Pioneering Research in Neurobiology: Aldo Perroncito's Findings on the Regeneration of the Peripheral Nervous System

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Camillo Golgi and his scientific school

At the beginning of 1873 Camillo Golgi recorded for the first time the conception of the ***black reaction*** (silver-chromate reaction) known nowadays as *Golgi impregnation* or *Golgi staining*.
The silver nitrate selectively stained in black only a few cells (between 1% and 5%): nerve cell could clearly appear with all its ramifications, revealing for the first time the complex architecture of the nervous system. Thanks to this important breakthrough for brain research Golgi was awarded the Nobel Prize for Medicine in 1906 *ex aequo* with Santiago Ramón y Cajal.

As a professor of Histology and General pathology at the University of Pavia, Golgi became also the director of the related laboratories at the General Pathology Institute, thus becoming one of the most important Institute of biological research in Italy. A large number of students and postgraduates trained at Golgi's laboratory. His school's research not only concerned the structure of the nervous system: for example, microbiology and the structure of the internal reticular apparatus (discovered by Golgi in 1898) were very productive fields.

Golgi and his students around 1900. Among others: Adelchi Negri (1st from left, 2nd row), Guido Sala (1st from left, 3rd row), Emilio Veratti (2nd from right, 1st row). **First from right, second raw, Aldo Perroncito**. Courtesy of V. Kienerk

Adelchi Negri attended the laboratory since his student days. In analogy with Golgi's description of malaria plasmodiums in human blood, he discovered the rabies corpuscles (Negri's bodies) in infected brains.

Emilio Veratti, full professor of General Pathology in Pavia after Golgi's retirement, described in detail the T-canalicular system of muscle fibre in relation to sarcoplasmatic reticular functions.
As a granted student in Golgi's laboratory, **Vittorio Marchi** carried out a study on the black-reaction impregnation of talamic and striatal neurons, subsequently creating a method which bears his name, allowing the description of central nervous pathways.
Together with Golgi, the student **Giulio Rezzonico** identified the myelin horny funnels (myelin annular apparatus).
Carlo Martinotti, Golgi's assistant for a year in 1888, described the ascending-axon cells of the cerebral cortex (Martinotti's cells).

A large number of leading researchers in histology and general pathology perfected their skills in Golgi's laboratory. Among them: **Battista Grassi**, the discoverer of the Anopheles mosquito responsible for the human malaria and **Antonio Carini**, who found the micro-organism that causes frequent pulmonary diseases during acquired immunodeficiency.

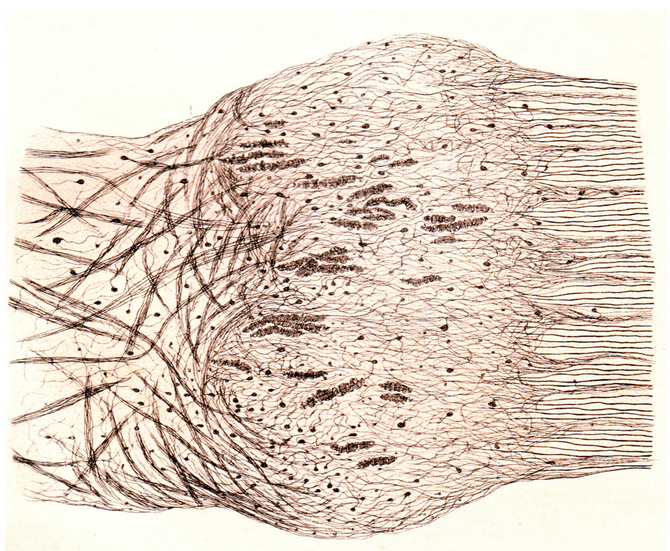
Prominent scholars who also attended the laboratory were: **Ferruccio Tartuferi**, **Casimiro Mondino**, **Ottorino Rossi**, **Achille Monti**, **Romeo Fusari, Luigi** and **Guido Sala**, **Antonio Pensa**.

Aldo Perroncito and the peripheral nerve regeneration

Aldo Perroncito (Turin 1882-Pavia 1929) enrolled in the University of Pavia in 1899 and since his first year joined the General Pathology Institute as an internal student. At that time, the assistants Giovanni Marenghi and Francesco Purpura were studying the problem of nerve regeneration. Perroncito faced the problem using the new reduced silver method of Ramón y Cajal. He set up a systemathic research plan by which he was able to describe the morfogenetic
kinetics of the peripheral nerve regeneration.
He recorded the first results in his degree dissertation entitled 'the regeneration of nerves'. He then carried out his research program for three years, with outsanding results.

Aldo Perroncito in his mid-eighteens

Perroncito studied the initial phases of the regeneration process: after severing the nerve he observed the early modification of the proximal stump, demostrating that the newly formed fibres derived from the pre-exixsting ones. The fibers were then in relation to the original cell bodies: Perrocinto definitely contractidited the 'poligenetic' or 'policatenarian' theory mainly supported by Albrecht Bethe: in fact according to this theory the nerves would derive from peripheral cell chain.

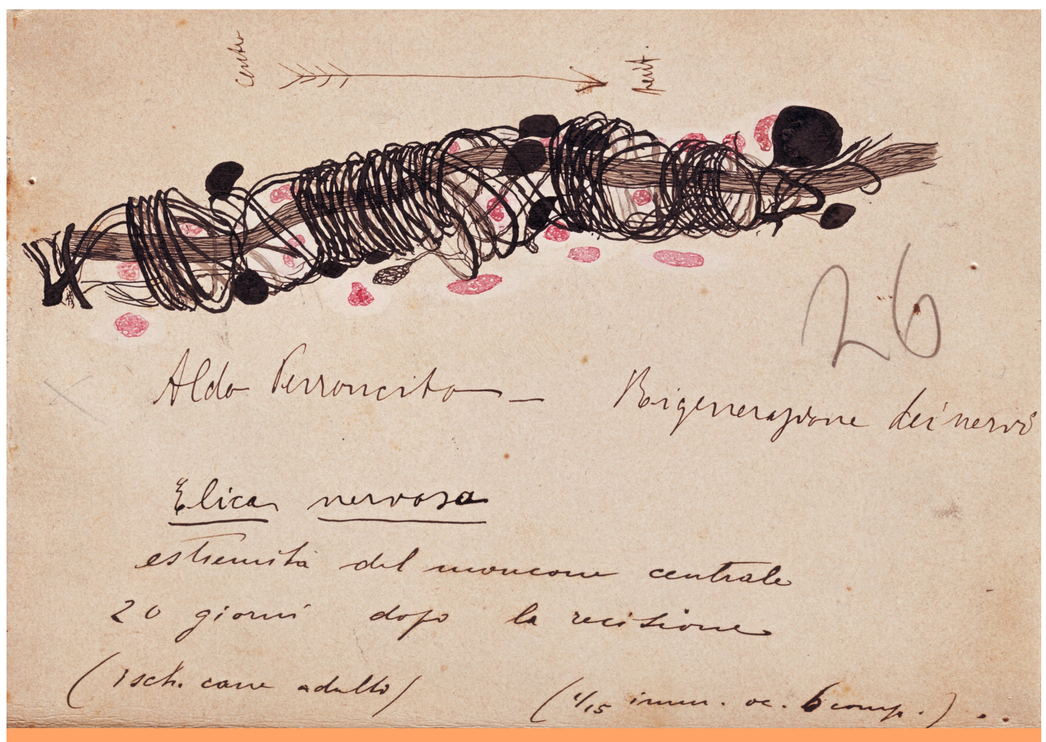


End of the central stump and the first section of the scar. From A. Perroncito, La rigenerazione dei nervi, 1907. Drawing by Aldo Perroncito.

Two hours after the experimental cut of the nerve, Perroncito noticed some morphological regeneration signs: in correspondence with the lesioned point (or immediately above it) he observed axons blowing up and the sprouting of newly formed fibres from the proximal stump, twisting themselves into spiral forms (the so called ***Perroncito spirals***). The fibers made their way down the necrotic area in various direction and, approaching the distal stump, they gradually come together in bundles, assuming a more regular course.
Finally they orient themselves along the axis of the nerve in the distal stump.
Ramón y Cajal and Georges Marinesco made similar experiments at about the same time, but Perroncito was the first to study analytically the initial phases of the regeneration process.

> ***"In honour of its discoverer, or at least of the investigator who first carefully studied it, we have called this curious phenomenon of the multiple production of nervous branches the phenomenon or apparatus of Perroncito"***

S. Ramón y Cajal Degeneration and Regeneration of the Nervous System, 1913.



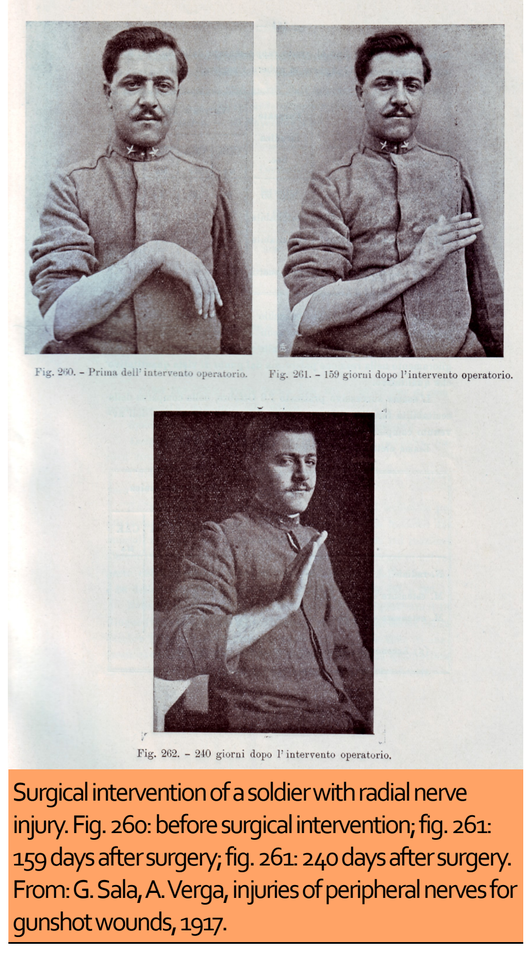
"Perroncito spirals", original drawing by Aldo Perroncito. Golgi Museum, Pavia, Italy.

Thanks to his work on regenerations, The Boston Medical School awarded Perroncito the prestigious **Warren Prize** in 1907. He then received other important honors in Italy and abroad.

Early application in clinics

Perroncito's studies have a strong theoretical and practical significance: they represent in fact fundamental research in neurobiology which directly influenced the subsequent reconstructive surgery of the peripheral nerve. By studying Perroncito conclusions, since 1910 **Giovanni Verga** in Pavia experimentally studied peripheral nerve regeneration in order to surgically restore the function of damaged nerves. He could then apply his findings on human beings while working as a surgeon at the Reserve Military Hospital settled in the Borromeo college of Pavia during the World War I. Camillo Golgi was the director of the hospital, where he had created a special neuropathological ward entrusted to his pupil **Guido Sala**, who also had studied nerve regenerations.

Sala and Verga worked together to treat peripheral nerves trauma patients, which had little chance of functional recovery before then. Their joint effort reached pioneered results of great scientific value, with important therapeutic outcomes.



Surgical intervention of a soldier with radial nerve injury. Fig. 260: before surgical intervention; fig. 261: 159 days after surgery; fig. 261: 240 days after surgery. From: G. Sala, A. Verga, injuries of peripheral nerves for gunshot wounds, 1917.