BEYOND THE IVORY TOWER

A Distant Mirror for the Brain

Carl Zimmer

This year's essay series highlights the benefits that scientists, science, and technology have brought to society throughout history.

History has a way of repeating itself—even the history of science. Today we are witnessing a revolution in neuroscience, as researchers chart the circuitry of memory, cognition, and emotion, offering the promise of a chemically based medicine of the mind (*1*). But these same words would have been just as apt over 300 years ago, when neurology first emerged as an experimental science (*2*). In the mid-1600s, humanity's understanding of the brain changed no less profoundly than it is changing today. Medieval concepts of the soul and spirits rapidly disappeared, replaced with a vision of the brain based on anatomy, chemistry, and physics.

The dawn of neurology in the 17th century offers some instructive lessons for 21st-century neuroscience.

Gazing into this distant mirror, we can see how many of the themes of modern neuroscience can actually be traced back to a time long before the luxuries of electroencephalograms (EEG) or magnetic resonanice imaging (MRI) existed. We can admire the brilliance of the minds that created a science of the mind itself. But not everything we see in this mirror is beautiful. The first neurologists did not hesitate to leap from scant evidence to wild speculation. They believed that the biology of the brain justified the social divide between the powerful and the powerless. And although they promised that neurology would usher in new treatments for madness and other mental disorders, they did nothing of the kind: In the late 1600s, neurology often served as a new bottle for ancient wines.

It is difficult to appreciate just how unimportant the brain was considered to be before the scientific revolution. Medieval and Renaissance physicians sought to understand the mind with a mix of Christian theology and Greek philosophy. The body was believed to be divided into three anatomical regions, each designed for its own soul. The vegetative soul in the liver was responsible for desires and appetites. The heart housed the vital soul, which produced passions and action. The rational soul was immaterial and immortal and, hence, could not reside in one specific place in the body. But its faculties—such as reason, memory, and imagination—were carried out by the body's invisible spirits. These spirits were believed to swirl in three hollow chambers in the head known as the ventricles (*3*).

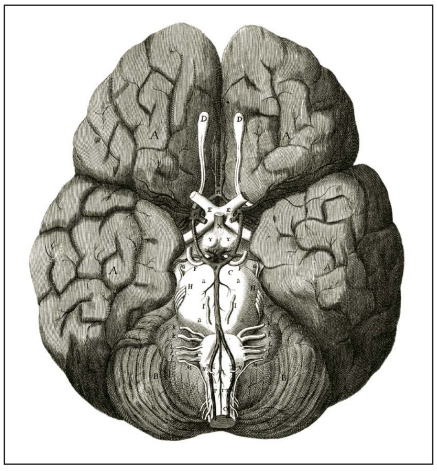
Anatomy, then, was the study of the houses of the souls. But anatomy alone was not enough to account for the life of the mind. Physicians also had to understand the fluids that coursed through the body. The four humors—black bile, yellow bile, blood, and phlegm—needed to be balanced for good health. Humors also gave each individual his or her temperament, be it the sad detachment of melancholy or the swift rage of choler. If the humors became corrupted or moved to the wrong place in the body, they could cause epilepsy or alter the temperament, even lead to madness. Physicians sought to cure many psychological disorders by bringing the humors back in balance, typically with bleeding and purging or by applying herbs.

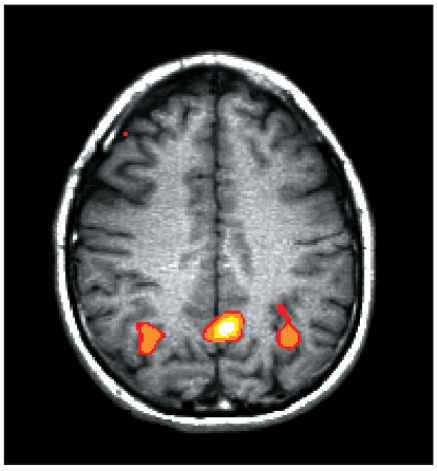
During the Renaissance, the theories of souls and humors were vigorously debated. Some Aristotelian scholars dared to suggest that the soul died with the body, whereas Plato's followers envisioned each individual soul resonating with spirits dispatched by the world soul. Yet in all these arguments, the brain was strangely absent. Its substance, which we recognize as consisting of billions of neurons trading complex signals, was seen as nothing more than phlegm. Even in the 17th century, the English philosopher Henry More went so far as to call it "a bowl of curds"—hardly the sort of material that could handle the lofty work of the soul.

The notebooks of the English physician Richard Napier (1559–1634) show how this mixture of medieval and ancient conceptions influenced psychological medicine on the eve of the scientific revolution (*4*). Napier described many psychological disorders, from patients who trembled or swooned to those who thought that rats were gnawing at their stomachs. He used horoscopes to diagnose madness, judging how the stars and planets affected the humors of his patients. In some cases, he conjured the archangel Raphael to reveal whether his patients were bewitched. But Napier was also something of a spiritual psychotherapist: he helped his patients reflect on their lives, comforted them with religious sermons, and prayed with them for a cure.

The thousands of patients who flocked to Napier are testimony to how widespread his beliefs were. Even as he treated his patients, however, the foundation of his beliefs was crumbling. Natural philosophers and physicians were forging a new medicine to take its place. Advances in physics, anatomy, and chemistry would all contribute to this change and would produce a modern conception of the brain.

In the early 1630s, René Descartes (1596–1650) constructed a description of the body that did not rely on vegetative or vital souls. He proposed that the body was





Brain imaging then and now. (**Left**) One of Christopher Wren's engravings of the brain (*7*). (**Right**) Modern functional MRI scan of the brain (*12*).

CREDIT: LEFT PANEL, REPRINTED WITH PERMISSION FROM (*11*). RIGHT PANEL FROM (*12*)

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made of particles that obeyed the laws of physics. A body was no different from a mechanical doll; neither needed a soul to drive its movements. Instead, Descartes envisioned nerves as a system of cords and inflating tubes that mechanically produced involuntary movements.

Descartes took a crucial step toward a science of the nervous system, despite the fact that he was woefully confused about the brain. He accepted the medieval notion of spirits flowing through the ventricles and even used it to determine where the rational soul was located. For Descartes, it was obvious that the pineal gland, which was believed to dangle over the ventricles, had to be where the rational soul influenced the spirits, steering them toward different nerves to produce voluntary movements.

Neurology could not become a true science until it had a sound anatomical foundation. Anatomy was going through its own revolution in the early 1600s, thanks to the work of William Harvey (1578–1657). Harvey trained at the University of Padua, where he learned Aristotle's methods of comparative zoology and functional anatomy. He returned to England and later became a royal physician to James I and Charles I, during which time he discovered the circulation of the blood.

As important as this discovery was, Harvey's methods—based on personal observation and experiment—were even more influential. By the 1650s, young natural philosophers were emulating Harvey, not Aristotle, in their studies of the liver, lungs, and other organs. And in the early 1660s, a group of Harvey's disciples applied his methods to the brain (*5*).

The group was led by the Oxford physician Thomas Willis (1621–1675). A royalist soldier during the Civil War, Willis had been rewarded at the Restoration with an appointment as professor of natural philosophy at Oxford. He used the new position to embark on a bold project: to map the brain and nerves and to work out their function (*6*). He and his colleagues—including his junior medical partner Richard Lower and his young friend Christopher Wren—dissected brains of humans, dogs, sheep, and other animals. Willis recorded their work in his 1664 book *The Anatomy of the Brain*, the first major work on the brain ever written (*7*). Over the next 8 years, he relied on his anatomical discoveries and careful bedside observations to write *Cerebral Pathology* on convulsive disorders and *Two Discourses Concerning the Soul of Brutes* on neurological and psychological disorders.

Together, this trilogy marks a defining moment in neuroscience. Willis dismissed Descartes' notions of the pineal gland and ventricles and demonstrated that these chambers could not house the spirits. Arguing that the brain itself was the site of mental functions, he carried out experiments to show that different functions were localized in different regions. Instead of Descartes' speculative sketch of involuntary movements, Willis offered a far more accurate account of reflexes. He even coined the term "neurology."

Willis also added chemistry to Descartes' mechanical nervous system. As a young physician, Willis had been strongly influenced by the work of alchemist-physicians such as Paracelsus and Joan Baptista Van Helmont. He also worked with Robert Boyle in 1650s Oxford. Willis envisioned the brain as an alembic (an apparatus alchemists used to distill substances) and the spirits that traveled through it as chemical messengers. He attributed the brain's disorders to disorders of chemistry. He saw epilepsy, for example, not as demonic possession, but as uncontrolled explosive reactions in the brain and nerves.

In recent decades, neuroscientists have looked back at Willis' work with growing admiration. He has even been called the Harvey of the nervous system. Not only did Willis create a masterful theory of the brain, but in his writings, we can see the first clinical descriptions of a wide range of neurological conditions, from myasthenia gravis to narcolepsy (*8*). By the late 17th century, the work of Willis and continental anatomists such as Nicolaus Steno and Franciscus Sylvius had led most physicians to accept the basic tenets of neurology. Philosophers such as John Locke (a student of Willis') even incorporated the reconceived brain into their epistemology.

Yet this revolution was, in some important ways, incomplete. Willis often transformed his observations into wild speculations, giving intricate accounts of the wanderings of invisible spirits as if he had traveled alongside them. Steno, a far more conservative student of the brain, castigated Willis and Descartes for their unwarranted certainty. "I frankly and openly confess that I know nothing about it [the function of the brain]," he declared and warned that it would be many generations before the brain was deciphered (*9*).

Willis sometimes saw in the brain what he wanted to see. He shared the common assumption of his time that peasants were dull-witted by nature. Trying to raise this prejudice to a medical fact, he argued that peasant brains were thick, preventing spirits from carving their proper pathways. Faced with the awkward fact that scholars sometimes fathered fools, Willis did not abandon his thick-brained theory. Instead, he claimed that too much study could deplete the spirits required for healthy sperm.

Willis imported not only social conventions into neurology, but also many aspects of traditional medicine. Hysteria, for example, was traditionally thought to be caused by a wandering womb, which could be cured by tying a bandage around the stomach to keep it in place. Willis declared the womb "wholly faultless" and recognized that hysteria was a disorder of the nervous system. But he still prescribed the same bandage—not to restrain the womb but to tame racing animal spirits in the nerves. Despite their revolutionary work, Willis and his peers could not surrender their belief in traditional remedies.

Even in 21st-century neuroscience, it's possible to see a continuity with the work of Willis and his 17th-century colleagues. Christopher Wren's anatomical drawings are replaced by digital atlases (see the figures on page 43). Willis' alchemy-influenced theories are replaced by neurochemistry. And like the first neurologists, today's brain researchers hope that their new knowledge will produce new treatments. Freud is the new Galen, his psychoanalytic tyranny overthrown by biological psychiatry (*10*).

Willis and his circle can stand as a model for how to study neuroscience—and how not to. His failings are the pitfalls all good neuroscientists try to avoid: unconsciously shoehorning neuroimaging results into social categories that may not have any biological meaning; creating a grand theoretical edifice that totters on scant evidence; designing therapies based on obsolete concepts of the brain. Most neuroscientists are aware of these pitfalls, but the public needs to become more familiar with them. People yearning to find personal meaning in the latest brain research (*11*) must understand that in many ways we still stand alongside Willis, Lower, and Wren, marveling at the brain while only beginning to comprehend it.

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