The maestro don Gonzalo Rodríguez-Lafora

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SUMMARY
Gonzalo Rodríguez-Lafora (1886–1971) was an influential Spanish neurologist, and has been called the last of Cajal's great Spanish disciples. Of course, he is best known now for describing (in 1911) the intracytoplasmic inclusion bodies in “Lafora disease.” In total, he published ∼200 papers covering a wide range of subjects in neurology, psychiatry, and neuropathology. He made seminal contributions not only to the clinical and scientific literature but also to the training of many noted disciples who paid him due homage as a true “maestro.” Throughout his intellectual endeavors, Lafora manifested a singular purpose and intensity and a burning devotion to scientific honesty.

KEY WORDS: Lafora disease, Epilepsy, Cajal, Madrid, Spain.

BRIEF LIFE HISTORY

Gonzalo Rodríguez-Lafora (1886–1971) (Fig. 1) was born in Madrid on 25 June 1886 to the son of an officer of the Spanish Army and spent part of his childhood in Puerto Rico when it was still a Spanish colony (before the Spanish-American War of 1898). As a youth, Lafora was already a tall and distinguished man whom many compared to Don Quixote. He showed signs of childhood poliomyelitis and could be seen in some photographs with a walking stick (Moya, 1972).

Luis Valenciano Gayá, a close colleague for many years, shed light on Lafora's personal development as a child and the source of the inquisitive, diligent, and austere nature that would come to be the core of Lafora's personality:

The first question that comes to mind when analyzing Lafora is how it was possible that he developed in his childhood and puberty in a manner so splendid that it was to unfold over the course of the majority of his life. The young student Lafora, marked by his stay in Puerto Rico, immersed himself in the world of his family's colonialism. In this setting he came in touch with the emotional and chronological history of Spain, his country of ancestry, by studying the authors of the “Generation of 1898” which included Baroja, Azorín, de Gaviria, de Unamuno, de Machado, and del Maetzu. The inquisitive and fiery spirits of these great men was passed on to Lafora, who even today, within or outside of Spain, continue to be honored. (Valenciano Gayá, 1972) (authors’ translation)

Lafora studied medicine at the Central University in Madrid and received his medical degree at the age of 21. After training with Cajal, Simarro, and Achúcarro in Madrid, he then went to Berlin, Munich, and Paris for further studies in neuropsychiatry. He visited Magnan, Pierre Marie, and Dejerine in Paris; Ziehen and Oppenheim in Berlin; and in 1909, he also studied clinical psychiatry with Kraepelin and visited Alzheimer's laboratory in Munich (Garcia-Albea & Trullen, 2003). During this training period, Lafora broadened his neuropsychiatry education, with special emphasis on neuropathology but without neglecting the psychological and clinical aspects of psychiatry (Ortiz-Hidalgo, 1986). On Achúcarro’s own recommendation, Lafora was appointed as the neuropathologist for the Government Hospital for the Insane in Washington, D.C. in 1910 (Fig. 2). Lafora remained there 3 years (Garcia-Albea & Trullen, 2003), and it is during this period of time that Lafora discovered the intraneuronal bodies present in familial myoclonic epilepsy that bear his name.

In 1915, Lafora returned to Spain to work with the Nobel laureate and neurohistologist Santiago Ramón y Cajal. Cajal helped Lafora install a cerebral physiology lab in a small room on the third floor of his house in Madrid (Ortiz-Hidalgo, 1986). During this period, Lafora worked as a clinical neurologist and pathologist. Before he passed away, Lafora published a total of ∼200 papers covering a wide range of subjects in neurology, psychiatry, and neuropathology. These include original
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works on sleep, neurosyphilis, histological alterations in dementias, and studies on schizophrenia. Most of his work was published in Spanish and did not become well known outside of Spain. In addition to his published research papers, Lafora was also the author of several books, such as *Mentally abnormal children* (1917) and *The modern treatment of neurosyphilis* (1921). With the help of Nicolás Achúcarro, Lafora established the National School for Handicapped Children, although due to political problems in Spain, it only operated for 2 years (Ortiz-Hidalgo, 1986). In 1920, Lafora, Jose María Sacristán, and Ortega y Gasset founded the journal *Archivos de Neurobiología*, which published Spanish scientific research articles in neuropathology, neurobiology, and psychiatry. Lafora also established the Spanish Neuropsychiatric Association. In addition to founding two national associations in Spain, Lafora was a prominent member of the Royal Academy of Medicine in Spain, the Royal Society of Medicine of London, the Neurological Society of Paris, and the National Society of Germany. He also wrote for the Madrid daily *El Sol*. In addition to his professional life as a neurologist, pathologist, and psychiatrist, Lafora was also an impressionist painter, specializing in cubism.

As a natural complement to his allegiance to the scientific method, Lafora considered truth such a high moral value that he found Spain’s hostile religious and political climate during the Spanish Civil War intolerable. He emigrated to Mexico in 1938, where he went into private practice as a neuropsychiatrist. He also founded the Laboratorio de Estudios Médicos y Biológicos as well as the Instituto de Biomedical Research at the Universidad Nacional Autónoma of Mexico (Fuentes-Delgado, 1972). Francisco Llavero compared Lafora to a quixotic idealist:

The friend, the teacher, the biographer, or the critical scientist that wishes to get to know the real personality of Dr. Lafora will find that he was like the quixotic defenders of the truth that never folded when it came to upholding the truth. For us, for his students, for the new generations, his repudiation of that which was even slightly untruthful was absolutely exemplary. (Llavero, 1972) (authors’ translation)
At the end of World War II, Lafora returned to Spain, and became a professor at the Cajal Institute in Madrid (Ortiz-Hidalgo, 1986). Lafora passed away at the age of 85 on December 28, 1971 in Madrid.

**LAFORA DISEASE**

In 1911, in two papers published in German, Lafora described intraneuronal inclusions present in one young patient afflicted with myoclonic epilepsy (Lafora, 1911, Lafora & Glueck, 1911). In the paper with Dr. Bernhard Glueck, Lafora differentiated between the more common paramyoclonus multiplex, as first described by Friedreich in 1881, but without epilepsy and myoclonic epilepsy:

The first exact descriptions [of myoclonic epilepsy] were provided by Unverricht in Germany and Koshenikow in Russia... It is remarkable to note, that as early as 1871 Emile Gaboriau described an imbecile with myoclonic epilepsy in his novel “La corde au cou.”... 108 cases were published until 1907. In many of these cases it was found to be a familial disease affecting 3–5 members of a family at 13–20 years of age... The main symptoms are brisk, sudden, interrupted, and arhythmic jerks... The jerks can affect all muscles of the organism, including the larynx and respiratory muscles, causing abrupt expirations and nonarticulated sounds... The prognosis is even poorer compared to paramyoclonus... The sick persons lose weight dramatically, develop bulbar symptoms and difficulties with swallowing, the patients pass away in status myoclonus or epilepticus... (Lafora & Glueck, 1911) (authors' translation)

Glueck and Lafora describe the history and findings in a 17-year-old young man in detail:

Grandfather alcoholic, father epileptic and alcoholic, mother nervous... of 15 brothers 4 died of starvation... developed constant myoclonus, progressive dementia, bilateral papilledema... reported torturing pain of both eyes and deterioration of vision... decreased hearing: hears the ticking of a pocket-watch 15 cm distant to the right and 30 cm to the left ear... underwent cranial surgery in order to lower intracranial pressure, but nothing abnormal was found... underwent cranial surgery in order to lower intracranial pressure, but nothing abnormal was found... nutrition per rectum became necessary... a total of 55 seizures were recorded, most of them without aura or loss of consciousness. (Lafora & Glueck, 1911) (authors' translation)

Most notable were the autopsy findings (emphasis added):

The granule and pyramidal cells in layers 2 and 3 show striking alterations, the Nissl substance is lost, the nucleus is positioned eccentrically, the protoplasmatic appendices are lost, so that the cells appear being round. In a great number of these cells, we find amyloid-bodies, which merely fill the whole cell and compress the nucleus, so that it is semilunar shaped... The amyloid bodies are round, composed of various layers, which tend to show radial stripes... one can see needle-shaped crystals... In contrast to the expected we found the most alterations in the cortical layers 2 and 3, whereas Betz cells are mostly spared... these findings suggest some interesting considerations: are the intracellular amyloid bodies the cause or the consequence of myoclonic seizures? The lack of these bodies in Betz cells and in the ganglion cells of the anterior medullary column, the greater number in sensitive or sensory centers like the visual cortex, the quadrigeminal plate, and the dorsal horn of the medulla force us to consider, that they are NOT products of tiring after convulsions...” (Lafora & Glueck, 1911) (authors' translation)

These intracellular “amyloid bodies” were later, of course, termed “Lafora bodies”: large, polyglucosan bodies found in the perikaryon of neurons, particularly in the cerebral cortex, thalamus, globus pallidus, and substantia nigra (Fig. 3). Interestingly, Lafora noted that compared to neurons, glial cells appeared to be spared: “We would like to stress the remarkable circumstance, that glial cells showed a very sparse reaction with respect to the amyloid-degenerated gangliocytes” (Lafora, 1911) (authors' translation). “Lafora disease” would later be recognized as one of the inherited progressive myoclonus epilepsy syndromes (Minassian, 2001). One other eponym attributed to
Lafora is Lafora’s sign, picking of the nose regarded as an early sign of cerebrospinal meningitis, although as Ortiz-Hidalgo points out, this is hardly pathognomonic (Ortiz-Hidalgo, 1986).

**LAFORA’S INFLUENCE ON HIS COLLEAGUES**

Although much detail is lost regarding Lafora’s personal life history, his influential presence has been described by several of his disciples/colleagues. Francisco Llavero describes Lafora as tall, with a Nordic-like head, thin and upright like a candle, distinguished by his apparent distance from people and objects. Don Gonzalo never looked at you with the tip of his eyes. Rather, he peered at you using his forehead, even though to do so required him to turn his entire posture towards you. He was always ready to listen and never left anyone in mid-thought. He also knew nothing of punctuality. How could he, as a scientist? (Llavero, 1965) (authors’ translation)

Diego Gutierrez Gomez, a student and colleague of Lafora, described the meticulous nature with which Lafora took up his work:

His diligence in work was impressive. While sitting bedside with a patient or at his desk in the office with journals or articles, he completely forgot the passage of time. His persistence in the search of a symptom or a bibliographic datum was obsessive. Nothing else mattered, not the hour of the day nor whomever was waiting for him on the other side of his door. He was simply exhaustive, persistent, until always arriving at the bottom of every question while the rest of us tried to jump on a doubtful fact or arrive at a conclusion precipitously. He forgot even the most essential necessities of life, and only with the help of some cigarettes and a few cups of coffee persisted at his work until he was left only half-satisfied, always the victim of an inimitable perfection. (Gomez, 1972) (authors’ translation)

Lafora became an assiduous champion of the scientific method. He would never settle for anything less than statistically significant proof beyond reasonable doubt, and would certainly condemn injecting personal views and unsubstantiated claims into scientific research. Nowhere better is this exemplified than in his manner of defending the *Archives of Neurobiology*, his beloved journal cofounded by himself, Sacristán, and Ortega y Gasset. Valenciano Gayá recalls that there [was] ample proof that Lafora resisted the attempts of publishers and other academics in the field to exert their influence and alter the journal from its original philosophies that Lafora and the cofounders had laid out. It would not have been possible without his constant insistence and diligence to resist the interests of other psychiatrists to insert their personal views into the journal and destroy the mother publication. (Valenciano Gayá, 1972) (authors’ translation)

Valenciano Gayá provides a brief description of Lafora’s nonacademic personality:

The fundamental characteristic of Lafora was his curiosity of all that occurred around him, from the most microscopic to the most macroscopic. There are scientists that fixate themselves upon narrow objective analysis and characterization in order to draw conclusions, and from here they proclaim themselves erudite. Lafora’s mind, however, works in an inverse process. His constant alertness and vigilance allows him to delve into any field that may arise before him, so his knowledge is merely a necessary result of his innate curiosity. As a result, aside from medicine, he is a scholar in literature and philosophy, music and painting, ancient artifacts, and even cuisine. (Valenciano Gayá, 1972) (authors’ translation)

Throughout all of his intellectual and personal endeavors, Lafora never lost sight of his role as an educator and endeavored never to miss an opportunity to train future physicians and fledgling scientists. Lafora attended conferences and clinical sessions comprised of young doctors and scientists, many of whom were his own students. Rey Ardid, one of Lafora’s many disciples, recalls that Lafora spent his whole life teaching, and those of us that had the good fortune of working at his side were able to grasp the enormous span of knowledge that he possessed. He was a master, a great master... He was a stoic man who shunned formalisms and constantly expressed sincerity. Without us ever asking, Lafora gave us everything and he devoted himself entirely to watching us grow, progress, and become successful in our own right. (Ardid, 1972) (authors’ translation)

Perhaps it is no surprise then that Lafora was nicknamed the “Maestro” by his fellow colleagues and students. In his last days, as Valenciano Gayá recounts, Lafora’s fervor was undiminished:

His last works are filled with nostalgia, his memories of a period of maximum productivity and capacity. But alas, his faculties were betraying him, his vision was getting worse, his penmanship was deteriorating... his own body became his worst enemy. Nevertheless, he persisted. He never turned himself in. (Valenciano Gayá, 1977) (authors’ translation)

**SUMMARY**

Don Gonzalo Rodríguez Lafora was an influential figure in Spanish neurology, psychiatry, and pathology. His tremendous contributions to Spanish neurology and psychiatry both through his writings and his disciples and students are evident. His devotion to teaching and mentoring was exemplary. This retrospective deepens our perspective on the man who discovered intracytoplasmic inclusion bodies in patients with myoclonic epilepsy.

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REFERENCES


