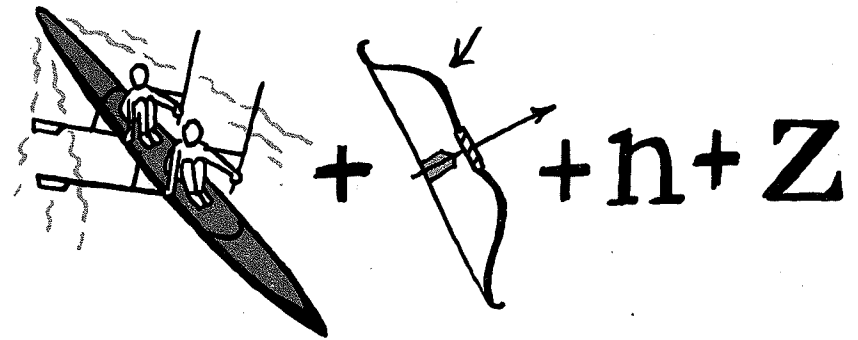


CHAPTER ONE

# The Dueling Neurosurgeons

One of the landmark cases in medical history involved King Henri II of France, whose suffering foreshadowed almost every important theme in the next four centuries of neuroscience. His case also provides a convenient introduction to the brain's layout and general makeup.



The world would have looked stunningly, alarmingly bright to the king of France, then suddenly dark. During the charge, little light penetrated the cocoon of his helmet. Darkness was safety. But when the visor was wrenched open, the sunlight punched his eyes, a slap as sharp as a hostage would feel the moment the bag was torn off his head. In his last split second of normal life, Henri's eyes might have registered a glimpse of the scene in front of him—the glint of sand kicked up by his horse's hooves; the throbbing white ribbons wrapped around his lance; the glare off the armor of his charging opponent. As soon as he was clobbered, everything dimmed. Just a handful of doctors in the world in 1559 could have foreseen the damage already diffusing through his skull. But even these men had never worked on a case so important. And over the next eleven days, until King Henri was past danger, most of the great themes of the next four centuries of neuroscience would play themselves out in the microcosm of his brain.

The unlikely king, unlikely queen, and unlikely royal mistress were celebrating a supposed end to violence that day. Queen Catherine looked like royalty itself in a gown of silk interwoven with gold fibers, but she'd actually grown up an orphan. As a fourteen-year-old in 1533, she'd watched helplessly as her family, the Medici of Florence, negotiated her marriage to an unpromising prince of France. She'd then endured a decade of barrenness with Henri before saving her life by squeezing out two heirs. And throughout it all, she'd had to endure the rivalry of her cousin Diane. Diane de Poitiers had been married to a man forty years her senior until just before Catherine's arrival in Paris. When he died, Diane donned black and white (French mourning colors) in perpetuity, a show of piety. Yet this thirty-five-year-old beauty lost no time in turning cougar on the fifteen-year-old Prince Henri, first enslaving him with sex, then parlaying this hold over him into real political power, much to the queen's disgust.

Le Roi, Henri II, had never been groomed for the throne; he'd become heir apparent only when his handsomer and more charming older brother died after a game of tennis. Henri furthermore had a tough early reign. Paranoid about Protestant spies, he'd started chopping off the tongues of "Lutheran scum" and burning them at the stake, making himself hated throughout France. He'd also prolonged a series of stupefyingly complex wars with Spain over Italian territories, bankrupting the realm. By the late 1550s Henri owed forty-three million livres to creditors—over twice his yearly income—with some loans at 16 percent interest.

So in 1559 Henri abruptly brought peace to France. He signed a treaty with Spain, and although many (including Catherine) fumed over Henri's giving away Italy, he stopped the ruinous military campaigns. Two important clauses in the treaty established alliances through marriages—an immediate wedding for Henri and Catherine's fourteen-year-old daughter to the king of Spain, and a second for Henri's spinster sister to an Italian duke. To celebrate the marriages, Henri organized a five-day jousting tournament. He had to borrow two million livres more, but workmen spent May and June ripping up cobblestones and packing down sand near Henri's palace in Paris to make a jousting list. (Protestants awaiting punishment in nearby dungeons could hear the clamor in their cells.) A few weeks before the tournament, carpenters erected some rickety timber galleries for royal guests and draped them with standards and banners. On the day of, peasants climbed onto rooftops to point and holler.

On the third day of festivities, a Friday, June 30, Henri himself decided to joust. Despite the heat he wore fifty pounds of gold-plated armor adorned with Diane's colors, mostly black-and-white swirls. Whatever his faults, Henri looked regal upon a horse, and he entered the list on a handsome, chestnut-colored steed. During his first run he unmanned (which is to say, unhorsed) his future brother-in-law with a blow from his lance; a short while later he unmanned a local duke, knocking him onto his arse as well. When young, Henri had had a

reputation as a brooding sort, but he was in high spirits that day, and arranged for a third and final joust against a powerful young Scotsman, Gabriel Montgomery.

The king and Montgomery put perhaps a hundred yards between them, and when a trumpet sounded, they took off. They clashed—and Henri got his bell rung. Montgomery bludgeoned him just below the neck, and Henri lost a stirrup and nearly careened off his horse.

Embarrassed, the king wheeled around and announced that "we" would tilt with Montgomery again—a bad idea for any number of reasons. It violated the laws of chivalry, as he'd already jousted the maximum three times. It also spooked his court. Catherine had dreamed the night before of Henri lying facedown in blood, and two of her astrologers had already prophesied the king's doom. (One of them, Nostradamus, had written a quatrain four years earlier that read, "The young lion overcomes the old / on the field of war in single combat. / He pierces his eyes in a cage of gold. / Two wounds one, then dies a cruel death.") Unnerved, Catherine sent a messenger to warn Henri off.

Finally, Henri had been suffering from vertigo and headaches recently, and his attendants found him shaken after his latest joust. Cruelly, though, a blow to the head can cloud someone's judgment when he needs it most, and like a linebacker or boxer of today, Henri insisted on jousting again. Montgomery demurred, and the crowd watched in embarrassment as Henri berated him and challenged him—on his allegiance, before God—to tilt again. At 5 p.m. they lined up. Some eyewitnesses later claimed that an attendant fastened the king's visor improperly. Others said that Henri wiped his brow and, in his fog, forgot to refasten the visor. Still others insisted that he cocked it up, in spite. Regardless, this time Henri didn't wait for the trumpet before charging.

During a joust, a low timber fence separated the combatants, and they charged each other left shoulder to left shoulder, shield hand to shield hand. They held their fourteen-foot wooden lances in their

right arms and had to angle them across their bodies to strike. A proper blow therefore not only jolted but twisted the opponent, and the force often broke the lance. Sure enough, the king's lance shattered when it met Montgomery, and Montgomery's lance exploded into splinters when it struck the king just below the neck. Both men jerked, and the courtiers in hose and doublets, the women adorned with ostrich feathers, the peasants hanging on the eaves, all of them whooped at the teeth-rattling blow.

The action, though, was not over. Given the commotion, no one quite knows what happened next. Perhaps Montgomery's broken shaft buckled upward like an uppercut, or perhaps a splinter of wood leapt up like shrapnel. But somewhere in the melee, something knocked open the king's gold-plated visor.

Now, many contemporaries blamed Montgomery for what happened next, because the moment his lance splintered he should have flung it aside. But the brain can react only so quickly to stimulus—a few tenths of a second at best—and a brain fogged from jousting would have responded more slowly still. Besides, Montgomery had an awful momentum, and even as the crowd's roar lingered, his horse took another gallop. An instant later the jagged lance butt in his hand struck the king dead between his eyebrows. It raked across his naked face, wrenching his skull sideways and digging into his right eye. *He pierces his eyes in a cage of gold.*

But Nostradamus spoke of two wounds, and a second, deeper wound, to Henri's brain, proved worse. Compared to those of most mammals, the four lobes of the human brain are grotesquely swollen. And while our skulls provide some good protection, the very hardness of the cranial bones also poses a threat, especially since the skull is surprisingly jagged on the inside, full of edges and ridges. What's more, the brain actually floats semifreely inside the skull; it's attached to the body really only at the bottom, near the stalk of the brainstem. We do have cerebrospinal fluid between the skull and brain to buoy and cushion it, but the fluid can absorb only so much energy. During

impact, then, the brain can actually slide counter to the skull's motion and slam into its bones at high speed.

As the butt of Montgomery's lance struck home, Henri would have felt both a blow and a twist, like a mean hook to the jaw. The blow likely sent a small shock wave through his brain, a ripple of trauma. The rotational force was likely even worse, since torque stresses the brain unequally at different points, tearing at its soft seams and opening up thousands of microhemorrhages. Henri, an expert equestrian, nevertheless kept his saddle after the impact: the muscle-memory circuits in his brain kept him balanced and kept his thighs squeezing the horse. But on a deeper level, the twist and the blow tore open millions of neurons, allowing neurotransmitters to leak out and flood the brain. This would have caused untold numbers of other neurons to fire in panic, a surge of electrical activity reminiscent of a mini-seizure. Although few men of science believed in such things, at least one doctor in Paris knew that Henri had suffered a mammoth concussion.

After the clash Montgomery yanked his horse's reins and whirled to see what he'd done. Henri had slumped down onto the neck of his Turkish steed, a horse forevermore known as Malheureux, *unlucky*. But however unlucky, Malheureux was disciplined, and when it felt its reins slacken upon Henri's collapse, it kept galloping. The now-unconscious king bobbed on his horse's back as if keeping time, his visor clanging down on the shards of wood protruding from his eye.

The two greatest doctors in Europe would soon converge on the king, but before they could do so, courtiers and sycophants of all stripes poured out of the stands toward Henri, each one craning for a glimpse and calculating whether his fortunes would rise or fall if Le Roi died. To most observers the entire French monarchy now looked as rickety as the timber grandstands. The dauphin (the heir apparent) was a frail, milquetoast boy of fifteen; he fainted at the mere sight of Henri's

injury. The shaky truce between Catherine and Diane depended entirely on Henri's living, as did the false peace between other political factions. The two royal weddings, not to mention the peace of Europe, threatened to unravel as well.

Eased down from his horse, Henri lay stunned. Montgomery pushed to the front of the crowd to beg, somewhat incongruously, that the king both forgive him and also cut off his head and hands. Upon surfacing to consciousness, the king instead absolved him, without beheading or beheading. Henri drifted in and out after that, and finally insisted on rising and walking (albeit with support) up the palace steps to his bedroom. His physicians set about removing a four-inch splinter from his eye, but had to leave many smaller ones in place.

Among those doctors attending the king was Ambroise Paré. A thin, prim man, Paré served as royal surgeon—a job less prestigious than it sounds. The son of a cabinetmaker, Paré hailed from a village



Dueling neurosurgeon Ambroise Paré.  
(National Library of Medicine)

in north France, where he'd trained as a "barber-surgeon." In short, barber-surgeons cut things, which differentiated them from proper physicians. He might start his day at 6 a.m. shaving beards and trimming periwigs, then amputate a gangrenous leg after lunch. In the early 1200s, the Catholic church had declared that no proper Christians, including physicians, could shed blood; physicians therefore looked down upon surgeons as butchers. Early in his career Paré had stood below even most surgeons because he spoke no Latin. Nor could he afford his licensure fee, so he became a battlefield surgeon at twenty-six, joining the army as a ragtag follower with no rank or regular salary. Injured soldiers paid what they could, be it casks of wine, horses, a half crown, or (sometimes) diamonds.

Paré took to soldiering like a house afire, hobnobbing with generals by day and getting drunk with lower-ranked officers at night. Over the next thirty years he worked in seventeen campaigns across Europe. But he made his first important discovery while a tyro. Most doctors in the early 1500s considered gunpowder poisonous, and cauterized any bullet wound, however slight, by dousing it with boiling elderberry oil. To his mortification, Paré ran out of elderberry oil one night after a battle. Begging their forgiveness, he patched up his patients' wounds with a paste of egg yolk, rose water, and turpentine instead. He expected every one of these "untreated" soldiers to die, but they were fine the next morning. In fact they were thriving compared to those treated with boiling oil, who writhed in pain. Paré realized he'd effectively run an experiment, with astounding results, since his trial group had fared much better than his controls.

That morning changed Paré's entire outlook on medicine. He refused to use boiling oil ever again, and set about perfecting his egg/turpentine paste instead. (Over the years the recipe changed somewhat, and eventually included earthworms and dead puppies.) On a deeper level, that morning taught Paré to experiment and to observe results for himself, no matter what ancient authorities said. It was a symbolic conversion, really: by abandoning boiling oil—with

all its medieval overtones—Paré effectively abandoned a medieval mentality that accepted medical advice on faith.

As is evident from his case reports, Paré lived in an era of near-cartoonish violence: one day might find him treating a twelve-year-old girl mauled by the king's pet lion; the next might find him literally standing on a duke's face, to get enough leverage to yank a broken spearhead out. But Paré handled it all with aplomb, and his willingness to experiment made him an innovative surgeon. He developed a new drill-and-saw contraption to "trepan" the skull—that is, open a hole in the bones and relieve pressure on the brain, whether from inflammation or fluid buildup. He also developed tests to distinguish—in particularly gory head wounds—between fat, which was harmless to scrape away, and oozing bits of fatty brain tissue, which weren't. (In short, fat floats on water, brain sinks; fat liquefies in a frying pan, brain shrivels.) When describing a patient's recovery, Paré usually pooh-poohed his own role: "I treated him, God healed him," he famously said. But his many near resurrections earned Paré quite a reputation, and Henri eventually appointed him "surgeon to the king."

Despite his expertise with head wounds, Paré still stood below the king's physicians in the medical hierarchy, and he deferred to them in the busy hours after the jousting disaster. The physicians force-fed Henri a potion of rhubarb and charred Egyptian mummy (a treatment Paré rolled his eyes at in private), and they opened the king's veins to bleed him, even as he bled spontaneously from his colon. The English ambassador noted the king had a "very evil rest" that first night, but most of the attending doctors remained optimistic that he'd suffered little damage beyond his right eye. And in fact, when the king surfaced into consciousness the next morning, he seemed to have his wits about him.

But Henri soon had to face the fact that Catherine had effectively seized control of France. He asked after Montgomery, and frowned to learn that the Scotsman, not trusting Catherine, had already fled.

Henri called out for his mistress, but Catherine had stationed soldiers at the palace door to bar Diane's entrance. Perhaps most startlingly, Henri learned that Catherine had ordered the decapitation of four criminals—then bade Henri's doctors to experiment on their heads with Montgomery's broken lance stump, to devise a strategy for treatment.

Meanwhile, a messenger on horseback was sprinting northeast through forest and field to Brussels, bound for the court of Philip II, the king of Spain. (Confusingly, Spanish kings lived in northern Europe, in conquered territory.) Although the recent peace treaty had secured Philip's marriage to Henri's daughter, Philip hadn't deigned to attend his own wedding in Paris, explaining that "kings of Spain do not run after brides." (Philip sent a proxy, a duke, to stand in at the ceremony instead. To legally "consummate" the marriage, the duke approached the princess's bedchamber that night, removed his boot and hose, and slipped his foot beneath the bedcovers to caress the girl's naked thigh. There was much ribald speculation in Paris about whether this satisfied her.)\* Despite his haughtiness toward Henri's family, Philip wanted Henri to live, and soon after the messenger arrived, Philip roused his best physician, the one man in Europe whose expertise with the brain rivaled Paré's.

As a teenager in Flanders, Andreas Vesalius had dissected moles, mice, cats, dogs, and whatever other animals he could snare. But animal dismemberment couldn't quite sate him, and before long he began pursuing his real passion, human dissection. He began robbing graves at midnight, sometimes fighting wild dogs over scraps. He also let himself get locked outside the city walls at night to rob skeletons from the gallows, clambering up thirty-foot gibbets to cut down swaying pickpockets and murderers, counting himself lucky if crows hadn't refashioned their anatomies too much already. He smuggled

\*This and all upcoming asterisks refer to the Notes and Miscellanea section, which begins on page 359 and goes into more detail on various interesting points.



Dueling neurosurgeon Andreas Vesalius.  
(National Library of Medicine)

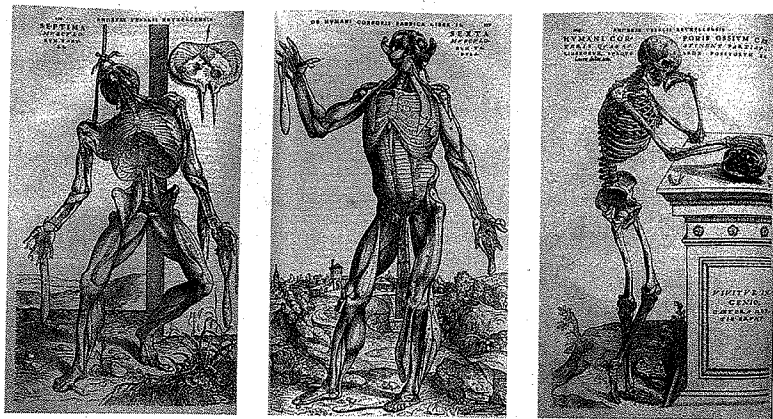
the cadavers back into the city beneath his garments, then stored them in his bedroom for weeks, to linger over their dissections like a cannibal gourmand over a meal. He delighted in clutching every organ, too, even crushing them between his fingers to see what oozed out. However creepy, his obsession revolutionized science.

Vesalius eventually enrolled in medical school, and like everyone else in the previous thirteen centuries, his medical training basically consisted of memorizing the works of Galen, a physician born in AD 129. Human dissection was taboo back then, but luckily for him, Galen served as a doctor for Roman gladiators, which was just about the best training possible for an anatomist: gladiator wounds could get pretty gnarly, and he probably saw more human innards than anyone alive then. He soon founded a school of anatomy, and his work was so innovative and all-encompassing that he stunted the field, since his

small-minded followers couldn't evolve past him. By the Renaissance, the birth pangs of a new science of anatomy had begun, but most "anatomists" still cut into the body as little as possible. Anatomy lectures were similarly a joke: they mostly consisted of an expert sitting on a throne and reciting Galen aloud while, beneath him, a lowly barber hacked open animals and held their greasy entrails up. Anatomy was theory, not practice.

Vesalius—a swarthy man with a virile black beard—adored Galen, but after immersing himself in human flesh, he began to notice discrepancies between the gospel of Galen and the evidence on the dissecting table. At first Vesalius refused to believe his own eyes, and told himself that he must have cut into some anomalous bodies. He even entertained the theory that the human body had changed since Galen's time, possibly because men now wore tight trousers instead of togas. Eventually, though, Vesalius admitted he was grasping, and that, however unthinkable it seemed, Galen had erred. Around 1540 he compiled a list of two hundred howlers, and determined from them that Galen had supplemented his gladiatorial work by dissecting sheep, apes, oxen, and goats, and then extrapolated to humans. This bestiary left human beings with extra lobes on the liver, a two-chambered heart, and fleshy "horns" on the uterus, among other mutations. Galen's shortcomings became glaringly obvious when Vesalius probed the brain. Galen had dissected mostly cow brains, cow brains being large and abundant in the butcher stalls of Rome. Unfortunately for Galen, humans have vastly more complex brains than cows, and for thirteen hundred years, physicians were left trying to explain how the brain worked based on a faulty notion of how it was put together.

Vesalius vowed to reform the science of anatomy. He began calling out, even exposing, prominent "anatomists" who never bothered dissecting bodies themselves. (About one, Vesalius sneered that he'd never seen the man with knife in hand, except when carving mutton at dinner.) More important, Vesalius reached a wider audience by



Drawings from Andreas Vesalius's *On the Fabric of the Human Body*, one of the most beautiful scientific books ever published. (National Library of Medicine)

composing one of the cherished works of Western civilization, *De Humani Corporis Fabrica* (On the Fabric of the Human Body).

Beyond the few crude diagrams in other books, this was the first anatomy text to include realistic drawings of the human form. And what drawings these were. Vesalius sought out the best local artist to illustrate his magnum opus, and since he was working in Padua then, this happened to be Titian, whose school of artists soon brought Vesalius's vision of the human form to life. Unlike in modern textbooks, the bodies in *Fabrica* don't lie flat and lifeless on a table. They rise and strut and pose like classical statues. Some do a veritable striptease with their flesh, peeling back layer after layer to reveal their inner organs and organic essence. In darker scenes, bodies sway from ropes or clasp their hands together in agonized prayer. One skeleton digs his own grave; another contemplates a skull, alas-poor-Yorick-like. Titian's apprentices labored over even the backgrounds of the pictures, planting the cavorting cadavers in the lovely, rolling landscapes near Padua. As in that era's painting and sculpture, the realism was unsurpassed, making *Fabrica* one of the greatest marriages of art and science\* ever produced. Pictures in the book's seventh and crowning volume, on

the brain and related structures, distinguished scores of important details for the first time. Other anatomists had passed their eyes over the brain, but in a literal sense Vesalius, like a great artist, was the first person to really see it.

Ever obsessive, Vesalius agonized over every detail of *Fabrica*, including what paper and font to use, and he crossed the Alps from Italy to Switzerland to oversee its printing. For the first bound copy, he found another artist to hand-paint the drawings and, after cladding the book in purple silk velvet, carried it farther north and presented it to the Holy Roman Emperor, Charles V. It was June 1543, and in a remarkable coincidence, Nicolaus Copernicus had published *On the Revolutions of the Heavenly Spheres* a week before. But whereas *On the Revolutions*, written by a seventy-year-old astronomer, demoted human beings from the center of the cosmos, *Fabrica*, written by a twenty-eight-year-old anatomist, elevated us, celebrating us as architectural marvels. This near-pagan glorification of the body didn't please everyone, not even some anatomists, who vilified Vesalius and demanded that he retract every criticism of Galen. (Vesalius's former mentor smeared him as *Vesanus*, Latin for "madman," with a pithy anatomical pun attached to its posterior.) Being ignorant of medical matters, Charles V adored *Fabrica* and promoted Vesalius to court physician.

By 1559, though, Charles had died, and Vesalius found himself serving in the court of Charles's son, the cold and remote Philip. He spent most days treating nobles for gout and VD and bowel obstructions, with little time for original work. So when word of Henri's disastrous joust arrived, Vesalius jumped, dashing down to Paris on a relay of mail carriages, covering two hundred miles in forty-eight hours.

He soon met Paré, and modern neuroscientists sometimes bite their knuckles at the thought of this encounter—two titans, meeting at last! They'd actually almost met before, in 1544, near Saint-Dizier, when the army Vesalius was serving with laid siege to Paré's army.



This time around, any “combat” would be *mano a mano*, and these two proud and ambitious men likely circled each other, sizing the other up. But they had little time to waste in posturing.

If contemporary sketches are accurate, the king’s bedchamber had deteriorated into a zoo. Dogs ran about, apothecaries chopped up herbs and mummy bits at the foot of the bed, and courtiers circled like vultures, interrupting Henri’s rest. Henri lay on a four-poster bed with sumptuous blankets and a nude bust perched above the headboard. Case notes report that his face had swelled grotesquely, and his neck had stiffened like old French bread. His left eye could still see, but the lance had blinded the right and exposed the bone around the socket; the pus-stained bandage there surely clashed with the silk pillows. Given modern knowledge of brain trauma, we can surmise that Henri had a metallic taste in his mouth. Worst of all he could no doubt feel some dim black thundercloud, a massive headache, throbbing in the back of his skull. In his lucid moments, Henri gamely conducted state business, dispatching letters, arranging for his sister’s marriage to proceed, even condemning some Lutheran scum. But as his brain swelled and the headache spread, he grew confused, and his vision came and went. He slept fitfully, and asked repeatedly for soothing music, which was never denied him, and for Diane, who was.

Miraculously, Paré and Vesalius found no fractures on Henri’s skull, not even a hairline crack. (Since ancient times, doctors had a few ways of searching for cracks. They might dab ink on the top of the head and watch whether it seeped through, or they might thwack the skull with a stick and listen, since cracked and intact skulls sound different, much like cracked and intact bells do.) Many court physicians rejoiced at this news and proclaimed that Henri would therefore live: like most doctors then, they believed that the brain could not suffer any serious damage in the absence of a skull fracture, much like an egg yolk can’t be damaged without the shell being cracked. (Some jurisdictions didn’t even recognize a blow to the head as murder unless it broke the skull.) And admittedly, skull fractures did *look* bloody

awful, much more sickening than nonfractures, so the reasoning made some sense.

Vesalius and Paré reasoned differently. Upon meeting the king, Vesalius produced a white cloth and asked Henri to bite down on it. Rather irreverently, he then ripped it from the royal mandible. Henri’s body convulsed, his hands shot to his head, he howled in pain. You can imagine the sound of a dozen swords being unsheathed at this affront, but the stunt convinced Vesalius that Henri would die. The author of *Fabrica* knew better than anyone how delicate the brain is—you can scoop it with a spoon, like ripe avocado—and long experience told him that people with pain so intense usually didn’t survive.

For his part Paré drew on battlefield experience. Not infrequently a soldier beamed by a shell or cannonball would betray no external symptoms—he might not even bleed. But his mind would wax and wane, and his brain would soon shut down. To probe this mystery, Paré would perform a quick autopsy. Autopsies were rare and usually illegal back then, but such laws were relaxed on the battlefield. And when Paré did his furtive autopsies, he often found swollen and bruised and sometimes even dead tissue inside these brains—signs of a controversial new diagnosis called a concussion. Paré had also seen cases where the head took a blow on one side but the brain damage was concentrated on the opposite side—a so-called *contrecoup* injury. These were in fact often the deadliest injuries. So in a prediction to outdo even Nostradamus, Paré suggested that Henri’s brain had suffered a mortal *contrecoup* concussion, with damage localized in the back. Each man drew on different expertise in judging the king a goner, but they both disregarded the ancient imperative about gory head injuries necessarily being the worst. Instead of focusing on fractures and blood loss, they focused on the brain alone.

As for actual treatments, they discussed trepanning the king’s skull to remove any excess fluids and “corrupted” blood, but the risks outweighed the benefits, and they gave the idea up. In the meantime

they examined the heads of the decapitated criminals. History doesn't record the exact methodology here—whether someone fixed each head inside a vise to provide a stable target, or perhaps strung the noggins up like piñatas to swing at—but Montgomery's lance stump got quite a workout battering their mugs. It was a macabre mix of medieval brutality and modern experimental savvy, and Paré and Vesalius eagerly examined the targets for clues. Alas, the heads offered little inspiration for treatment.

The two men could have learned a lot more by simply observing the king, whose suffering foreshadowed many great discoveries over the next four centuries of neuroscience. Henri continued to drift in and out of coherence, limning the borders of the unconscious. He suffered from seizures and temporary paralysis, two then-mysterious afflictions. Strangely, the paralysis or seizures would derange only half of his body at any one time, a clear hint (in retrospect) that the brain controls the body's halves independently. Henri's vision also went in and out, a clue that the back of the brain (where Paré expected to find the contrecoup damage) controls our sense of sight. Worst of all, Henri's headache kept widening, which told Paré that his brain was swelling and that blood vessels inside the skull had ruptured. As we know today, inflammation and fluid pressure can crush brain cells, destroying the switches and circuits that run the body and mind. This explains why brain injuries can be lethal even if the skull suffers no fracture. Skull fractures can in fact save people's lives, by giving the swollen brain or pools of blood room to expand into. The history of neuroscience has proved the brain amazingly resilient, but one thing it cannot stand is pressure, and the secondary effects of trauma, like swelling, often prove more deadly than the initial blow.

King Henri II of France finally succumbed to an intracranial hemorrhage at 1 p.m. on July 10. Queen Catherine ordered every church to say six requiem masses daily and ordered all church bells—which had been bleating for the king—silenced. Amidst this sudden, sinister quiet, Vesalius and Paré began their famous autopsy.

To cut open a king—to even suggest such a thing—was bold. In that era, anatomists might open someone up for one of two reasons, a public lecture or an autopsy. Both activities had a stink of the disreputable about them. By the mid-1500s a few cities, especially in Italy, had relaxed the old prohibition on dissections for teaching purposes, but only barely: authorities might allow one per year (usually in winter, to prevent spoilage), and then only of criminals, since an official sentence of “death and dissection” would wring a little more posthumous punishment out of the rogue. Most kingdoms limited autopsies to suspected cases of poisoning, infanticide, or other heinous acts. And in some cases an “autopsy” did not require actually cutting open the body. Why Catherine gave in to Paré and Vesalius and permitted a full, invasive autopsy of Henri isn't clear, since everyone knew who had killed him and how, but history remains grateful she did.

Vesalius had laid out the proper steps for opening the skull in *Fabrica*. This usually involved lopping the head off to make examining the brain easier, but out of deference to the king, he merely elevated the chin in this case, by placing a wooden block beneath the royal nape. Someone grabbed a fistful of the king's graying hair to steady the skull, while someone else (presumably Vesalius, the expert dissector) began sawing an inch above the eyebrows. After circling the head and removing the skull vault, he encountered the thin membranes (the meninges) surrounding the brain. In *Fabrica* Vesalius suggested that students nick the meninges with their thumbnails and unwrap them. He then encouraged students to plunge their fingers in and squeeze and fondle every fold: dissection was as much a tactile as a visual pleasure for him. But with Henri, Vesalius restrained himself once again—probably in part because Henri's brain didn't look all that appetizing. The front and sides looked normal, but in the rear—antipodal to the blow\*—Vesalius and Paré found pools of blackened fluids beneath the meninges, like blisters about to burst. The brain itself had also yellowed and putrefied back there, a puslike mass that measured one thumb's width across by two thumbs' widths high.

Equally important, they found that the wooden shards from Montgomery's lance had never penetrated the brain.

It's not always clear what Vesalius and Paré understood, in modern terms, of how brain damage kills. In their reports they often lapsed into talk of imbalanced humors and "animal spirits" escaping Henri's body. They knew nothing of neurons or localization. And the shards from Montgomery's lance probably led to an infection that weakened Henri and hastened his death—a complication they couldn't have grasped. But the duo understood well enough that the "commotion" and "corruption" in the back of Henri's brain, along with the resultant pooling of blood, had ultimately killed him. Trauma to the brain alone, they determined, could be deadly, even without a skull fracture. And in proving this, they vastly outdid the mutterings of that old phony, Nostradamus. Nostradamus had bloviated about lions and cages of gold. Vesalius and Paré had predicted what sort of damage they'd find inside Henri's brain and exactly where they'd find it—and find it they did. They proved science the superior clairvoyant.

The fallout from Henri's death poisoned most everything he loved. After him, French kings were forbidden from jousting, for their own protection. Diane de Poitiers had to surrender the jewels and estates and place at court she'd earned as Henri's mistress. The new French king, the frail François II, died just seventeen months later, after contracting an earache while hunting. The next king in line, Charles IX, was ten years old, so Catherine assumed power as regent—putting an Italian, a Medici, in charge of France.

Henri's death had actually crushed Catherine: despite his shabby treatment of her, she loved him. (She even swapped her original royal symbol, a rainbow, for a broken lance.) But her policies over the next few years betrayed his hopes for peace and precipitated decades of civil war between Catholic Royalists and Protestants. These wars reached their nadir with the St. Bartholomew's Day Massacre in

August 1572, which Catherine likely engineered. Although intended as a surgical strike against key Protestant leaders, the killing fed on itself, and mobs spread across the countryside, butchering thousands; historians call it less a day of massacre than a season. One Protestant targeted was none other than Gabriel Montgomery, who, while in exile after manslaughtering Henri, had renounced Catholicism. After the St. Bart's massacre Montgomery fled to England, but he returned the next year to battle the royalists, capturing Normandy and threatening to conquer all of northern France. A lengthy pursuit ended with royalist troops capturing him in 1574, and Catherine had the pleasure of seeing the man she still blamed for her husband's death quartered and then beheaded.

As for the scientists, Paré had treated François II on his deathbed in 1560. The boy's earache had led to a buildup of fluid on the brain, but once again Paré declined to trepan a king of France. No one quite knows why he refused, and nasty rumors have always circulated that Paré (à la *Hamlet*) slipped poison into the young king's ear, probably at Catherine's request, so she could reign as regent. But there's another reason Paré did not perform emergency neurosurgery. The risks involved with trepanning were high, and he knew he would likely incur the blame for any mishap. That was doubly true since Paré had converted to Protestantism by this time, and therefore—far from being someone that Catherine would entrust with a murder—actually held a precarious position in Her Majesty's government. Indeed, Paré barely survived the St. Bartholomew's Day Massacre a dozen years later.

Nevertheless, during the intervals of peace in Paris, Paré thrived. He wrote a handbook for military surgeons and an anatomy textbook that plagiarized Vesalius. (Paré didn't see this as a big deal, calling his appropriation "as harmless as the lighting of one candle from the flame of another.") He also campaigned against mummies and unicorn horns and other bogus cures. Most important, Henri's autopsy inspired Paré to write a book about head wounds. It called attention

to the danger of contrecoup injuries and pooling fluids, and it continued the vital work of pairing specific brain injuries with specific symptoms—the modus operandi of neuroscience for the next four centuries. The world's finest surgeon spent his twilight in Paris, having served four kings, and he died in his bed in one of his five houses.

Vesalius met a nastier end. Within a month of Henri's autopsy, King Philip quit cold Brussels for sunny Spain. Vesalius followed, and soon wished he hadn't. There are two competing stories about what finally drove Vesalius from Spain. The less likely story says that Vesalius got a little too anxious to start the autopsy of a noblewoman one night—and found her heart still beating when he cut her open. Her family supposedly called in the Inquisition, and Vesalius saved his neck only by agreeing to make a pilgrimage to Jerusalem.

The second story, while probably more truthful, is even stranger. The Spanish heir apparent, Don Carlos, called the Infante, was a weak and febrile boy. No one had much sympathy for him, however, since he was also a psychopath. Born with teeth, he delighted in gnashing his nursemaids' nipples until they bled and became infected, and he spent much of his childhood roasting animals alive. By his teenage years he'd moved on to deflowering young girls. One night in 1562 the Infante tore down the stairs to snatch a maiden he'd spied, but karma tripped him. He somersaulted and smashed his noggin at the bottom of the staircase, lying there bleeding for some time. Spanish doctors failed to cure the prince, so Philip sent Vesalius. Vesalius found a tiny but deep red wound at the base of the prince's skull, and he suggested trepanation to alleviate pressure. The Spanish doctors, spiteful at a foreigner's interference, refused. Instead, they allowed the local townsfolk to dig up the desiccated, century-old corpse of Friar Diego, a cook at a local monastery and a reputed miracle-worker. The townsfolk then entered the Infante's bedchamber to slip Diego beneath the boy's sheets—and the boy, who was more or less out of his wits by then, snuggled up to and began dreaming of visits from the friar. A few days later he'd improved little, and Vesalius finally prevailed upon

the other doctors to puncture the skull near the eye socket and drain some pus. The Infante recovered within a week after this, but the doctors and townsfolk universally credited Diego, who was later canonized for Vesalius's miracle.

The whole farce disgusted Vesalius and convinced him to quit Spain. So he arranged a holy pilgrimage to escape. He first visited Padua, where he'd produced *Fabrica*, and arranged to get his old job as professor back. Nevertheless, perhaps feeling guilty about using a pilgrimage as a ruse, Vesalius continued to the Holy Land, landing at Jaffa in the summer of 1564. He visited Jerusalem and the plains of Jericho, and sailed back satisfied, but he never reached Padua. He'd booked passage on a cut-rate tourist ship with inadequate supplies, and when storms ravaged the vessel on the return voyage, passengers began expiring from a lack of victuals and fresh water. Like something out of Géricault's *The Raft of the Medusa*, corpses were being heaved overboard, and for once in his life the sight of dead bodies spooked Andreas Vesalius. He went half mad, and scrambled ashore as soon as the ship staggered to Zakynthos, an island in what's now western Greece. According to different accounts, he either died at the gates of Zante, a port city, or crawled to a filthy inn where the locals, wary of the plague, let him die alone. Either way, it was an anticlimactic death. There was no autopsy to determine what had killed him.

In the end, about the only person, place, or thing to gain from Henri's death was the incipient field of neuroscience. On a basic level, Henri's autopsy confirmed beyond a doubt that contrecoup injuries existed, and that the brain could suffer trauma even if the skull remained undamaged. It's a lesson, sadly, we're still relearning today. Rope-a-dope boxers and quarterbacks and hockey enforcers continue to shake off concussions on the theory of *no blood, no harm*. But each concussion effectively softens up the brain and ups the chances of more concussions. After multiple blows, neurons start to die and spongy holes open up; people's personalities then disintegrate, leaving them depressed, diminished, suicidal. Four centuries have passed, but

macho modern athletes\* might as well trade pads for armor and go joust with Henri.

On a deeper level, Henri's death helped inaugurate a new approach to neuroscience. You can't call Vesalius and Paré modern: each revered Galen along with Hippocrates and the rest of the Greek medical chorus. But each of them also evolved past the ancients, by emphasizing experiments and observation. Vesalius bequeathed a new map of the brain, Paré new diagnoses and surgical techniques; and while Henri's was not the first autopsy, in terms of prestige—prestige of both the patient and the practitioners—it was the summa of early medical science. The treatment of royals often defined what became standard care for everyone else, and after Henri's death, autopsies started to spread throughout Europe. This expansion made it easier to correlate specific brain damage with altered behavior, and with every new autopsy, neuroscientists learned to pinpoint people's symptoms more precisely.

Soon scientists even moved beyond the brain's gross anatomy, into a realm that Paré and Vesalius never dreamed of, the microscopic. Like physicists drilling down into the fundamental particles of the universe, neuroscientists began to drill down, down, down into the fundamental matter of the brain, parsing it into tissues and cells and axons and synapses before finally arriving at the brain's basic currency, its neurotransmitters.

PART II

CELLS, SENSES,  
CIRCUITS