The Beautiful Brain and the Influence of Santiago Ramón y Cajal on Medicine

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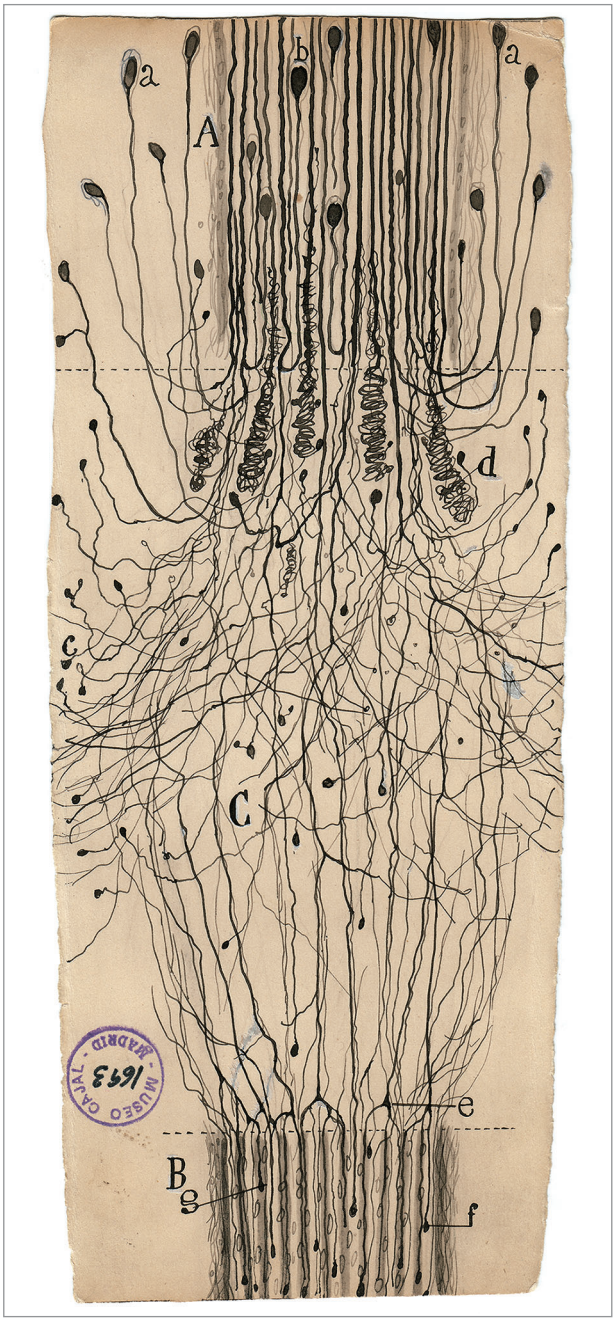
The Beautiful Brain: The Drawings of Ramón y Cajal is an aptly titled exhibit featuring drawings of brain cells by Santiago Ramón y Cajal, the grand master of neurohistology who flourished more than 100 years ago. The exhibit opened at the Weisman Art Museum of the University of Minnesota in January 2017 and will travel to university museums and galleries in Canada and the United States through the spring of 2019. The exhibit consists of 82 exquisitely detailed drawings of brain cells and neural elements from other tissues selected from more than 3200 drawings. The exhibit is exceptionally well conceived, executed, and presented, and the accompanying catalog is of the highest quality.

Cajal communicates the beauty of the brain by painstakingly reproducing on paper what he saw unfolding in his monocular microscope: a vast, neverending, and always-changing landscape of neurons with varied and intricate processes ordered, arranged, and interweaving in a dazzling whole. His unique vision was realized with use of a stain developed by Camillo Golgi in 1873. Unlike previous stains, Golgi's was applied to a whole tissue block and allowed for the visualization of large portions of a cell, and in "fortunate" cases (as Cajal called them), visualization of the whole cell. By 1888, Cajal had modified the stain and staining procedures to better visualize cellular structures and was incessantly drawing neural elements from various tissues and species, producing images published in 2 volumes, first in Spanish (1899-1904), then French (1909), then finally translated to English in 1995 (*Histology of the Nervous System*, volumes I and II. Oxford University Press).

The most dramatic aesthetic feature of Cajal's drawings is the elegant fine detail of the cell and its processes: dendrites and dendritic spines or axon collaterals of cortical neurons; end-feet of glial astrocytes engulfing blood vessels; planar, fan-shaped Purkinje cells in the cerebellum; a packed variety of cells in the retina; or neurons in the gut, to name only a few. Modern methods also produce beautiful multicolored cells, as nicely illustrated in the exhibit, but they are no match in elegance to a complete single neuron passionately animated by Cajal. British physiologist Charles Sherrington, a contemporary, characterized Cajal's talent this way: "The intense anthropomorphism of his descriptions of what the preparations showed was at first startling to accept. He treated the microscopic scene as though it were alive and were inhabited by beings which felt and did and hoped and tried even as we do."[1]

Then as now scientists disagreed about how exactly the brain worked. One view, held by Golgi, was that neurons directly contacted each other to form an uninterrupted circuit. Cajal correctly intuited that the neurons he saw and drew

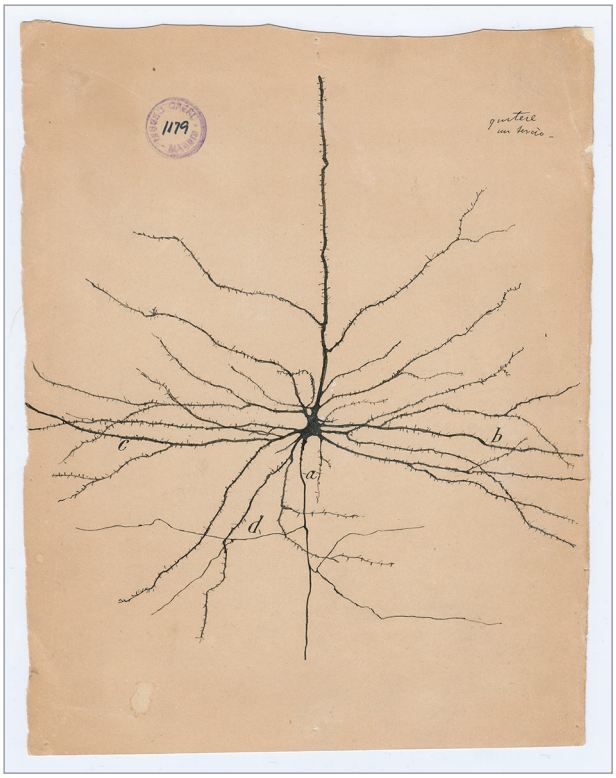


A cut nerve outside the spinal cord, drawn by Santiago Ramón y Cajal. 1913, ink and pencil on paper.
Courtesy of Instituto Cajal (CSIC).

were separate from each other and somehow communicated, an intuition that would need to wait until the advent of electronic microscopy in the 1950s for confirmation because of the limitations of light microscopy for visualizing typical synaptic cleft distances (~20 nm). Cajal's belief in neuronal separation gave impetus to the so-called Neuron Doctrine propounded by Waldeyer and laid the foundation for a modern understanding of brain function as a network of neurons interacting by chemical transmission. (Direct communication between neurons in gap junctions is now well established too, but chemical synaptic transmission is the rule.) Golgi and Cajal shared the Nobel Prize in 1906 but never resolved their scientific disagreement. In his autobiography Cajal later remarked "What a cruel irony of fate to pair, like Siamese twins united at the shoulders, scientific adversaries of such contrasting character."[2]

The influence of Cajal's work on basic neuroscience is unquestionable; his contributions to neuropathology and to our understanding of the degeneration and regeneration of neural tissue have stood the test of time and have been championed by prominent figures such as Río Hortega and Wilder Penfield who made their own historical contributions to neuroscience. One can also draw a direct line between Cajal's depiction of neurons and their assumed interactions in local circuits and contemporary sophisticated science that examines in exquisite detail the integrative function of various local brain circuits.[3,4]

Cajal's influence on clinical medicine and on the thinking of practicing neurologists and psychiatrists is admittedly more indirect, providing the intellectual background against which brain disorders have been investigated and treated. At the time of the 1906 Nobel Prize it seemed inevitable that clinical neurological thinking would be influenced by Cajal's revelations of brain cellular organization; that discussion of the anatomical and physiological basis of neurological disorders would come to incorporate facts newly revealed by Cajal's observations; and that clinical experience with neurological disorders would have enriched and informed the discussion of competing theories of neuronal organization. For unclear reasons, none of that occurred.



The pyramidal neuron of the cerebral cortex, drawn by Santiago Ramón y Cajal. 1904, ink and pencil on paper.
Courtesy of Instituto Cajal (CSIC).

Santiago Ramón y Cajal, 1876.
Courtesy of Instituto Cajal (CSIC).

The case of epilepsy, meticulously detailed by British neurologist John Hughlings Jackson,[5] offers an example of the missed opportunities. The localized onset and orderly spread ("deliberate march") of clinical seizure activity during some seizures would appear to support Cajal's idea of a network of anatomically separate but interacting neurons, but the "contemporaneousness of development of movements of several regions" seen in other seizure types would appear to support Golgi's concept of a neural reticulum comprising anatomically connected neurons, a notion supported by the identification of gap junctions in the motor cortex using electron microscopy.[6] Jackson discussed motor seizures in terms of movement representations in the brain and Cajal only briefly referred to the somatotopic arrangement of the motor cortex. Ironically, in early attempts to understand how neurons communicate and function in circuits, Cajal and others did not make the connections between neural organization and clinical neurology, a still-challenging task and important goal for neuroscientists and clinical neurologists alike.

Cajal's contributions to neuroscience were nevertheless groundbreaking and his drawings true revelations of the brain's beauty, unsurpassed in elegance and meaning. *The Beautiful Brain* is a must-see and its catalog a must-have: a rare confluence of breathtaking art and science.

1. Sherrington C. A memoir of Dr. Cajal. In: Cannon DF, ed. *Explorer of the Human Brain, The Life of Santiago Ramón y Cajal (1852-1934)*. New York, NY: Henry Schuman; 1949:xiii-xiv.

2. Cajal S. *Ramón y. Recuerdos de mi vida*. Madrid, Spain: Moya; 1917.

3. Shepherd G, Grillner S, eds. *Handbook of Brain Microcircuits*. New York, NY: Oxford; 2010.

4. Georgopoulos AP, Stefanis CN. Local shaping of function in the motor cortex: motor contrast, directional tuning. *Brain Res Rev*. 2007;55(2):383-389.

5. Jackson JH. REMARKS on the RELATIONS of DIFFERENT DIVISIONS of the CENTRAL NERVOUS SYSTEM to ONE ANOTHER and to PARTS of the BODY: Delivered before the Neurological Society, December 8th, 1897. *Br Med J*. 1898;1 (1932):65-69.

6. Sloper JJ, Powell TP. Gap junctions between dendrites and somata of neurons in the primate sensori-motor cortex. *Proc R Soc Lond B Biol Sci*. 1978; 203(1150):39-47.

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Submissions: The Arts and Medicine editors welcome proposals for features in the section. Submit yours at artsandmedicine@jamanetwork.com.

Exhibit Schedule

Weisman Art Museum, University of Minnesota, Minneapolis. January 28-May 21, 2017.

Morris and Helen Belkin Art Gallery, The University of British Columbia, Vancouver, Canada. September 5-December 3, 2017.

Grey Art Gallery, New York University, New York. January 9-March 31, 2018.

MIT Museum, Cambridge, Massachusetts. May 2, 2018-January 1, 2019.

Ackland Art Museum, University of North Carolina at Chapel Hill. January 27-April 7, 2019.

Catalog

Swanson L, Newman E, Araque A, Dubinsky J. *The Beautiful Brain: The Drawings of Santiago Ramon y Cajal*. Abrams Books; January 2017.