begins tamping the powder directly with the iron bar. In no time he strikes fire in the rock, and the charge blows upward in his face.[2]

The explosion is so brutal that the entire gang freezes on their feet. It takes a few seconds to piece together what is going on. The bang is unusual, and the rock is intact. Also unusual is the whistling sound, as of a rocket hurled at the sky. But this is more than fireworks. It is assault and battery. The iron enters Gage's left cheek, pierces the base of the skull, traverses the front of his brain, and exits at high speed through the top of the head. The rod has landed more than a hundred feet away, covered in blood and brains. Phineas Gage has been thrown to the ground. He is stunned, in the afternoon glow, silent but awake. So are we all, helpless spectators.

"Horrible Accident" will be the predictable headline in the Boston *Daily Courier* and *Daily Journal* of September 20, a week later.

"Wonderful Accident" will be the strange headline in the *Vermont Mercury* of September 22. "Passage of an Iron Rod Through the Head" will be the accurate headline in the *Boston Medical and Surgical Journal*. From the matter-of-factness with which they tell the story, one would think the writers were familiar with Edgar Allan Poe's accounts of the bizarre and the horrific. And perhaps they were, although this is not likely; Poe's gothic tales are not yet popular, and Poe himself will die the next year, unknown and impecunious. Perhaps the horrible is just in the air.

Noting how surprised people were that Gage was not killed instantly, the Boston medical article documents that "immediately after the explosion the patient was thrown upon his back"; that shortly thereafter he exhibited "a few convulsive motions of the extremities," and "spoke in a few minutes"; that "his men (with whom he was a great favourite) took him in their arms and carried him to the road, only a few rods distant (a rod is equivalent to 5½ yards, or 16½ feet), and sat him into an ox cart, in which he rode, sitting erect, a full three quarters of a mile, to the hotel of Mr. Joseph Adams"; and that Gage "got out of the cart himself, with a little assistance from his men."

Let me introduce Mr. Adams. He is the justice of the peace for Cavendish and the owner of the town's hotel and tavern. He is taller than Gage, twice as round, and as solicitous as his Falstaff shape suggests. He approaches Gage, and immediately has someone call for Dr. John Harlow, one of the town physicians. While they wait, I imagine, he says, "Come, come, Mr. Gage, what have we got here?" and, why not, "My, my, what troubles we've seen." He shakes his head in disbelief and leads Gage to the shady part of the hotel porch, which has been described as a "piazza." That makes it sound grand and spacious and open, and perhaps it is grand and spacious, but it is not open; it is just a porch. And there perhaps Mr. Adams is now giving Phineas Gage lemonade, or maybe cold cider.

An hour has passed since the explosion. The sun is declining and the heat is more bearable. A younger colleague of Dr. Harlow's, Dr. Edward Williams, is arriving. Years later Dr. Williams will describe the scene: "He at that time was sitting in a chair upon the piazza of Mr. Adams' hotel, in Cavendish. When I drove up, he said, 'Doctor, here is business enough for you.' I first noticed the wound upon the head before I alighted from my carriage, the pulsations of the brain being very distinct; there was also an appearance which, before I examined the head, I could not account for: the top of the head appeared somewhat like an inverted funnel; this was owing, I discovered, to the bone being fractured about the opening for a distance of about two inches in every direction. I ought to have mentioned above that the opening through the skull and integuments was not far from one and a half inch in diameter; the edges of this opening were everted, and the whole wound appeared as if some wedge-shaped body had passed from below upward. Mr. Gage, during the time I was examining this wound, was relating the manner in which he was injured to the bystanders; he talked so rationally and was so willing to answer questions, that I directed my inquiries to him in preference to the men who were with him at the time of the accident, and who were standing about at this time. Mr. G. then related to me some of the circumstances, as he has since done; and I can safely say that neither at that time nor on any subsequent occasion, save once, did I consider him to be other than perfectly rational. The one time to which I allude was about a fortnight after the accident, and then he persisted in calling me John Kirwin; yet he answered all my questions correctly."[3]

The survival is made all the more amazing when one considers the shape and weight of the iron bar. Henry Bigelow, a surgery professor at Harvard, describes the iron so: "The iron which thus traversed the skull weighs thirteen and a quarter pounds. It is three feet seven inches in length, and one and a quarter inches in diameter. The end which entered first is pointed; the taper being seven inches long, and the diameter of the point one quarter of an inch; circumstances to which the patient perhaps owes his life. The iron is unlike any other, and was made by a neighbouring blacksmith to please the fancy of the owner."[4] Gage is serious about his trade and its proper tools.

Surviving the explosion with so large a wound to the head, being able to talk and walk and remain coherent immediately afterward—this is all surprising. But just as surprising will be Gage's surviving the inevitable infection that is about to take over his wound. Gage's physician, John Harlow, is well aware of the role of disinfection. He does not have the help of antibiotics, but using what chemicals are available he will clean the wound vigorously and regularly, and place the patient in a semi-recumbent position so that drainage will be natural and easy. Gage will develop high fevers and at least one abscess, which Harlow will promptly remove with his scalpel. In the end, Gage's youth and strong constitution will overcome the odds against him, assisted, as Harlow will put it, by divine intervention: "I dressed him, God healed him."

Phineas Gage will be pronounced cured in less than two months. Yet this astonishing outcome pales in comparison with the extraordinary turn that Gage's personality is about to undergo. Gage's disposition, his likes and dislikes, his dreams and aspirations are all to change. Gage's body may be alive and well, but there is a new spirit animating it.

GAGE WAS NO LONGER GAGE

Just what exactly happened we can glean today from the account Dr. Harlow prepared twenty years after the accident.[5] It is a trustworthy text, with an abundance of facts and a minimum of interpretation. It makes sense humanly and neurologically, and from it we can piece together not just Gage but his doctor as well. John Harlow had been a schoolteacher before he entered Jefferson Medical College in Philadelphia, and was only a few years into his medical career when he took care of Gage. The case became his life-consuming interest, and I suspect that it made Harlow want to be a scholar, something that may not have been in his plans when he set up his medical practice in Vermont. Treating Gage successfully and reporting the results to his Boston colleagues may have been the shining hours of his career, and he must have been disturbed by the fact that a real cloud hung over Gage's cure.

Harlow's narrative describes how Gage regained his strength and how his physical recovery was complete. Gage could touch, hear, and see, and was not paralyzed of limb or tongue. He had lost vision in his left eye, but his vision was perfect in the right. He walked firmly, used his hands with dexterity, and had no noticeable difficulty with speech or language. And yet, as Harlow recounts, the "equilibrium or balance, so to speak, between his intellectual faculty and animal propensities" had been destroyed. The changes became apparent as soon as the acute phase of brain injury subsided. He was now "fitful, irreverent, indulging at times in the grossest profanity which was not previously his custom, manifesting but little deference for his fellows, impatient of restraint or advice when it conflicts with his desires, at times pertinaciously obstinate, yet capricious and vacillating, devising many plans of future operation, which are no sooner arranged than they are abandoned. . . . A child in his intellectual capacity and manifestations, he has the animal passions of a strong man." The foul language was so debased that women were advised not to stay long in his presence, lest their sensibilities be offended. The strongest admonitions from Harlow himself failed to return our survivor to good behavior.

These new personality traits contrasted sharply with the "temperate habits" and "considerable energy of character" Phineas Gage was known to have possessed before the accident. He had had "a well balanced mind and was looked upon by those who knew him as a shrewd, smart businessman, very energetic and persistent in executing all his plans of action." There is no doubt that in the context of his job and time, he was successful. So radical was the change in him that friends and acquaintances could hardly recognize the man. They noted sadly that "Gage was no longer Gage." So different a man was he that his employers would not take him back when he returned to work, for they "considered the change in his mind so marked that they could not give him his place again." The problem was not lack of physical ability or skill; it was his new character.

The unraveling continued unabated. No longer able to work as a foreman, Gage took jobs on horse farms. One gathers that he was prone to quit in a capricious fit or be let go because of poor discipline. As Harlow notes, he was good at "always finding something which did not suit him." Then came his career as a circus attraction. Gage was featured at Barnum's Museum in New York City, vaingloriously showing his wounds and the tamping iron. (Harlow states that the iron was a constant companion, and points out Gage's strong attachment to objects and animals, which was new and somewhat out of the ordinary. This trait, what we might call "collector's behavior," is something I have seen in patients who have suffered injuries like Gage's, as well as in autistic individuals.)

Then far more than now, the circus capitalized on nature's cruelty. The endocrine variety included dwarfs, the fattest woman on earth, the tallest man, the fellow with the largest jaw; the neurological variety included youths with elephant skin, victims of neurofibromatosis—and now Gage. We can imagine him in such company, peddling misery for gold.

Four years after the accident, there was another theatrical coup. Gage left for South America. He may have worked on horse farms, and was a sometime stagecoach driver in Santiago and Valparaiso. Little else is known about his expatriate life except that in 1859 his health was deteriorating.

In 1860, Gage returned to the United States to live with his mother and sister, who had since moved to San Francisco. At first he was employed on a farm in Santa Clara, but he did not stay long. In fact, he moved around, occasionally finding work as a laborer in the area. It is clear that he was not an independent person and that he could not secure the type of steady, remunerative job that he had once held. The end of the fall was nearing.

In my mind is a picture of 1860s San Francisco as a bustling place, full of adventurous entrepreneurs engaged in mining, farming, and shipping. That is where we can find Gage's mother and sister, the latter married to a prosperous San Francisco merchant (D. D. Shattuck, Esquire), and that is where the old Phineas Gage might have belonged. But that is not where we would find him if we could travel back in time. We would probably find him drinking and brawling in a question-able district, not conversing with the captains of commerce, as astonished as anybody when the fault would slip and the earth would shake threateningly. He had joined the tableau of dispirited people who, as Nathanael West would put it decades later, and a few hundred miles to the south, "had come to California to die."[6]

The meager documents available suggest that Gage developed epileptic fits (seizures). The end came on May 21, 1861, after an illness that lasted little more than a day. Gage had a major convulsion which made him lose consciousness. A series of subsequent convulsions, one coming soon on the heels of another, followed. He never regained consciousness. I believe he was the victim of *status epilepticus*, a condition in which convulsions become nearly continuous and usher in death. He was thirty-eight years old. There was no death notice in the San Francisco newspapers.

WHY PHINEAS GAGE?

Why is this sad story worth telling? What is the possible significance of such a bizarre tale? The answer is simple. While other cases of neurological damage that occurred at about the same time revealed that the brain was the foundation for language, perception, and motor function, and generally provided more conclusive details, Gage's story hinted at an amazing fact: Somehow, there were systems in the human brain dedicated more to reasoning than to anything else, and in particular to the personal and social dimensions of reasoning. The observance of previously acquired social convention and ethical rules could be lost as a result of brain damage, even when neither basic intellect nor language seemed compromised. Unwittingly, Gage's example indicated that something in the brain was concerned specifically with unique human properties, among them the ability to anticipate the future and plan accordingly within a complex social environment; the sense of responsibility toward the self and others; and the ability to orchestrate one's survival deliberately, at the command of one's free will.

The most striking aspect of this unpleasant story is the discrepancy between the normal personality structure that preceded the accident and the nefarious personality traits that surfaced thereafter and seem to have remained for the rest of Gage's life. Gage had once known all he needed to know about making choices conducive to his betterment. He had a sense of personal and social responsibility, reflected in the way he had secured advancement in his job, cared for the quality of his work, and attracted the admiration of employers and colleagues. He was well adapted in terms of social convention and appears to have been ethical in his dealings. After the accident, he no longer showed respect for social convention; ethics in the broad sense of the term, were violated; the decisions he made did not take into account his best interest, and he was given to invent tales "without any foundation except in his fancy," in Harlow's words. There was no evidence of concern about his future, no sign of forethought.

The alterations in Gage's personality were not subtle. He could not make good choices, and the choices he made were not simply neutral. They were not the reserved or slight decisions of someone whose mind is diminished and who is afraid to act, but were instead actively disadvantageous. One might venture that either his value system was now different, or, if it was still the same, there was no way in which the old values could influence his decisions. No evidence exists to tell us which is true, yet my investigation of patients with brain damage similar to Phineas Gage's convinces me that neither explanation captures what really happens in those circumstances. Some part of the value system remains and can be utilized in abstract terms, but it is unconnected to real-life situations. When the Phineas Gages of this world need to operate in reality, the decision-making process is minimally influenced by old knowledge.

Another important aspect of Gage's story is the discrepancy between the degenerated character and the apparent intactness of the several instruments of mind—attention, perception, memory, language, intelligence. In this type of discrepancy, known in neuropsychology as *dissociation,* one or more performances within a general profile of operations are at odds with the rest. In Gage's case the impaired character was dissociated from the otherwise intact cognition and behavior. In other patients, with lesions elsewhere in the brain, language may be the impaired aspect, while character and all other cognitive aspects remain intact; language is then the "dissociated" ability. Subsequent study of patients similar to Gage has confirmed that his specific dissociation profile occurs consistently.

It must have been hard to believe that the character change would not resolve itself, and at first even Dr. Harlow resisted admitting that the change was permanent. This is understandable, since the most dramatic elements in Gage's story were his very survival, and then his survival without a defect that would more easily meet the eye: paralysis, for example, or a speech defect, or memory loss. Somehow, emphasizing Gage's newly developed social shortcomings smacked of ingratitude to both providence and medicine. By 1868, however, Dr. Harlow was ready to acknowledge the full extent of his patient's personality change.

Gage's survival was duly noted, but with the caution reserved for freakish phenomena. The significance of his behavioral changes was largely lost. There were good reasons for this neglect. Even in the small world of brain science at the time, two camps were beginning to form. One held that psychological functions such as language or memory could never be traced to a particular region of the brain. If one had to accept, reluctantly, that the brain did produce the mind, it did so as a whole and not as a collection of parts with special functions. The other camp held that, on the contrary, the brain did have specialized parts and those parts generated separate mind functions. The rift between the two camps was not merely indicative of the infancy of brain research; the argument endured for another century and, to a certain extent, is still with us today.

Whatever scientific debate Phineas Gage's story elicited, it focused on the issue of localizing language and movement in the brain. The debate never turned to the connection between impaired social conduct and frontal lobe damage. I am reminded here of a saying of Warren McCulloch's: "When I point, look where I point, not at my finger." (McCulloch, a legendary neurophysiologist and a pioneer in the field that would become computational neuroscience, was also a poet and a prophet. This saying was usually part of a prophecy.) Few looked to where Gage was unwittingly pointing. It is of course difficult to imagine anybody in Gage's day with the knowledge *and* the courage to look in the proper direction. It was acceptable that the brain sectors whose damage would have caused Gage's heart to stop pumping and his lungs to stop breathing had not been touched by the iron rod. It was also acceptable that the brain sectors which control wakefulness were far from the iron's course and were thus spared. It was even acceptable that the injury did not render Gage unconscious for a long period. (The event anticipated what is current knowledge from studies of head injuries: The style of the injury is a critical variable. A severe blow to the head, even if no bone is broken and no weapon penetrates the brain, can cause a major disruption of wakefulness for a long time; the forces unleashed by the blow disorganize brain function profoundly. A penetrating injury in which the forces are concentrated on a narrow and steady path, rather than dissipate and accelerate the brain against the skull, may cause dysfunction only where brain tissue is actually destroyed, and thus spare brain function elsewhere.) But to understand Gage's behavioral change would have meant believing that normal social conduct required a particular corresponding brain region, and this concept was far more unthinkable than its equivalent for movement, the senses, or even language.

Gage's case was used, in fact, by those who did not believe that mind functions could be linked to specific brain areas. They took a cursory view of the medical evidence and claimed that if such a wound as Gage's could fail to produce paralysis or speech impairments, then it was obvious that neither motor control nor language could be traced to the relatively small brain regions that neurologists had identified as motor and language centers. They argued—in complete error, as we shall see—that Gage's wound directly damaged those centers.[7]

The British physiologist David Ferrier was one of the few to take the trouble to analyze the findings with competence and wisdom.[8]

Ferrier's knowledge of other cases of brain lesion with behavioral changes, as well as his own pioneering experiments on electrical stimulation and ablation of the cerebral cortex in animals, had placed him in a unique position to appreciate Harlow's findings. He concluded that the wound spared motor and language "centers," that it did damage the part of the brain he himself had called the prefrontal cortex, and that such damage might be related to Gage's peculiar change in personality, to which Ferrier referred, picturesquely, as "mental degradation." The only supportive voices Harlow and Ferrier may have heard, in their very separate worlds, came from the followers of phrenology.

An Aside on Phrenology

What came to be known as phrenology began its days as "organology" and was founded by Franz Joseph Gall in the late 1700s. First in Europe, where it enjoyed a succès de scandale in the intellectual circles of Vienna, Weimar, and Paris, and then in America, where it was introduced by Gall's disciple and onetime friend Johann Caspar Spurzheim, phrenology sailed forth as a curious mixture of early psychology, early neuroscience, and practical philosophy. It had a remarkable influence in science and in the humanities, throughout most of the nineteenth century, although the influence was not widely acknowledged and the influenced took care to distance themselves from the movement.

Some of Gall's ideas are indeed quite astounding for the time. In no uncertain terms he stated that the brain was the organ of the spirit. With no less certitude he asserted that the brain was an aggregate of many organs, each having a specific psychological faculty. Not only did he part company with the favored dualist thinking, which separated biology from mind altogether, but he correctly intuited that there were many parts to this thing called brain, and that there was specialization in terms of the functions played by those parts.[9] The latter was a fabulous intuition since brain specialization is now a well-confirmed fact. Not surprisingly, however, he did not realize that the function of each separate brain part is not independent and that it is, rather, a contribution to the function of larger systems composed of those separate parts. But one can hardly fault Gall on this matter. It has taken the better part of two centuries for a "modern" view to take some hold. We can now say with confidence that there are no single "centers" for vision, or language, or for that matter, reason or social behavior. There are "systems" made up of several interconnected brain units; anatomically, but not functionally, those brain units are none other than the old "centers" of phrenologically inspired theory; and these systems are indeed dedicated to relatively separable operations that constitute the basis of mental functions. It is also true that the separate brain units, by virtue of where they are placed in a system, contribute different components to the system's operation and are thus not interchangeable. This is most important: What determines the contribution of a given brain unit to the operation of the system to which it belongs is not just the structure of the unit but also its *place* in the system.

The whereabouts of a unit is of paramount importance. This is why throughout this book I will talk so much about neuroanatomy, or brain anatomy, identify different brain regions, and even ask you to suffer the repeated mention of their names and the names of other regions with which they are interconnected. On numerous occasions I will refer to the presumed function of given brain regions, but such references should be taken in the context of the systems to which those regions belong. I am not falling into the phrenological trap. To put it simply: The mind results from the operation of each of the separate components, and from the concerted operation of the multiple systems constituted by those separate components.

While we must credit Gall with the concept of brain specialization, an impressive idea indeed given the scarce knowledge of his time, we must blame him for the notion of brain "centers" that he inspired. Brain centers became indelibly associated with "mental functions" in the work of nineteenth-century neurologists and physiologists. We also must be critical of various wild claims of phrenology, for instance, the idea that each separate brain "organ" generated mental faculties that were proportional to the size of the organ, or that all organs and faculties were innate. The notion of size as an index of the "power" or "energy" of a given mental faculty is amusingly wrong, although some contemporary neuroscientists have not shied away from using precisely the same notion in their work. The extension of this claim, the one that most undermined phrenology—and that many people think of when they hear the word—was that the organs could be identified from the outside by telltale bumps in the skull. As for the idea that organs and faculties are innate, you can see its influence throughout the nineteenth century, in literature as well as elsewhere; the magnitude of its error will be discussed in chapter 5.

The connection between phrenology and Phineas Gage's story deserves special mention. In his search for evidence about Gage, the psychologist M. B. MacMillan[10] uncovered a lead about one Nelson Sizer, a figure in phrenological circles of the 1800s who lectured in New England and who visited Vermont in the early 1840s, before Gage's accident. Sizer met John Harlow in 1842. In his otherwise rather boring book,[11] Sizer writes that "Dr. Harlow was then a young physician and assisted as a member of the committee at our lectures on phrenology in 1842." There were several followers of phrenology at medical schools in the eastern United States then, and Harlow was well acquainted with their ideas. He may have heard them speak in Philadelphia, a phrenology haven, or in New Haven or Boston, where Spurzheim had come in 1832, shortly after Gall's death, to be hailed as scientific leader and social sensation. New England wined and dined the hapless Spurzheim to the grave. His premature death came in a matter of weeks, although gratitude followed: the very night of the funeral, the Boston Phrenological Society was founded.

Whether or not Harlow ever heard Spurzheim, it is tantalizing to learn that he had at least one phrenology lesson directly from Nelson Sizer while the latter visited Cavendish (where he stayed—where else—at Mr. Adams's hotel). This influence may well explain Harlow's bold conclusion that Gage's behavioral transformation was due to a specific brain lesion and not to a general reaction to the accident. Intriguingly, Harlow does not rely on phrenology to support his interpretations.

Sizer did come back to Cavendish (and stayed again at Mr. Adams's hotel—in Gage's recovery room, naturally), and he was well aware of Gage's story. When Sizer wrote his book on phrenology in 1882, Phineas Gage was mentioned: "We perused [Harlow's] history of the case in 1848 with intense and affectionate interest, and also do not forget that the poor patient was quartered at the same hotel and in the same room."[11] Sizer's conclusion was that the iron bar had passed "in the neighborhood of Benevolence and the front part of Veneration." Benevolence and Veneration? Now, Benevolence and Veneration were not sisters in some Carmelite convent. They were phrenological "centers," brain "organs." Benevolence and Veneration gave people proper behavior, kindness and respect for other persons. Armed with this knowledge, you can understand Sizer's final view of Gage: "His organ of Veneration seemed to have been injured, and the profanity was the probable result." How true!

A LANDMARK BY HINDSIGHT

There is no question that Gage's personality change was caused by a circumscribed brain lesion in a specific site. But that explanation would not be apparent until two decades after the accident, and it became vaguely acceptable only in this century. For a long time, most everybody, John Harlow included, believed that "the portion of the brain traversed, was, for several reasons, the best fitted of any part of the cerebral substance to sustain the injury"[12]: in other words, a part of the brain that did nothing much and was thus expendable. But nothing could be further from the truth, as Harlow himself realized. He wrote in 1868 that Gage's mental recovery "was only partial, his intellectual faculties being decidedly impaired, but not totally lost; nothing like dementia, but they were enfeebled in their manifestations, his mental operations being perfect in kind, but not in degree or quantity." The unintentional message in Gage's case was that observing social convention, behaving ethically, and making decisions advantageous to one's survival and progress require knowledge of rules and strategies *and* the integrity of specific brain systems. The problem with this message was that it lacked the evidence required to make it understandable and definitive. Instead the message became a mystery and came down to us as the "enigma" of frontal lobe function. Gage posed more questions than he gave answers.

To begin with, all we knew about Gage's brain lesion was that it was probably in the frontal lobe. That is a bit like saying that Chicago is probably in the United States—accurate but not very specific or helpful. Granted that the damage was likely to involve the frontal lobe, where exactly was it within that region? The left lobe? The right? Both? Somewhere else too? As you will see in the next chapter, new imaging technologies have helped us come up with the answer to this puzzle.

Then there was the nature of Gage's character defect. How did the abnormality develop? The primary cause, sure enough, was a hole in the head, but that just tells why the defect arose, not how. Might a hole anywhere in the frontal lobe have the same result? Whatever the answer, by what plausible means can destruction of a brain region change personality? If there are specific regions in the frontal lobe, what are they made of, and how do they operate in an intact brain? Are they some kind of "center" for social behavior? Are they modules selected in evolution, filled with problem-solving algorithms ready to tell us how to reason and make decisions? How do these modules, if that is what they are, interact with the environment during development to permit normal reasoning and decision making? Or are there in fact no such modules?

What were the mechanisms behind Gage's failure at decision making? It might be that the knowledge required to reason through a problem was destroyed or rendered inaccessible, so that he no longer could decide appropriately. It is possible also that the requisite knowledge remained intact and accessible but the strategies for reasoning were compromised. If this was the case, which reasoning steps were missing? More to the point, which steps are there for those who are allegedly normal? And if we are fortunate enough to glean the nature of some of these steps, what are their neural underpinnings?

Intriguing as all these questions are, they may not be as important as those which surround Gage's status as a human being. May he be described as having free will? Did he have a sense of right and wrong, or was he the victim of his new brain design, such that his decisions were imposed upon him and inevitable? Was he responsible for his acts? If we rule that he was not, does this tell us something about responsibility in more general terms? There are many Gages around us, people whose fall from social grace is disturbingly similar. Some have brain damage consequent to brain tumors, or head injury, or other neurological disease. Yet some have had no overt neurological disease and they still behave like Gage, for reasons having to do with their brains or with the society into which they were born. We need to understand the nature of these human beings whose actions can be destructive to themselves and to others, if we are to solve humanely the problems they pose. Neither incarceration nor the death penalty—among the responses that society currently offers for those individuals—contribute to our understanding or solve the problem. In fact, we should take the question further and inquire about our own responsibility when we "normal" individuals slip into the irrationality that marked Phineas Gage's great fall.

Gage lost something uniquely human, the ability to plan his future as a social being. How aware was he of this loss? Might he be described as self-conscious in the same sense that you and I are? Is it fair to say that his soul was diminished, or that he had lost his soul? And if so, what would Descartes have thought had he known about Gage and had he had the knowledge of neurobiology we now have? Would he have inquired about Gage's pineal gland?

Two

Gage's Brain Revealed

THE PROBLEM

At about the time of the Phineas Gage affair, the neurologists Paul Broca in France and Carl Wernicke in Germany captured the attention of the medical world with their studies of neurological patients with brain lesions. Independently, Broca and Wernicke each proposed that damage to a well-circumscribed area in the brain was the cause of newly acquired language disorders in these patients.[1] The impairment in language became known technically as aphasia. The lesions, Broca and Wernicke thought, were thus revealing the neural underpinnings of two different aspects of language processing in normals. Their proposals were controversial and there was no rush to endorse them but the world did listen. With some reluctance and with much amendment they gradually became accepted. Harlow's work on Gage, however, or David Ferrier's comments, for that matter, never received the same attention, and never fired the imagination of their colleagues in the same way.

There were several reasons why. Even if a philosophical bent allowed one to think of the brain as the basis for the mind, it was difficult to accept the view that something as close to the human soul as ethical judgment, or as culture-bound as social conduct, might depend significantly on a specific region of the brain. Then there was the fact that Harlow was an amateur compared with Professors Broca and Wernicke, and could not marshal the convincing evidence required to make his case. Nowhere was this more obvious than in the failure to provide a precise location for the brain damage. Broca could state with certainty where in the brain the damage was that had caused language impairment, or aphasia, in his patients. He had studied their brains at the autopsy table. Likewise Wernicke, who had seen at postmortem that a back portion of the left temporal lobe was partially destroyed in patients exhibiting a language impairment—and noted that the aspect of language faculties affected was other than that identified by Broca. Harlow had not been able to make any such observation. Not only did he have to venture a relationship between Gage's brain damage and his behavioral impairment, but he had to conjecture where the damage was in the first place. He could not prove to anybody's satisfaction that he was right about anything.

Harlow's predicament was made worse by Broca's recently published findings. Broca had shown that lesions in the left frontal lobe, third frontal gyrus, caused language impairment in his patients. The entry and exit of the iron suggested that the damage to Gage's brain

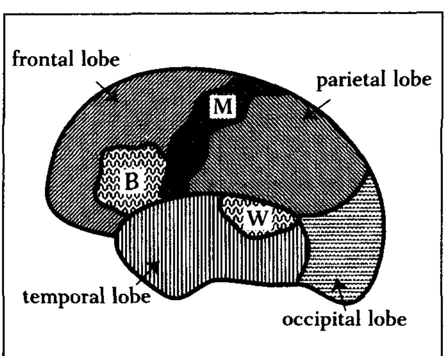


Figure 2-1. B = Broca area; M = motor area; W = Wernicke area. The four lobes are identified in the illustration. Harlow's critics claimed that Gage's lesion involved Broca's area, or the motor area, or even both, and used this claim to attack the idea that there was functional specialization in the human brain.

might be in the left frontal lobe. Yet Gage had no language impairment, while Broca's patients had no character defect. How could there be such different results? With the scarce knowledge of functional neuroanatomy of the time, some people thought the lesions were in approximately the same place, and that the different results merely revealed the folly of those who wanted to find functional specializations in the brain.

When Gage died in 1861, no autopsy was performed. Harlow himself did not learn of Gage's death until about five years later. The Civil War had been raging in the intervening years and news of this sort did not travel fast. Harlow must have been saddened by Gage's death and crushed at the lost opportunity of studying Gage's brain. So crushed, in fact, that he proceeded to write Gage's sister with a bizarre request. He petitioned her to have the body exhumed so that the skull could be recovered and kept as a record of the case.

Phineas Gage was once again the involuntary protagonist of a grim scene. His sister and her husband, D. D. Shattuck, along with a Dr. Coon (then the mayor of San Francisco) and the family physician, looked on as a mortician opened Gage's coffin and removed his skull. The tamping iron, which had been placed alongside Gage's body, was also retrieved, and sent with the skull to Dr. Harlow back East. Skull and iron have been companions at the Warren Medical Museum of the Harvard Medical School in Boston ever since.

For Harlow, being able to exhibit skull and iron was the closest he could come to establishing that his case was not an invention, that a man with such a wound had indeed existed. For Hanna Damasio, some hundred twenty years later, Gage's skull was the springboard for a piece of detective work that completed Harlow's unfinished business and serves as a bridge between Gage and modern research on frontal lobe function.

She began by considering the general trajectory of the iron, a curious exercise in itself. Entering from the left cheek upward into the skull, the iron broke through the back of the left orbital cavity (the eye socket) located immediately above. Continuing upward it must have penetrated the front part of the brain close to the midline, although it was difficult to say where exactly. Since it seems to have been angled to the right it may have hit the left side first, then some of the right as it traveled upward. The initial site of brain damage probably was the orbital frontal region, directly above the orbital cavities. In its travel, the iron would have destroyed some of the inner surface of the left frontal lobe and perhaps of the right frontal lobe. Finally, as it exited, the iron would have damaged some part of the dorsal, or back, region of the frontal lobe, on the left side for sure and perhaps also on the right.

The uncertainties of this conjecture were obvious. There was a range of potential trajectories the iron might have taken through a "standard," idealized brain, and no way of knowing whether or how that brain resembled Gage's. The problem was made worse because although neuroanatomy jealously preserves topological relationships among its components, there are considerable degrees of individual topographic variation that make each of our brains far more different than cars of the same make. This point is best illustrated with the paradoxical sameness and difference of human faces: Faces have an invariant number of components and an invariant spatial arrangement (the topological relations of the components are the same in all human faces). Yet they are infinitely diverse and individually distinguishable because of small anatomical differences in size, contour, and position of those invariant parts and configuration (the precise topography changes from face to face). Individual brain variation, then, increased the likelihood that the above conjecture was erroneous.

Hanna Damasio proceeded to take advantage of modern neuroanatomy and state-of-the-art neuroimaging technology.[2] Specifically, she used a new technique she developed to reconstruct brain images of living humans in three dimensions. The technique, known as Brainvox,[3] relies on computer manipulation of raw data obtained from high-resolution magnetic resonance scans of the brain. In living normals or in neurological patients, it renders an image of the brain that is in no way different from the picture of that brain that you would be able to see at the autopsy table. It is an eerie, disquieting marvel. Think of what Prince Hamlet would have done, if he had been allowed to contemplate his own three pounds of brooding, indecisive brain, rather than just the empty skull the gravedigger handed him.

An Aside on the Anatomy of Nervous Systems

It may be useful here to outline the anatomy of the human nervous system. Why should any time be spent on this? In the previous chapter, when I discussed phrenology and the connection between brain structure and function, I mentioned the importance of neuroanatomy or brain anatomy. I emphasize it again because

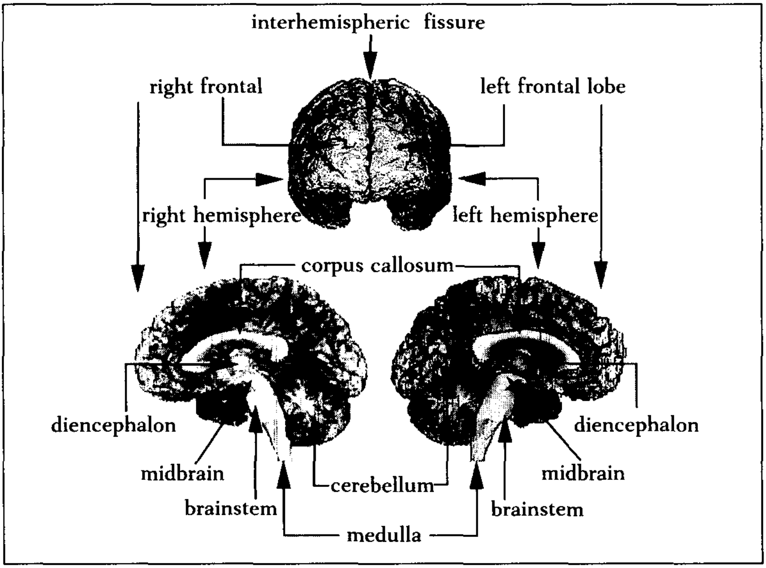


Figure 2-2. Human living brain reconstructed in three dimensions. The top center image shows the brain seen from the front. The corpus callosum is hidden underneath the interhemispheric fissure. The bottom images at the left and at the right show the two hemispheres of the same brain, separated at the middle as in a split-brain operation. The main anatomical structures are identified in the figure. The convoluted cover of the cerebral hemispheres is the cerebral cortex.

neuroanatomy is the fundamental discipline in neuroscience, from the level of microscopic single neurons (nerve cells) to that of the macroscopic systems spanning the entire brain. There can be no hope of understanding the many levels of brain function if we do not have a detailed knowledge of brain geography at multiple scales.

When we consider the nervous system in its entirety we can separate its central and peripheral divisions easily. The three-dimensional reconstruction in figure 2-2 represents the cerebrum, the main component of the central nervous system. In addition to the cerebrum, with its left and right cerebral hemispheres joined by the corpus callosum (a thick collection of nerve fibers connecting left and right hemispheres bidirectionally), the central nervous system includes the

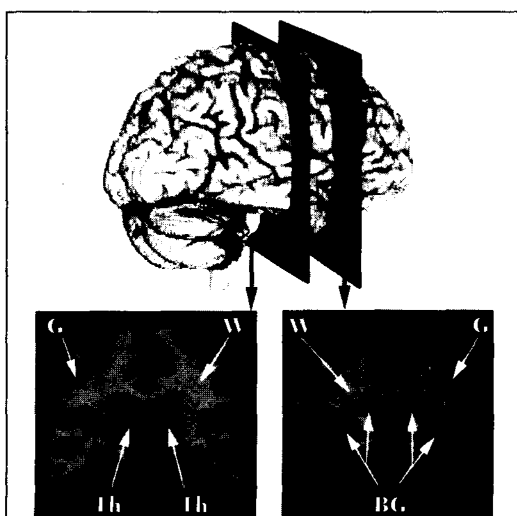


Figure 2-3. Two sections through a reconstructed living human brain obtained with magnetic resonance imaging (MRI) and the Brainvox technique. The planes of section are identified in the image at the top and center. The difference between gray (G) and white matter (W) is readily visible. Gray matter shows up in the cerebral cortex, the gray ribbon which makes up the entire contour of every hump and crevice in the section, and in deep nuclei such as the basal ganglia (BG) and the thalamus (Th).

diencephalon (a midline collection of nuclei, hidden under the hemispheres, which includes the thalamus and the hypothalamus), the midbrain, the brain stem, the cerebellum, and the spinal cord.

The central nervous system is "neurally" connected to almost every nook and cranny of the remainder of the body by nerves, the collection of which constitute the peripheral nervous system. Nerves ferry impulses from brain to body and from body to brain. As will be discussed in chapter 5, however, brain and body are also interconnected chemically, by substances such as hormones and peptides, which are released in one and go to the other via the bloodstream.

When we section the central nervous system we can make out without difficulty the difference between its dark and pale sectors. (Figure 2-3). The dark sectors are known as the gray matter although their real color is usually brown rather than gray. The pale sectors are known as the white matter. The gray matter corresponds largely to collections of nerve cell bodies, while the white matter corresponds largely to axons, or nerve fibers, emanating from cell bodies in the gray matter.

The gray matter comes in two varieties. In one variety the neurons are layered as in a cake and form a *cortex*. Examples are the cerebral cortex which covers the cerebral hemispheres, and the cerebellar cortex which envelops the cerebellum. In the second variety of gray matter the neurons are not layered and are organized instead like

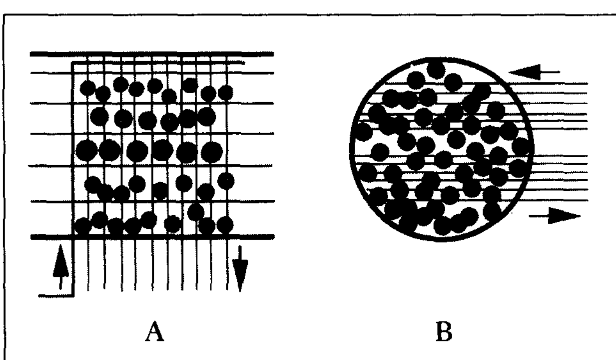


Figure 2-4. A = diagram of the cellular architecture of cerebral cortex with its characteristic layer structure; B = diagram of the cellular architecture of a nucleus.

cashew nuts inside a bowl. They form a *nucleus.* There are large nuclei, such as the caudate, putamen, and pallidum, quietly hidden in the depth of each hemisphere; or the amygdala, hidden inside each temporal lobe; there are large collections of smaller nuclei, such as those that form the thalamus; and small individual nuclei, such as the substantia nigra or the nucleus ceruleus, located in the brain stem.

The brain structure to which neuroscience has dedicated the most effort is the cerebral cortex. It can be visualized as a comprehensive mantle to the cerebrum, covering all its surfaces, including those located in the depth of crevices known as fissures and sulci which give the brain its characteristic folded appearance. (See Fig. 2-2.) The thickness of this multilayer blanket is about 3 millimeters, and the layers are parallel to one another and to the brain's surface. (See Fig. 2-4). All gray matter below the cortex (nuclei, large and small, and the cerebellar cortex) is known as subcortical. The evolutionarily modern part of the cerebral cortex is called the neocortex. Most of the evolutionarily older cortex is known as limbic cortex (see below). Throughout the book I will usually refer either to cerebral cortex (meaning neocortex), or to limbic cortex and its specific parts.

Figure 2-5 depicts a frequently used map of the cerebral cortex based on its varied cytoarchitectonic areas (regions of distinctive

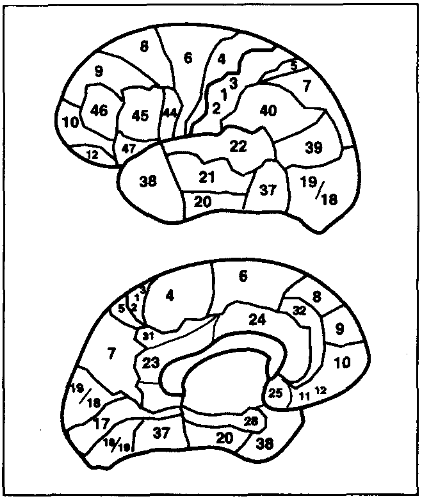


Figure 2-5. A map of the main brain areas identified by Brodmann in his studies of cellular architecture (cytoarchitectonics). This is neither a phrenology map nor a contemporary map of brain functions. It is simply a convenient anatomical reference. Some areas are too small to be depicted here, or they are hidden in the depth of sulci and fissures. The top image corresponds to the external aspect of the left hemisphere, and the bottom one to the internal aspect.

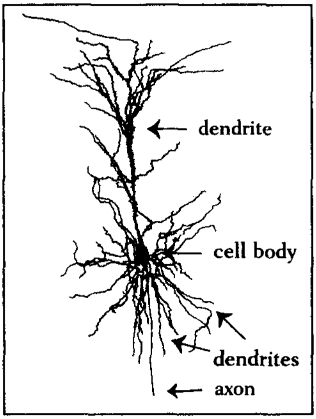
cellular architecture). It is known as Brodmann's map and its areas are designated by number.

One division of the central nervous system to which I will refer often is both cortical and subcortical and is known as the limbic system. (The term is something of a catchall for a number of evolutionarily old structures, and although many neuroscientists resist using it, it often comes in handy.) The main structures of the limbic system are the cingulate gyrus, in the cerebral cortex, and the amygdala and basal forebrain, two collections of nuclei.

The nervous (or neural) tissue is made up of nerve cells (neurons) supported by glial cells. Neurons are the cells essential for brain activity. There are billions of such neurons in our brains, organized in local circuits, which, in turn, constitute cortical regions (if they are arranged in layers) or nuclei (if they are aggregated in nonlayered collections). Finally, the cortical regions and nuclei are interconnected to form systems, and systems of systems, at progressively higher levels of complexity. In terms of scale, all neurons and local circuits are microscopic, while cortical regions, nuclei, and systems are macroscopic.

Neurons have three important components: a cell body; a main output fiber, the axon; and input fibers, or dendrites. (See Fig. 2-6)

Figure 2-6. Diagram of a neuron with its main components: cell body, dendrites, and portion of axon.



Neurons are interconnected in circuits in which there are the equivalent of conducting wires (the neurons' axon fibers) and connectors (synapses, the points at which axons make contact with the dendrites of other neurons).

When neurons become active (a state known in neuroscience jargon as "firing"), an electric current is propagated away from the cell body and down the axon. This current is the action potential, and when it arrives at a synapse it triggers the release of chemicals known as neurotransmitters (glutamate is one such transmitter). In turn, neurotransmitters operate on receptors. In an excitatory neuron, the cooperative interaction of many other neurons whose synapses are adjacent and which may or not release their own transmitters, determines whether or not the next neuron will fire, that is, whether it will produce its own action potential, which will lead to its own neurotransmitter release, and so forth.

Synapses can be strong or weak. Synaptic strength decides whether or not, and how easily, impulses continue to travel into the next neuron. In general, in an excitatory neuron, a strong synapse facilitates impulse travel, while a weak synapse impedes or blocks it.[4]

A neuroanatomical issue I must mention to conclude this aside has to do with the nature of neuron connectivity. It is not uncommon to find scientists who despair of ever understanding the brain when they are confronted by the complexity of connections among neurons. Some prefer to hide behind the notion that everything connects with everything else and that mind and behavior probably emerge from that willy-nilly connectivity in ways that neuroanatomy will never reveal. Fortunately, they are wrong. Consider the following: On the average, every neuron forms about 1,000 synapses, although some can have as many as 5,000 or 6,000. This may seem a high number, but when we consider that there are more than 10 billion neurons and more than 10 *trillion* synapses, we realize that each neuron is nothing if not modestly connected. Pick a few neurons in the cortex or in nuclei, randomly or according to your anatomical preferences, and you will find that each neuron talks to a few others but never to most or all of the others. In fact, many neurons talk only to neurons that are not

Levels of Neural Architecture
Neurons
Local Circuits
Subcortical Nuclei
Cortical Regions
Systems
Systems of Systems

very far away, within relatively local circuits of cortical regions and nuclei, and others, although their axons sail forth for several millimeters, even centimeters, across the brain, will still make contact with only a relatively small number of other neurons. The main consequences of this arrangement are as follows: (1) whatever neurons do depends on the nearby assembly of neurons they belong to; (2) whatever systems do depends on how assemblies influence other assemblies in an architecture of interconnected assemblies; and (3) whatever each assembly contributes to the function of the system to which it belongs depends on its place in that system. In other words, the brain specialization mentioned in the aside on phrenology in chapter 1 is a consequence of the place occupied by assemblies of sparsely connected neurons within a large-scale system.

In short, then, the brain is a supersystem of systems. Each system is composed of an elaborate interconnection of small but macroscopic cortical regions and subcortical nuclei, which are made of microscopic local circuits, which are made of neurons, all of which are connected by synapses. (It is not uncommon to find the terms "circuit" and "network" used as synonyms of "system." To avoid confusion, it is important to specify whether a microscopic or macroscopic scale is intended. In this text, unless otherwise stated, systems are macroscopic and circuits are microscopic.)

THE SOLUTION

Since Phineas Gage was not around to be scanned, Hanna Damasio thought of an indirect approach to his brain.[5] She enlisted the help of Albert Galaburda, a neurologist at Harvard Medical School, who went to the Warren Medical Museum and carefully photographed Gage's skull from different angles, and measured the distances between the areas of bone damage and a variety of standard bone landmarks.

Analysis of these photographs combined with the descriptions of the wound helped narrow down the range of possible courses for the iron bar. The photographs also allowed Hanna Damasio and her neurologist colleague, Thomas Grabowski, to re-create Gage's skull in three-dimensional coordinates and to derive from them the most likely coordinates of the brain that best fitted such a skull. With the help of her collaborator Randall Frank, an engineer, Damasio then performed a simulation in a high-power computer work station. They re-created a three-dimensional iron rod with the precise dimensions of Gage's tamping iron, and "impaled" it on a brain whose shape and size were close to Gage's, along the now narrowed range of possible trajectories that the iron might have followed during the accident. The results are shown in Figures 2-7 and 2-8.

Figure 2-7. Photograph of Gage's skull obtained in 1992.

Figure 2-8. TOP PANELS: A reconstruction of Gage's brain and skull with the likely trajectory of the iron rod marked in dark gray. BOTTOM PANELS: A view of both left and right hemispheres as seen from the inside, showing how the iron damaged frontal lobe structures on both sides.

We can now confirm David Ferrier's claim that in spite of the amount of brain lost, the iron did not touch the brain regions necessary for motor function or language. (The intact areas of both hemispheres included the motor and premotor cortices, as well as the frontal operculum, on the left side known as Broca's area.) We can state with confidence that the damage was more extensive on the left than on the right hemisphere, and on the anterior than the posterior sectors of the frontal region as a whole. The damage compromised prefrontal cortices in the ventral and inner surfaces of both hemispheres while preserving the lateral, or external, aspects of the prefrontal cortices.

Part of a region which our recent investigations have highlighted as critical for normal decision-making, the ventromedial prefrontal region, was indeed damaged in Gage. (In neuroanatomical terminology, the orbital region is known also as the *ventromedial* region of the frontal lobe, and this is how I will refer to it throughout the book. "Ventral" and "ventro-" come from *venter,* "belly" in Latin, and this region is the underbelly of the frontal lobe, so to speak; "medial" designates proximity to the midline or the inside surface of a structure.) The reconstruction revealed that regions thought to be vital for other aspects of neuropsychological function were not damaged in Gage. The cortices in the lateral aspect of the frontal lobe, for instance, whose damage disrupts the ability to control attention, perform calculations, and shift appropriately from stimulus to stimulus, were intact.

This modern research allowed certain conclusions. Hanna Damasio and her colleagues could say with some foundation that it was selective damage in the prefrontal cortices of Phineas Gage's brain that compromised his ability to plan for the future, to conduct himself according to the social rules he previously had learned, and to decide on the course of action that ultimately would be most advantageous to his survival. What was missing now was the knowledge of how Gage's mind might have worked when he behaved as dismally as he did. And for that we had to investigate the modern counterparts of Phineas Gage.