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The history of neuropathology in Italy

D. Schiffer

CNBO - Policlinico di Monza Foundation, University of Turin, Vercelli, Italy

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Abstract. The history of Italian Neuropathology begins in the XIX century with Lombroso with his studies of criminal and prostitutes, inspired by the positivism of the era, and on the brain of epileptic patients. It reached its peak at the beginning of XX century with Camillo Golgi, Nobel laureate for his impregnation of neurons and the theory of the diffuse neuronal net. Neuropathology was then cultivated in Asylums and Universities where the main subject of interest were dementias and degenerative diseases, followed by vascular and inflammatory diseases. Some Laboratories arose in the country, especially in neurological institutes and some people later began to emigrate, especially to France and Germany and then to USA in order to improve their Neuropathology. Starting in the late fifties of the XX century there was a progressive enrichment of Neuropathology with histochemistry, electron microscopy, immunohistochemistry and then molecular biology and the number of Laboratories increased consistently. As in other developed countries, Neuropathology with the enlargement of its scientific fields, began to split in sub-disciplines. It remained as a wide spectrum of knowledge, but neuropathologists were obliged to specialize in specific areas of the discipline. The continuous change of the set up of the university studies in the country in the last twenty years did not favor Neuropathology from which, moreover, some new independent disciplines originated.

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Correspondence to
D. Schiffer
CNBO – Policlinico di Monza Foundation,
University of Turin,
Via Pietro Micca, 29,
Vercelli 13100, Italy
davide.schiffer@unito.it

The systematic study of brain pathology began in Italy in the XIX century and, as in England, France and Germany, was performed in old psychiatric hospitals where it became a common practice at the end of the century. A great amount of autopsy material from clinically studied patients was collected in those institutions, and it is still traceable today. During this period, some mental hospitals became famous in Italy, and the figure of Cesare Lombroso began to acquire international recognition. Lombroso was active in Pavia starting in 1872 and later in Turin, where he established the renowned anthropological museum, beginning in 1876. His studies of brains of criminals and prostitutes led him to develop his famous anthropological conception, in line with the prevailing positivism of the century, which attributed an anatomical and phenotypical basis to human psychological profiles. At the same time, he was deeply devoted to the study of epileptic brains and described neuronal heterotopias and cortical dysplasias according to quite modern criteria. Lombroso is remembered today mainly because his research contributed to providing an anatomical basis for the human mind, describing the differences among human beings in cellular and genetic terms. His book on the identification of genius with psychic abnormality (Genius and Folly) received significant recognition. However, he believed - and this was an important trait of his mind - that finding an anatomical basis for the psychological differences in human beings was not grounds for adhering to racism by subjecting these differences to a scale of values. On the contrary, he always showed an attitude of human compassion for criminals and prostitutes, who he recognized as suffering human beings.

From mental hospitals, where dementias were the most important subjects of interest, neuropathology began to move to university institutes of pathology and then of neurology, where it covered all the fields of neurological diseases. At this time, the figure of the Nobel laureate Camillo Golgi emerged: he was well-known not only for his theory of the "diffuse neural net", in opposition to the neuron doctrine of Ramon y Cajal, but also for the discovery of the cell apparatus which today bears his name. He was also a practical pathologist, especially interested in malaria and in the description of clinico-pathological cases. Golgi developed scientific connections

Figure 1.

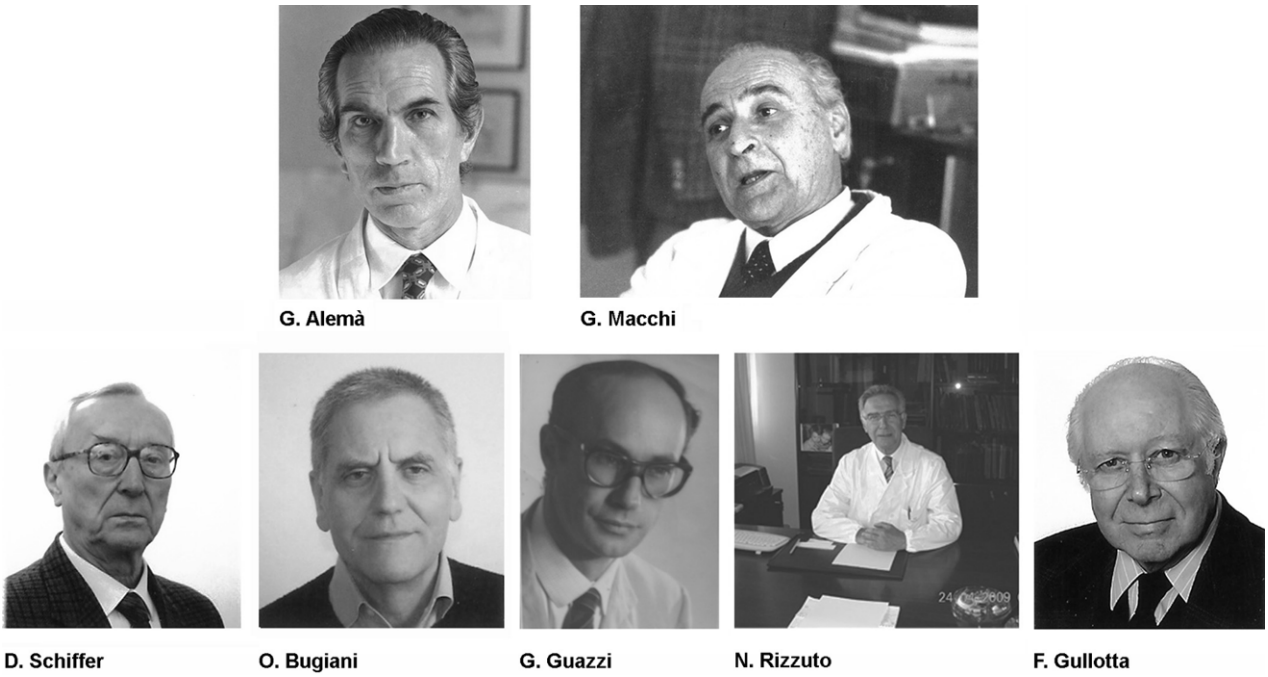

Figure 2.

with many Italian and foreign scientists, including Lombroso, from whom, however, he later parted due to disagreements about the modalities of scientific observations. Golgi was rather taken with the idea of scientific holism, which was the basis of his disagreement with Cajal, who emphasized the supremacy of neuronal individuality. Golgi shared scientific interests with eminent anatomists and clinicians of the time, such as Scarpa, Pensa, Tanzi, Lugaro, and Bizzozzero, as is well described in a book dedicated to Golgi's era [1].

At the beginning of the XX century, the neuropathological scene was dominated by

Figure 3.

disputes concerning the distinctions between tumor, vascular, inflammatory and degenerative diseases on a sheer morphological basis, even though still within the framework of Virchow's concepts of disease. Ettore Marchiafava and Amico Bignami described Marchiafava-Bignami's disease in 1907, initiating a period of commercial rivalry between French and Italian wines. In 1910 Perusini and Bonfiglio rediscovered Alzheimer's disease to which they added many characteristics. In those times, the main subject of debate was the distinction between inflammatory and degenerative diseases, with the endings -itis and -osis, and the issue of neuronal atrophy and its causes. Many publications were dedicated to the definition of so-called systemic-abiotrophic-degenerative diseases following the ideas of Oscar and Cécile Vogt, Dietrich Bonhoeffer and Ludo Van Bogaert. The influence of French and mainly German neuropathology was widely acknowledged. As time went by, cases of dementias never ceased to be published from mental hospitals, as was the case with Giovanni Fattovich from the Asylum of Trieste. Ugo Cerletti, the discoverer of electroshock, was strongly interested in neuropathology, as were numerous neurologists and psychiatrists: Ernesto Lugaro with his studies on glia ("neuroglial death") and his pupil Dino Bolsi with silver impregnation studies on oligodendroglia and microglia migration during development.

In Italy the term neuropathology has always been the subject of misunderstanding, as it has been used from the beginning to indicate neurology as distinct from psychiatry, and institutes of neuropathology were never established. Neuropathology became an academic discipline in universities only in the eighties and developed in neurological institutions through dedicated laboratories. As a matter of fact, the period between the two world wars was dominated by distinguished neurologists who were active in the field of neuropathology: Giovanni Berlucchi (Pavia), Mario Gozzano (Rome) and above all Vito Maria Buscaino (Neaples), who developed original and inventive ideas about extra-pyramidal and demyelinating diseases. In the

early thirties, a scientific dispute took place in Italian and German neurological journals between the fierce Neapolitan neurologist and several German neuropathologists. It was about the so-called "zolle di disintegrazione a grappolo" (disintegration cluster clods), which were considered characteristic of certain myelinopathies by Buscaino and an artifact according to the German opponents. Ultimately, the Germans were proven to be right, but the written debate was passionate and showed how deep the involvement of scientists from both sides in neuropathology was at that time.

In the second half of the XX century, the progressive development of neurosurgery and the establishment of neurosurgical departments in universities further stimulated the growth of neuropathological laboratories. An emerging figure in this period was that of Giorgio Macchi who moved from anatomy (Parma) to neurology (Perugia, Rome) and became one of the greatest worldwide experts on the thalamus; later he was one of the founders of the Italian Association of Neuropathology. Other distinguished neuropathologists were Giovanni Alemà (Rome), well-known for the clinico-pathologic case description, and Antonio Allegranza (Milan), a pathologist active in neuropathology in the mental Hospital of Milan-Affori.

From the fifties to the seventies the expansion of neuropathology encouraged some young people from neurology and a smaller number from pathology to emigrate in order to improve their specific knowledge: Davide Schiffer went to Neustadt/Schwarzwald, Germany, and Filippo Gullotta moved to Munich and then to Bonn and finally Münster where he became a professor of neuropathology. He rendered great help to Italian neuropathology by hosting and training many young aspiring Italian neuropathologists in his institute. Giancarlo Guazzi spent many years in Antwerp with Ludo Van Bogaert in the Bunge Institut. Nicolò Rizzuto and Orso Bugiani first went to the same institute in Antwerp and later to the USA, Guglielmo Scarlato went to Köln and Corrado Angelini and Roberto Cotrufo went to the USA. The return of skilled neuropathologists to Italy allowed the rise and growth of laboratories, some of which covered the entire spectrum of Neuropathology, such as those of Turin (Davide Schiffer), Genoa-Milan (Orso Bugiani) and Verona (Nicolò Rizzuto), or specialized in neuro-muscular diseases, such as those of Milan (Guglielmo Scarlato) and Padoa (Corrado Angelini). Many others emigrated for good, completing their academic careers abroad but remaining involved with Italian neuropathology and also indirectly helping by hosting young Italian disciples. Amico Bignami, Pier Luigi Gambetti, and Bernardino Ghetti became professors of neuropathology in Boston, Cleveland and Indianapolis, respectively. Later Francesco Scaravilli and Maria Grazia Spillantini immigrated to England where they acquired university positions of prestige. In the field of muscular diseases the name of Salvatore Di Mauro, who was a real guiding light for many young Italians in New York, must not be forgotten. In the sixties the Italian Association of Neuropathology was finally established as a section of the SIN (Italian Society of Neurology).

In the eighties throughout the world, neuropathology began to differentiate and to split into or to merge with other disciplines or sub-disciplines, such as neuro-muscular diseases, neuro-oncology, neuro-immunology. Many laboratories enriched themselves with new technical skills, such as immunohistochemistry, electron microscopy, in vitro cultures, or special skills in specific sectors. New laboratories arose serving specific clinical necessities or taking advantage of the expansion of the neurosciences, which began to appear as a wide discipline covering the entire spectrum of the nervous system, and the tremendous development of immunology, molecular biology and genetics. In Italy, neuropathology did not split into a clinical and an experimental branch, but acquired an undefined relationship with the neurosciences because many new laboratories were devoted less to classic neuropathology and more to the all-embracing field of neurosciences. The number of scholars increased, but the figure of the neuropathologist who was able to cope with every aspect of neuropathology became rather rare. Neuropathology, therefore, conceived as "the discipline which studies the organic substrates of neurological diseases at a cellular, sub-cellular and molecular level" still had a life even more than before and even in its undefined borders with neurosciences. Individual neuropathologists capable of addressing diagnostic and research problems re-

lated to tumors, inflammatory diseases, vascular diseases and neurodegeneration, however, became rarer than before. The current situation is that few large laboratories exist, rather there are more numerous and smaller specialized ones, as illustrated by a recent report [2].

In the last twenty years the organization of university studies has changed many times in Italy. The official position of neuropathology, which in the eighties had achieved the dignity of a university discipline and was included in the curriculum in the field of neurology, was questioned by general pathologists, and the Department of Education moved it from neurology to general pathology. As a result neuropathology disappeared as a university discipline and three schools of specialization were closed. The teaching of neuropathology to undergraduate students was therefore incorporated into pathology, although it was kept by neurologists in the School of Specialization in Neurology. It must be said that today, also as a consequence of many inopportune measures taken by political managers of education in the past, the situation is somewhat confused. Moreover, some disciplines, such as myopathology and neuro-immunology, split from neuropathology as a result of establishing separate associations with aging.

In this transitional period new figures came on the scene, such as Maria Teresa Giordana (tumors and degenerative diseases), GianLuigi Mancardi (demyelinating diseases), Marina Bentivoglio (neuroanatomy, degenerative diseases), Fabrizio Tagliavini (prion diseases, dementias), Francesco Monaco (prion diseases), Felice Gingaspero and Bianca Pollo (tumors), Tabaton, Giaccone (dementias), Marina Melone (neurobiology), Simonati (development), Giovanna Cenacchi (electron microscopy), Amalia Bruni (dementias) and others. Some, such as Caterina Giannini (tumors), immigrated to the USA. Many laboratories are active today in all fields of neuropathology and are located in neurological, neurosurgical and pathology institutions, both in universities and in non-university settings. Some of the latter have acquired enormous importance in the scientific life of the country today. It is impossible to name them all, but it is sufficient to say that the number of presentations at national meetings is consistently over one hundred.

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