Golgi, Camilo

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Camilo Golgi (1843-1926)

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Bartolomeo Camillo Golgi was born, the third of four sons, in Corteno (today Corteno Golgi), a small mountain village in the province of Brescia, Italy on 7 July 1843 (Figure 1). His father Alessandro was a doctor from Paviawho, through the demands of work, had taken on the general practice at Corteno in 1838. Golgi studied medicine at the University of Pavia where he graduated in 1865 at the age of 22. After his graduation, Golgi started his clinical activities at the Ospedale San Matteo in various medical, surgical and dermatological wards.

Figure 1: Corteno, birthplace of Camillo Golgi.

However, he soon became assistant at the Psychiatric Clinic headed by the pre-eminent psychiatrist Cesare Lombroso, who sparked his vocation to study the brain. Following the tenets of positivist scientific philosophy, anatomical and anthropological data became, at that time, the tools by which biology could explore neuropsychiatric diseases. Thus Golgi, in collaboration with Lombroso, began to investigate the aetiology of mental and neurological illness from an

experimental and anti-metaphysical point of view. Meanwhile in the free time that his hospital duties allowed, Golgi attended the Institute of General Pathology directed by Giulio Bizzozero, the rising exponent of the new experimental medicine which had as its emblem the microscope. From Bizzozero Golgi acquired a passion for histological investigation, the direct means of penetrating the formidable unknown of the architecture of the nervous system, that 'object' whose *hidden structure* enclosed the secret of all psychic and behavioural phenomena. Although three years younger than Golgi, Bizzozero thus became his master, patron and the 'catalyst' of his mind.

Under the direction of Bizzozero, Golgi began to publish works between 1870 and 1872, the most important of which were dedicated to the study of the neuroglia and which were flatteringly quoted in international literature. By 1872 Golgi had acquired a solid reputation as a clinician and histopathologist but this was not considered enough to earn him a satisfactory position at the University.

In 1872, pressured by his father, Golgi took part in and won the competition for the post of Chief Physician at the Pio Luogo degli Incurabili, a hospital for chronic diseases, at Abbiategrasso near Milan. Everything indicated that, with Golgi's arrival in a small town hospital, his research activities were about to end for good. However, after some initial difficulties, Golgi set up a rudimentary laboratory consisting of a microscope and a few instruments in the kitchen of his small quarters.

On 16 February 1873, Golgi hurriedly wrote the following words to his friend Nicolò Manfredi (part of this letter was published in Mazzarello, 1999): "I spend long hours at the microscope. I am delighted that I have found a new reaction to demonstrate, even to the blind, the structure of the interstitial stroma of the cerebral cortex. I let the silver nitrate react with pieces of brain hardened in potassium dichromate. I have obtained magnificent results and hope to do even better in the future." This is the first record of the invention of the black reaction (but it is also a *discovery* of a chemical-biological phenomenon) known nowadays as 'Golgi staining' or 'Golgi impregnation', which was a breakthrough for brain structure research. The black reaction consists of a first phase of hardening the tissue in potassium dichromate followed by the impregnation of the nervous elements by silver nitrate. The final result is a preparation in which the silhouette of the nerve cell appears in all its morphological complexity with all its ramifications, which could be followed and analysed even at a great distance from the cell body. The great advantage of this technique is that, for reasons that are still unknown, a precipitate of silver chromate randomly stains only a few cells in black (usually from 1% to 5%), and completely spares other surrounding cells, allowing the individual elements to emerge from the nervous puzzle. The discovery of the black reaction provided the spark to a truly scientific revolution that allowed the morphology and the basic architecture of the cerebral tissue to be displayed in all its complexity, thus contributing to the foundations of modern neuroscience.

Aided by his black reaction, Golgi, while in Abbiategrasso, discovered the branching of the axon and the fact that dendrites are not fused in a network. Furthermore he performed studies on the structure of the cerebellum (Figure 2) (describing the so-called Golgi cells of the cerebellar cortex) and olfactory bulbs, and observed striatal and cortical lesions in a case of chorea. Meanwhile he began to elaborate on a general theory of brain organization, the so-called 'diffuse nervous net', according to which the axons are connected (through direct fusion or intimate contact) in a diffuse network along which the nervous impulse is propagated. Although this concept was in polemical opposition to the 'neuron theory', ironically the indefatigable paladin of this theory, the Spaniard Santiago Ramón y Cajal, became such by using the Golgi stain.

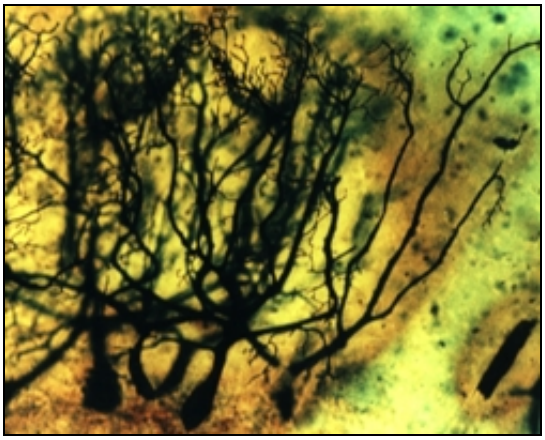

Figure 2: Microphotograph from an original preparation of the cerebellum from Golgi's lab.

After the discovery of the black reaction, Golgi (Figure 3) became Professor of Histology at the University of Pavia in 1876 (in the same year, for few months, he also taught anatomy at the University of Siena) and from 1879 onwards, he also became Professor of General Pathology and honorary chief with direct clinical responsibilities of a medical ward at the San Matteo Hospital.

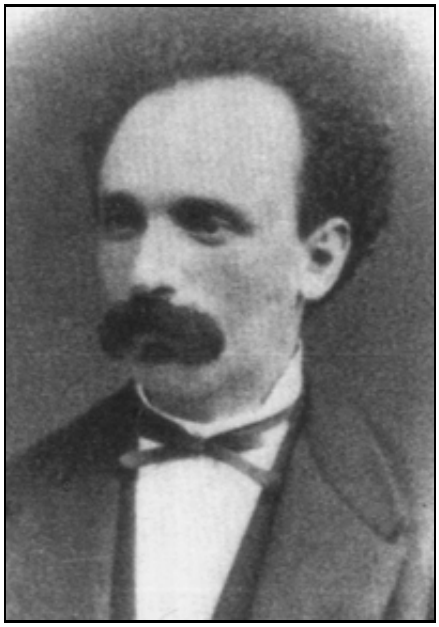

Figure 3: Camillo Golgi in 1875.

In 1878 he described two kinds of tendinous sensory corpuscles: the Golgi tendon organ (Figure 4) (proprioceptors) and the Golgi-Mazzoni corpuscles (transductor of pressure stimuli). Then he invented the staining method with potassium dichromate and mercuric chloride (1878-79), discovered the myelin annular apparatus (horny funnel of Golgi-Rezzonico, 1879) and analysed several regions of the nervous system in detail providing beautiful illustrations of them (Golgi, 1885, reprinted in 1886).

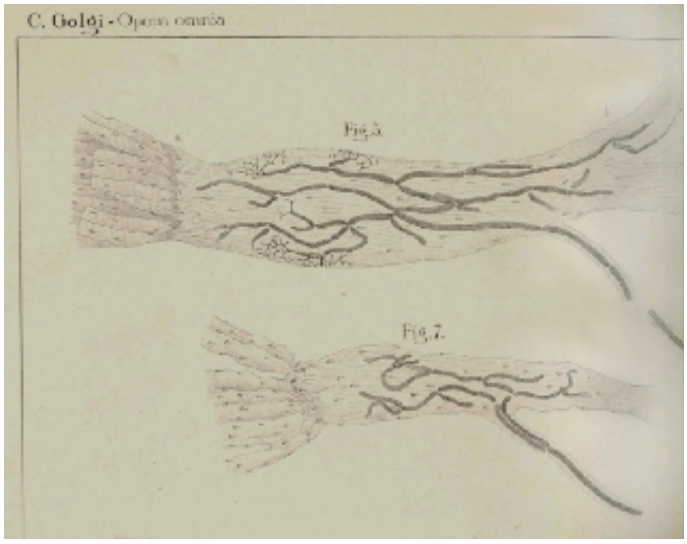

Figure 4: Golgi tendon organ (from *Opera Omnia*, 1903).

Between 1885 and 1892 he concentrated on studying human malaria (Figure 5). He was soon able not only to determine the entire intraerythrocytic cycle of development of the malaria parasite *Plasmodium* (Golgi cycle), but he also discovered the temporal relation between the recurrent febrile bout and the segmentation of the parasite (Golgi law). Meanwhile he concentrated on the study of kidney histology, histopathology and histogenesis (1884-89) and discovered the important relationship between the vascular pole of the Malpighian glomerulus and the distal tubule, which plays an important role in the regulation of blood pressure.

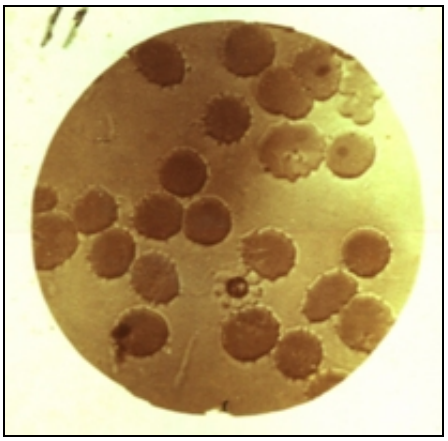

Figure 5: Original microphotograph of Golgi from a blood preparation, showing a 'daisy-like' formation from a malaria patient.

A skilled physician who always refused private work, he also published important clinical studies on peritoneal blood transfusion, intestinal worm infection, regeneration and pathological changes of the kidney. He also observed independently from the Swedish histologist Erik Müller, the canaliculi of the parietal cells of the gastric glands, often called Müller-Golgi tubules. At the end of 1893 he was elected, for the first time, Rector of the University of Pavia, and held the position until 1896. Thereafter Golgi returned to the study of the nervous system and using a variant of his black reaction he was able to observe, in 1897, a 'reticulum' in the cytoplasm of cells of spinal ganglia, the so-call 'internal reticular apparatus', subsequently christened the 'Golgi apparatus' or 'Golgi complex'. Meanwhile Golgi observed the perineuronal net that constitutes a reticular structure enveloping many neurons.

In the twentieth century, Golgi's scientific creativity faded, although he did continue to publish some papers until 1923. His time was divided between new responsibilities in the direction of Pavia University (of which he was again made Rector from 1901 to 1909) and the Senato del Regno (the

Senate of the Italian Kingdom), of which he was elected member from 1900.

In 1906 he reached the pinnacle of his international fame, when he received the Nobel Prize for Physiology or Medicine, which, ironically, was also won by his eternal scientific rival Ramón y Cajal. During the First World War, Golgi directed the Military Hospital Collegio Borromeo of Pavia, and promoted the rehabilitatory treatment for the war-wounded. In 1918 he retired from the University of Pavia at the age of 75, but continued to teach histology as Professor Emeritus until the beginning of the 1920s.

During his life he was elected honorary doctor of the Universities of Cambridge, Geneva, Kristiania (Oslo), Athens and Paris (Université de la Sorbonne). He was also Dean of the Medical Faculty of the University of Pavia and member of a number of international academies and scientific societies. He died in Paviaon 21 January 1926.

In Golgi's laboratory, Carlo Martinotti identified the cell named after him in the cerebral cortex, Aldo Perroncito described the phases of regeneration in the nerves, Emilio Veratti observed the sarcoplasmic reticulum and Adelchi Negri discovered the intraneuronal inclusions (the Negri bodies) in animals and humans infected with the rabies virus (Figure 6).

Figure 6 Golgi's school around 1900. Adelchi Negri is the first from the left, second row. Emilio Veratti is the second from the right, first row. A very young Aldo Perroncito is the first from the right, second row.

Many other scientists spent periods of study and specialization in Golgi's laboratory such as Giovanni Battista Grassi, the discoverer of the *Anopheles* that transmit human malaria, Antonio Carini who discovered the *Pneumocystis carinii*, and Fritjof Nansen, a Norwegian zoologist and Nobel Prize winner for Peace in 1922.

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Favourite sentences

"I have never felt regret for having been silent; only for having spoken" (Golgi, from a private document, Museum for the History of the University of Pavia).

"I maintain that my method, based on the sequentially combined action of potassium dichromate and silver nitrate, is one of the most precious methods available in microscopy, and I believe that it is destined to play an important role in the solution of the problems that continuously emerge in the study of the central nervous system" (Golgi, 1875).

"The histological evidence compels us to accept the existence not of isolated actions of individual cells but of the simultaneous actions of large groups of cells, at least in most regions of the central nervous system" (Golgi, 1885).

"Even if my statements clash with the widespread tendency to individualize the nervous elements, I cannot deflect from the idea of a unitary action of the nervous system, and I don't mind if this brings me close to an old conception of how the nervous system works" (Golgi, 1910; see Mazzarello, 1999).

"We, who have grown up in the faith of infinite progress, but who have been educated by experience and disciplined by scientific logic, look confidently upon you [students], on whom rests the task of consolidating and widening acquired knowledge, to participate, by spreading intellectual education with a mind free from political prejudice, in transforming of society, which we believe will be achieved, not through political commotions and revolutions, but because of the inescapable law of evolution" (Golgi, 1901; see Mazzarello, 1999).

"The most solid scientific knowledge . . . are never conquered with flights of fancy, which can only lead to an appearance of progress, but with minute, methodical, daily work, which, leading to the solid acquisition of a single fact, creates the unshakeable knowledge of the laws of life" (Golgi, 1902; see Mazzarello, 1999).

"Besides rigorous scientific thinking, in me there moves an intuitive form of thinking that has always guided me, without exception" (Golgi, 1910; see Mazzarello, 1999).

". . . civilization was the product not of single nation, but of all nations, and . . . the intellectual and moral wealth of mankind derives from the concurrence of all forces and from the achievements of the mind and genius of all nations" (Golgi, 1916; see Mazzarello 1999).

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