GOLGI, CAJAL, AND THE 1906 NOBEL PRIZE

James L. Culberson and Dennis O. Overman
Department of Anatomy
West Virginia University Medical Center
Morgantown, WV

The award of a Nobel Prize is always a special event in the history of a particular science, and the award of the 1906 prize in Physiology and Medicine was an extraordinary event. Not only was this the first time the prize had been shared by two laureates, but as related in the texts of their Nobel lectures, the two winners held radically differing views concerning the subject of their prize. Camillo Golgi from Pavia, Italy and Santiago Ramón y Cajal from Madrid were co-recipients of the 1906 Physiology or Medicine Prize, presented for their research on the structure of the nervous system. The following account provides some additional details about these two scientists, information concerning the actual award of the prizes in 1906, and a reference list for anyone interested in further exploration of this intriguing bit of neuroscientific history.

The Nobel Laureates

Camillo Golgi was born July 9, 1843 in the Alpine village of Cortena, Italy; his father was a distinguished medical practitioner. He studied medicine at nearby Pavia and graduated in 1866. His medical school thesis dealt with possible causes of mental disorders, and with the classification of mental problems based on anatomical and etiological factors. He remained at Pavia for an additional six years, publishing work on perivascular spaces of the brain, psammomas, pellagra, and neuroglial cells, and left there only when financial demands required that he assume a higher paying position. In 1872 he moved to a hospital for incurables at Abbialegroasso, where he was effectively isolated from most scientific activities and laboratories. Despite this environment it was here that Golgi made the discovery for which he is best known to neuroscientists. Working by candlelight, in his kitchen laboratory, he developed the black reaction ("la reazione nera"), which revealed for the first time the structural features of entire neurons. He subsequently used the method in studies of cerebral cortex, cerebellum, peripheral nerves, spinal cord and olfactory bulb, and in the first published papers to mention the technique (1873 and 1874), described the well-known Golgi Type I and Type II neurons. It is of interest that Golgi's original descriptions were inaccurate regarding details of structure and that he later erred in correlating these two types of nerve cells with function.

Golgi returned to a faculty position at Pavia in 1875, and except for a brief time in the Anatomy Chair in Siena, remained there until his death in 1926. His work shifted during the 1880's to focus on pathology, although he continued to study neural structure as well until the late 1890s. His many important contributions included discovery of the internal reticular apparatus of cells, studies of endoperitoneal blood transfusion, description of several muscle and tendon nerve endings (including muscle spindles), a paper on the neuropathology of chorea, and a series of studies on the kidneys and urinary system. His most important pathologic studies dealt with malaria, especially descriptions of the malarial parasite and part of its life cycle. Golgi continued to offer "free" courses in histology, and to do research until his death in 1926. He published his last paper, which concerned seasonal changes in the yolk spheres of frog eggs, in 1923.

Santiago Ramón y Cajal was born May 1, 1852 in Petilla, a small isolated village in the

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Pyrenees. His father was an ambitious struggling "second-class" surgeon who completed a medical degree and moved to a professorship in medicine at Zaragoza. Young Cajal earned a well-reserved reputation as a stubborn, mischievous youth, resisting successfully his father's best efforts at enforcing (by barbaric methods!) a classical education, while aggressively, (often secretly) pursuing his own interests in art and nature. After several school failures and apprenticeships with tracemers, the senior Ramon began tutoring his son personally and managed to discover a spark of interest in anatomy and illustration. Cajal finally did study medicine at Zaragoza and received a medical degree (without distinction) in 1873. Medical service followed, including a long bout with malaria precipitated by a stint in Cuba. Then he returned to Madrid to take an additional medical degree. He took his first faculty position in Anatomy at Zaragoza in 1877. There followed positions in Anatomy at Valencia (1884) and Barcelona (1887). Cajal's first paper, on inflammation, issued from his meager home laboratory while he was at Zaragoza (1880). At the age of 35, in Barcelona, he initiated the neurohistologic studies that would make him the leading medical scientist of modern Spain. Learning of Golgi's chrome-silver stain from Simmaro, a Madrid neuropathologist, Cajal soon modified the capricious technique, first by using double impregnation, and then by applying the method to embryonic neural tissue, in which axons are unmyelinated and thus easier to stain.

When his early neuroanatomic discoveries, published in Spanish, went unrecognized by the scientific community, Cajal took his slides to a German Anatomical meeting in 1889 where he won immediate respect and an instant reputation. In 1892 he assumed the chair of histology and pathological anatomy in Madrid and remained there for the rest of his career. Prolific publications by Cajal and his students during the 1880's and 1890's provided many of the descriptive details of the nervous system as we know it today, and the major props which support the neuron doctrine rest firmly on his work. He was recognized throughout the European world, with prizes or honors from Oxford, Cambridge, Moscow, Paris, Berlin, and the United States before his receipt of the Nobel Prize. Cajal's monumental works on the histology of the nervous system, on degeneration and regeneration of nerves, and his insightful autobiography and counsels for scientists (see references) are recognized classics of neuroscience and history of science. It remains astonishing but true that modern neuroanatomists still must check Cajal, to discover what he saw 80-90 years ago, before assuming the novelty of their own observations.

Selection of Laureates and Presentation of Awards

The funds and criteria for award of the Nobel prizes were provided by the unusual will of Alfred Nobel, an eccentric Swedish inventor and businessman who died in 1896, leaving the bulk of his estate for this purpose. After five years of wrangling over the details of implementation of Nobel's intentions, the first Nobel prizes were awarded in 1901. The identification of candidates and selection of the winner(s) in Physiology or Medicine was (and remains) the responsibility of a committee from the Royal Caroline Institute.

According to Koch (1960), both Golgi and Cajal were recommended for the Physiology and Medicine prize several times during the early years of the twentieth century. The 1906 Nobel Committee had the task of selecting winners from a distinguished list of 18 nominees; of these 18, seven actually were awarded the prize in 1906 or in subsequent years. As had been the case in previous years, there were some nominators and committee members who favored either Golgi or Cajal alone, and others who preferred to award the prize jointly. The final majority vote of the committee (Oct. 25, 1906) resulted in the award going to both scientists.

In accordance with the statutes of the Nobel Foundation, the formal presentation of the Nobel prizes (except the Peace Prize) is always scheduled for December 10, the date of the anniversary of the death of Alfred Nobel. The award ceremony in 1906 was preceded by the Nobel Banquet, held in the early evening at the Grand Hotel in Stockholm. In the presence of many of the important guests who would attend the later award presentation, each of the
laureates was honored with a series of toasts, expressing warm greetings and respect for their work. Count K.A.H. Mörner of the Royal Caroline Institute (speaking in French) recognized Golgi, who responded (by Cajal's account) in French and then Italian, "with olympic pride and pretentious mien!" (16). Cajal's introduction by Professor Sundberg was followed by a gracious response in French, which included acknowledgement of the other outstanding investigators who he considered at least equally worthy of this honor.

The presentation event was a formal evening affair held in the grand salon of the Royal Academy of Music, in Stockholm. It featured music by the Royal Orchestra in addition to the presentation of the awards. The guest list was headed by King Otto II and his retinue, and included members of Swedish ministries, diplomats, members of the Nobel family, high ranking local and national civilian and military officials, and representatives of learned societies for literature, sciences, letters and the arts.

Interspersed with musical selections, there was an introductory speech (in Swedish), focused on Nobel and his ideals, by Mr. Tornebladh from the Administrative Council of the Nobel Foundation. The laureates were presented individually by representatives of the selection committees for each prize. Golgi and Cajal again were introduced by Count Mörner, President of the Nobel Committee of the Royal Caroline Institute. Mörner's brief speech of introduction (in Swedish) provided some background information about nervous system structure and function for the largely non-scientific audience, and summarized for them the open questions addressed and/or answered by the work of the two laureates in Physiology and Medicine. The award itself, comprising a medal, certificate and cash, was presented by the King. Golgi and Cajal presumably would have needed to rely on interpreters to understand most of the evening's events, although Count Mörner did address each of them in his respective native tongue when he announced them for the official award and its motivation.

The Lectures

The Nobel lectures were presented to more appropriate, scientific audiences on December 11 (Golgi) and December 12 (Cajal). Both talks were delivered in French, and the two men presented fascinating contrasts in their approach to and interpretation of contemporary understanding of neural structure.

Golgi's lecture was entitled "The Neurone Doctrine-Theory and Facts". He began with the observation that he would speak directly to the theory which he had always opposed, "at a time when this doctrine is generally recognized to be going out of favour" (11). In a discourse that could be described as rambling, although it was organized around the theme of assessing arguments for the neuron doctrine, he sought to provide observational evidence which raised questions about the basic assumptions of the theory. Is the neurone an embryological unit? Is the adult neuron a single cell? Is the neuron a physiological unit? These queries were raised in sequence, and each was answered with a series of observations, mostly Golgi's own, which suggested that there could be no affirmative answer, because too many questions remained open. While presumably speaking about the neurone doctrine, Golgi defended (or sought to clarify) his erroneous correlation of Type I and Type II neurones with motor and sensory function respectively, resurrected his "diffuse reticular network", and explained (again in an attempt to clarify) his prior descriptions of dendritic processes as structures for nutrition of the cell body. In all, he sought to raise as many questions as possible without providing any recent solid evidence to counter prevailing support for the neurone doctrine.

Cajal spoke the following day on 'The Structure and Connexions of Neurons'. He began with a clear straightforward statement of the structural and functional meaning of his work. He then proceeded to support his conclusions with illustrated examples of the work which led him to his position. He described neuronal connectivity in the spinal cord, retina, and cerebellum and concluded this segment of his talk with illustrations and thoughtful comments regarding centrifugal fiber systems which he had
demonstrated and studied in several nerve centers. He spoke often of the importance of methodology and presented a modern (1906) view of the internal neurofibrillar structure of neurons. Finally he addressed a series of contemporary arguments against the neuron doctrine based on neuroembryology and studies of regeneration. He effectively dismissed these by providing evidence, based on what he considered better methods, that studies of both developing neurons and of regenerating nerves actually provided excellent support of the concept of the nerve cell as a morphological entity.

Perhaps the greatest contrast between the two published lectures is the difference in references to other neuroscientists. Indeed, Cajal suggests in his autobiography that Golgi made a display of pride and self-worship which produced a deplorable effect on the assembly (16). Golgi essentially ignored all work done since his own, and he had done little with the nervous system for about 10 years. In his defense, it seems possible that Golgi may have been taken aback when expected to present a Nobel address on the nervous system, and thus may have worked from his own old ideas. He may have been unaware of many of the studies he ignored in his talk. Today we certainly can find many of the ideas from his lecture defective at innumerable points, and Cajal observed that the same was true for knowledgeable scientists who were present at the lecture.

Cajal on the other hand, was very generous in extending recognition to many workers, including Golgi, who had added to knowledge of nervous system structure. In reading his lecture in fact, one is often obliged to read through two or three lines of names of those scientists who he cites for their contributions to a particular idea.

Concluding Comments

The presentation of the Nobel prize recognized the fact that both Golgi and Cajal made very important contributions to late 19th - early 20th century understanding of the nervous system. It is interesting that although they were contemporaries and shared Latin origins and academic medical backgrounds, they held very little else in common. Although we have no record of actual enmity between them (this has sometimes been assumed), there is also no sense of collegiality nor discussion of shared interests. While we must rely mostly on Cajal’s account, it seems that during their Nobel visit to Sweden, they interacted only formally and as required by protocol. It is not clear whether this stemmed more from Golgi’s proud manner, or from Cajal’s feeling that Golgi was so unwilling to acknowledge what so many other scientists were achieving in neuroanatomy in 1906.

Certainly today, when Golgi’s Opera Omnia (5) is consulted, it is likely to be done in a historical context, by someone interested in the early background of some idea or technic. Cajal’s work, on the other hand, is used and cited regularly by many modern neuroscientists, who use it as they use their other current references, to support contemporary observations and to recognize the priority of discovery, theory, or descriptions. Perhaps this contrast, drawn between the modern use of the scientific production of the two, is the best index for us to apply in judging their relative contributions to our modern understanding of the nervous system.

References


NEUROBIOLOGY OF THE CEREBELLAR SYSTEMS: A CENTENARY OF RAMON Y CAJAL’S DESCRIPTION OF THE CEREBELLAR CIRCUITS

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PROGRAM AND ABSTRACTS