A Lot of Nerve

Scientific style and personality loom large in *Nerve Endings* and *The War of the Soups and the Sparks,* two new books documenting discoveries about the neuron's anatomical structure and its modes of transmitting nerve impulses. These volumes tell a story that begins in the late 19th century and is still being written today. Both accounts meld individual biographies of scientists with descriptions of experimental procedures and raise questions about the ways in which styles of research, creativity and intuition have contributed to the practice of experimental neuroscience.

In *Nerve Endings*, Richard Rapport, a neurosurgeon by training, focuses on the life and work of the Spanish artist and scientist Santiago Ramón y Cajal and to a lesser extent on Cajal's Italian rival, Camillo Golgi. Cajal's late 19th-century conception of a discrete nervous cell, separated from other cells by a gap (later called a synapse), came to replace the older reticular theory, which postulated that nervous tissue comprised a seamless, continuous web—an unbroken network, or *reticulum*—through which nerve impulses could travel in any direction. Golgi's adamant advocacy of the reticular theory was the source of his conflict with Cajal.

Golgi, after attending medical school, began his scientific career in experimental pathology by joining the even younger histologist Giulio Bizzozero, who was doing original research at the University of Pavia. In 1872, at age 28, Golgi left the university and, to support himself, took a job as chief physician at a mental hospital near Pavia. In his spare time, working in the kitchen of his hospital apartment, he strove to find a stain for neural tissue that could more clearly isolate neural structures. The following year he achieved what he termed the *black reaction* by using a silver nitrate stain that affected only a small percentage of neurons, allowing him to trace nerve structures more precisely than had been done before. He was then able to detect branching of axons (now understood to be the single fibers that conduct impulses away from the cell body) and to confirm the existence of protoplasmic extensions, or dendrites (now known to be the fibers on a cell body that receive signals sent from the axons of other cells). However, he was convinced that dendrites did not actually participate in neural transmission but instead merely played a supportive role in the network. His silver nitrate stain was nonetheless a formidable advance and was in widespread use by the 1880s. For his accomplishments, Golgi accepted a chair in histology at the University of Pavia.

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Cajal, who was nine years younger than Golgi, took to drawing, watercolors and photography as a young boy. Eventually he turned toward anatomical studies, employing his artistic skills for medical illustration. After his medical training at the University of Zaragoza, he taught histology, and in 1887 he began experimenting with the Golgi stain in his own kitchen laboratory. Cajal pioneered an improved method that he referred to as the double impregnation procedure. It involved soaking embryonic nerve tissue and cerebellar tissue first in fixative and then in silver nitrate, and then repeating this process. This method provided a deeper stain of nerve tissue, allowing Cajal to visually track the paths of axons and map the structure of neuronal cell bodies in greater detail. He found that axons ended in gray matter, meaning that the bulges (boutons) on the ends of axons conformed to patterns of dendrites on nearby cells. Most strikingly, he noted that the ends of axons were not seamlessly connected to other neurons but were separated from them by a gap. He also proposed a theory of dynamic polarization, in which nerve impulses were transmitted in one direction only, from the neuron's dendrites to the axon.

Cajal made many artistic renderings of his observations, some of which are helpfully reprinted in this volume. As Rapport reminds us, however, the gaps between neurons were not actually visible to Cajal, and it was only 50 years later with the aid of an electron microscope that they could be directly seen. How then did Cajal intuit such gaps? Rapport suggests that Cajal, because he was relatively isolated from the scientific mainstream and was not wedded to the reticular theory, did not have preconceived notions of what he might find. He used his imaginative capacity to see what others could not.

Nonetheless, the validity of Cajal's findings was not so easily apparent to others. He resorted to creating his own journal to publish his results, but his writings in Spanish attracted little attention. He therefore translated his work into French (which was considered a more acceptable language for reporting scientific findings) and submitted it to prominent German journals. As Rapport tells it, acceptance of the neuron theory began when the renowned histologist Albert von Kölliker was converted from the reticularist position at an 1889 Anatomical Society meeting in Berlin. Yet Golgi still adamantly opposed the neuron theory, a rejection that Rapport suggests may have been due to Golgi's rigid personal style. Indeed, even in 1906, by which time the theory had become widely accepted, Golgi attacked it in the speech he gave when he and Cajal were awarded the Nobel Prize. …

Reference

Lanzoni, S. (2006). A lot of nerve. *American Scientist, 94,* 80.