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Gonzalo Rodríguez Lafora (1886-1971)

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ABSTRACT

Gonzalo Rodríguez Lafora, born in Madrid in 1886, was introduced to the field of neuropathology through his acquaintance with Simarro and Madinaveitia. After earning his medical degree in 1907, he continued his studies with Achúcarro and Gayarre in 1908. He moved to Berlin shortly afterwards, where he worked at La Charité with Ziehen and Oppenheim. He also studied neuropathology under Brodmann and Vogt. Somewhat later in Munich, he worked with Kraepelin and completed his training in neuropathology under Alzheimer.

It was Achúcarro who suggested hiring Lafora as head of the neuropathology department at the Government Hospital for the Insane, a position which the former had held since 1908. Alzheimer was another firm supporter of Lafora's appointment. Lafora accepted and travelled to Washington D.C. in May 1910. In 1911, while working in Washington, he studied a case of familial myoclonus epilepsy. He described its symptoms, its autosomal recessive transmission pattern, and the presence of polyglucosan bodies in cells, and he formulated the hypothesis that the disease was a congenital metabolic disorder. He published his findings in Germany and completed further investigations in cooperation with Glueck.

The German school, especially Stürmer and Alzheimer, questioned the veracity of his study at first. The authors therefore sent their prepared microscope slides to those researchers. Alfons Maria Jakob confirmed that Lafora's findings were correct and attached his name to the disease.

Although Lafora is best known for describing progressive myoclonus epilepsy, he made many other valuable contributions to clinical neurology and neuropathology, developing healthcare practices and a medical approach to sex education, education for the intellectually disabled, and issues in legal medicine.

KEYWORDS
Gonzalo Rodríguez Lafora, Lafora disease, progressive myoclonus epilepsy

The present overview is based on L. Valenciano's detailed biography of Dr Gonzalo Rodríguez Lafora.[1]

Lafora was born in Madrid in 1886 (Figure 1). When he was 4 years old he moved to San Juan, Puerto Rico; his father served in the military and had been posted to that city. Gonzalo was the second of four siblings.

After their father's death in 1892, the family moved back to Madrid, the city where the future doctor would complete his primary and university studies. At a very young age, Lafora underwent surgery to reduce the sequelae left by the bout of poliomyelitis he suffered when he was two.

He was admitted to the Faculty of Medicine in Madrid in the autumn of 1900, when he was not yet 15. He supplemented the dubious official programme by attending Simarro and Madinaveitia's laboratory, frequently missing his lectures at the Faculty as a result. Lafora, who nevertheless had an outstanding academic record, received his medical degree in 1907.

Upon launching his professional career he dropped his father's surname: he signed his documents and was known as Gonzalo R. Lafora. He completed additional training in histology and neuropathology under the guidance of Achúcarro and Gayarre. In late 1908, he was awarded a grant to study nervous system anatomy in Berlin and Munich.

He first moved to Berlin, where he worked in Ziehen's neuropsychiatry department in La Charité while studying

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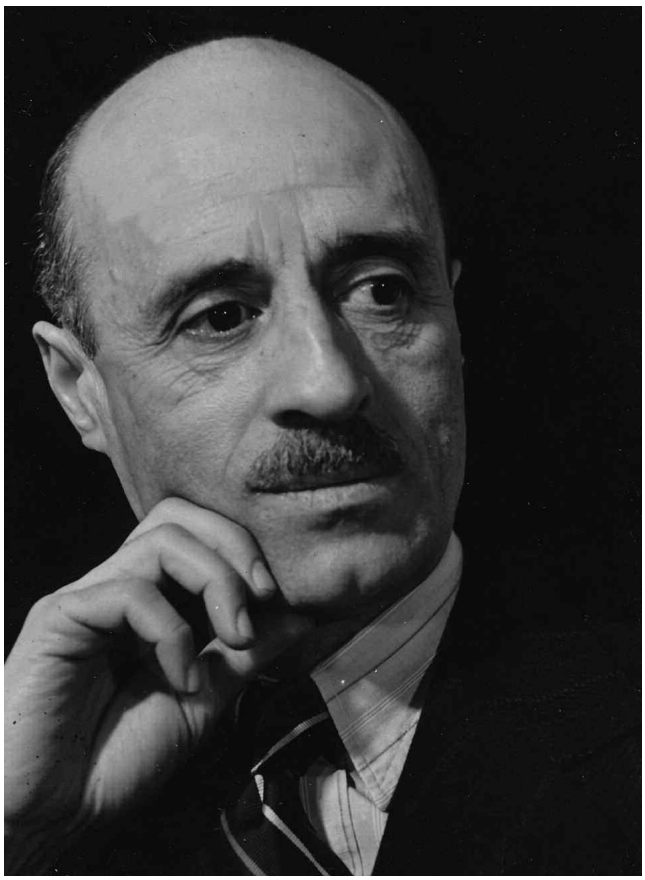


Figure 1. Gonzalo Rodríguez Lafora (1886-1971)

clinical neurology with Oppenheim as well as neuropathology under Brodmann and Vogt. Lafora translated Ziehen's treatise *Introduction to physiological psychology* into Spanish. Shortly afterwards, he moved to Munich, where he added to his knowledge of clinical psychiatry under Kraepelin and of neuropathology under Alzheimer. It is obvious that his stay in Munich was a key phase in Lafora's development as a scientist. He continued his training, working at Dejerine's and Pierre Marie's departments in Paris for short periods of time.

In November 1909, Lafora heard from his professor and friend Achúcarro, who was at the Government Hospital for the Insane in Washington, D.C. at the time. In his letter, Achúcarro asked Lafora to take over his position as head of the neuropathology department. Lafora accepted and held that position from May 1910 to late 1912.

During his stay in Washington, in 1911, he came across a case of familial myoclonus epilepsy. He described the patient's symptoms in great detail, highlighting the autosomal recessive inheritance pattern of the disease as well as its anatomical and pathological features. In his description of the case, Lafora stated that the symptoms had not previously been described and that they were caused by an inheritable congenital metabolic disorder.

He returned to Spain in late 1912. Lafora's scientific output soon caught Cajal's eye, and in 1913, Cajal created a new workplace especially for Lafora, the Laboratory of Experimental Nervous System Physiology, within his own research centre. Lafora was also named interim assistant in the psychology section of the department of legal medicine (Central University) and, shortly afterwards, vice-secretary of the National Council for Handicapped Children. As a result of his work with that council, he published *Los niños mentalmente anormales* (mentally abnormal children), the first book published in Spain addressing intellectual disability from a medical perspective. In 1916, the Board for Advanced Studies (*Junta para Ampliación de Estudios*) appointed him director of the Nervous System Physiology and Anatomy Laboratory. Unfortunately, the laboratory only remained operational for two years.

On top of his investigative work and social projects, Lafora actively practiced clinical medicine at Hospital Provincial with Achúcarro as well as a small clinic located in Calle de San Bartolomé in Madrid.

His interests in medicine and social issues led him to create the Medical-Pedagogical Institute and the Carabanchel Neuropathic Sanatorium in the 1920s. His bid for the directorship of the neurology and psychiatry departments at Hospital Provincial was eventually successful.

In 1923, the Spanish Cultural Institute appointed him as its representative of Spanish intellectual circles. He presented a series of lectures at the Faculty of Medicine in Buenos Aires, the most influential of which were titled 'Experimental research on localisation of apraxia', 'Psychoanalysis as scientific research method', and 'Myoclonias and amylaceous inclusions in the nerve cells'.

Lafora went into exile in Mexico at the outbreak of the Spanish Civil War due to his progressive and democratic views, although he was not a affiliated with any political party. He spent the next nine years in Mexico City. He was given a warm welcome by the Cárdenas government and the Mexican medical community alike: he was named an honorary member of the Mexican Society of Neurology and Psychiatry and the National Academy of Medicine, chaired by Rosendo Amor.

Lafora gave many lectures in his host country and was allowed to practise medicine freely in the private sector. He published numerous articles in a wide range of Mexican medical journals: *Archivos de Neurología y Psiquiatría de México*, *Revista de Ciencia*, and *Revista de Medicina*. He was also asked to speak at conferences in the United States: once at the University of Los Angeles in 1939, and twice in Washington D.C. at St. Elizabeths Hospital (formerly known as the Government Hospital for the Insane) in 1942 and 1946.

Lafora returned to Spain in 1947, where he had to be "politically sanitised", meaning he had to prove he was not a member of any political parties with socialist or Marxist leanings. The process took three years, but he was allowed to practise medicine during this time. In the end, the Council of Ministers concluded their examination of his file and deemed him politically acceptable. As a result, he was able to return to his duties at Hospital Provincial and he resumed his position as head of the neuropathology department at the Cajal Institute. Although he retired in 1955, he remained active in teaching and research. Dr Lafora died in 1971 at the age of 85.

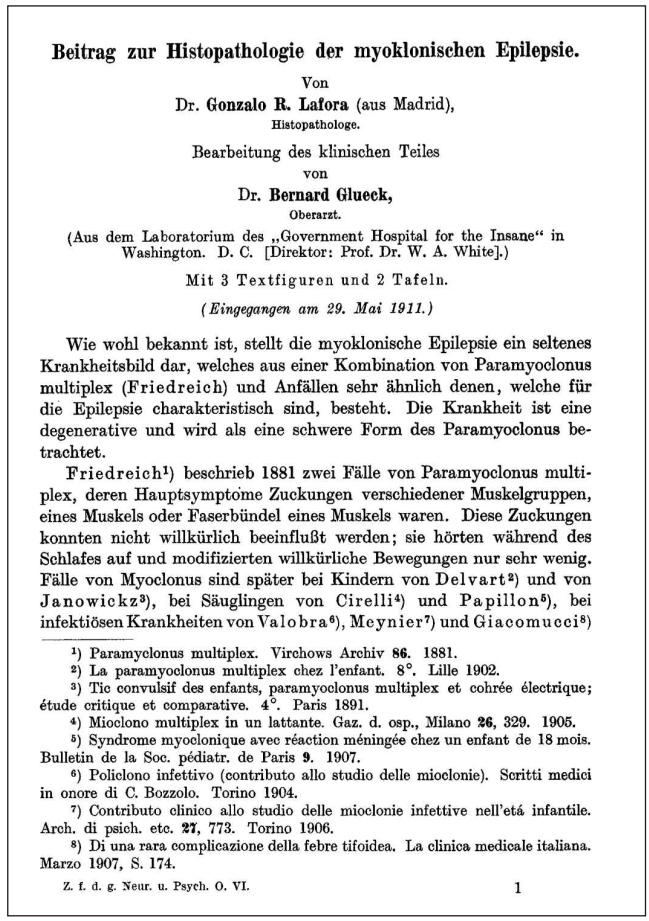
He took it upon himself to relaunch the journal *Archivos de Neurobiología*, which he himself had founded with Ortega y Gasset and Sacristán in 1919. The first issue of the journal's second incarnation was published in 1954, following a 16-year hiatus due to the vicissitudes of the Spanish Civil War and post-war period.

Lafora had been a member of the Spanish Society of Neurology (SEN) since its founding in 1949 and became the chair of the 'neurology in society' group in 1950. Between 1952 and 1958 he held the positions of second vice-president and member of the Board of Directors of the SEN. He also presented lectures in 3 biannual meetings: 'Problems in caring for neurologically disabled patients. Management strategies in society and medicine' (2nd Biannual Meeting of the SEN; Madrid, 29 and 30 June 1952); 'History of neurology in Spain', with B. Rodríguez Arias and L. Barraquer Bordas (5th Biannual Meeting of the SEN; Murcia, 22 and 23 November 1958); and 'Current clinical knowledge on viral encephalitis', with B. Rodríguez Arias (7th Biannual Meeting of the SEN; Pamplona, 16 and 17 October 1962).

Lines of research

While the bulk of Lafora's education focused on neuropathology, he developed an interest in clinical neurology during his stays in Munich and Washington. An examination of his published works shows that most of his anatomical studies included a section presenting detailed descriptions of symptoms.

His first article, '*Sur la karyorrhexis neuroglique*',[2] was published 3 years after he finished his medical degree. While in Germany in 1911, he published his study on 'amyloid' bodies in cells he discovered in a patient with familial myoclonus epilepsy while working in Washington, D.C.[3,4] Shortly after that, Glueck and Lafora expanded that study by adding the medical history, indicating the disease's autosomal recessive inheritance pattern, and hypothesising that it could be due to an inborn error of metabolism (Figure 2). The patient was a 16-year-old boy who experienced myoclonia, partial occipital seizures, generalised seizures, and progressive dementia. He died few years later due to myoclonic status



Beitrag zur Histopathologie der myoklonischen Epilepsie.

Von

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Bearbeitung des klinischen Teiles

von

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Oberarzt.

(Aus dem Laboratorium des „Government Hospital for the Insane" in Washington. D. C. [Direktor: Prof. Dr. W. A. White].)

Mit 3 Textfiguren und 2 Tafeln.

(Eingegangen am 29. Mai 1911.)

Wie wohl bekannt ist, stellt die myoklonische Epilepsie ein seltenes Krankheitsbild dar, welches aus einer Kombination von Paramyoclonus multiplex (Friedreich) und Anfällen sehr ähnlich denen, welche für die Epilepsie charakteristisch sind, besteht. Die Krankheit ist eine degenerative und wird als eine schwere Form des Paramyoclonus betrachtet.

Friedreich[1]) beschrieb 1881 zwei Fälle von Paramyoclonus multiplex, deren Hauptsymptome Zuckungen verschiedener Muskelgruppen, eines Muskels oder Faserbündel eines Muskels waren. Diese Zuckungen konnten nicht willkürlich beeinflußt werden; sie hörten während des Schlafes auf und modifizierten willkürliche Bewegungen nur sehr wenig. Fälle von Myoclonus sind später bei Kindern von Delvart[2]) und von Janowickz[3]), bei Säuglingen von Cirelli[4]) und Papillon[5]), bei infektiösen Krankheiten von Valobra[6]), Meynier[7]) und Giacomucci[8])

[1]) Paramyclonus multiplex. Virchows Archiv **86**. 1881.
[2]) La paramyoclonus multiplex chez l'enfant. 8°. Lille 1902.
[3]) Tic convulsif des enfants, paramyoclonus multiplex et cohrée électrique; étude critique et comparative. 4°. Paris 1891.
[4]) Mioclono multiplex in un lattante. Gaz. d. osp., Milano **26**, 329. 1905.
[5]) Syndrome myoclonique avec réaction méningée chez un enfant de 18 mois. Bulletin de la Soc. pédiatr. de Paris **9**. 1907.
[6]) Policlono infettivo (contributo allo studio delle mioclonie). Scritti medici in onore di C. Bozzolo. Torino 1904.
[7]) Contributo clinico allo studio delle mioclonie infettive nell'etá infantile. Arch. di psich. etc. **27**, 773. Torino 1906.
[8]) Di una rara complicazione della febre tifoidea. La clinica medicale italiana. Marzo 1907, S. 174.

Z. f. d. g. Neur. u. Psych. O. VI. 1

Figure 2. First page of the article '*Beitrag zur Histologie der myoklonischen Epilepsie' (Zeitschrift für die gesamte Neurologie und Psychiatrie)* by Lafora and Glueck.[5]

epilepticus. Lafora reported: "...presence of amyloid bodies in cells of the cerebral cortex and central grey nuclei [which are] more numerous in the visual cortex" (Figure 3). Lafora's study shows that these 'amyloid' bodies can be stained using different types of dyes, and on this basis, he stated the following: "All these reactions demonstrate the amyloid substance of these bodies. It is therefore very likely that amyloid bodies are a mere consequence of metabolic disorders of the nervous system."[5] (Figure 3)

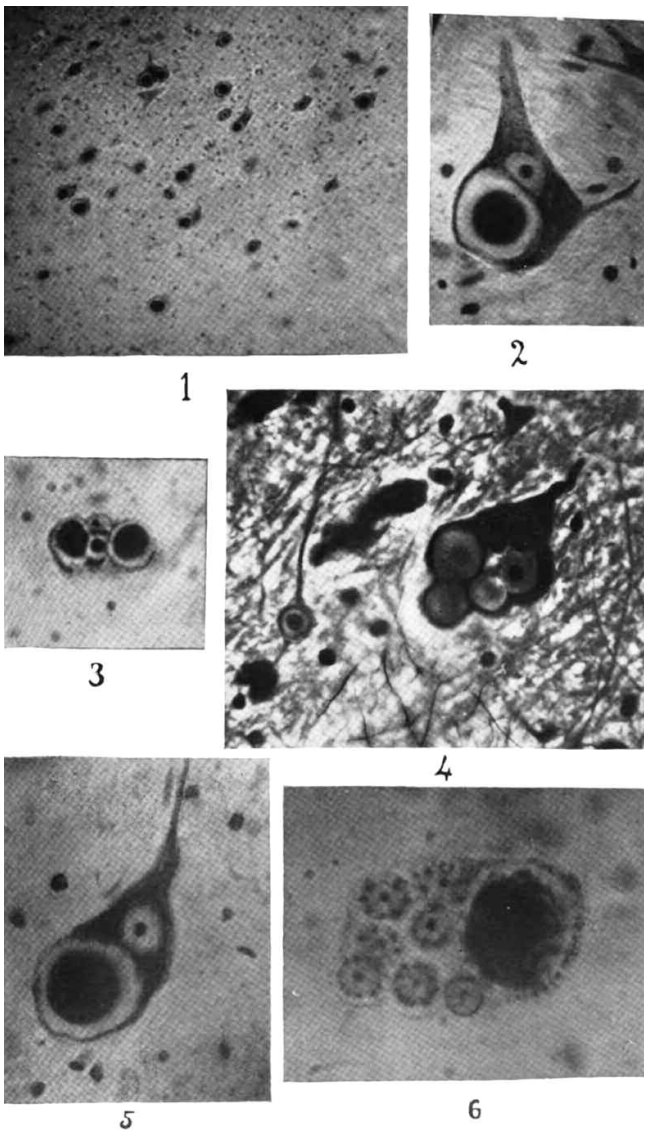

Figure 3. Anatomical pathology of myoclonic epilepsy, originally published in the article 'The presence of amyloid bodies in the protoplasm of the ganglion cells: a contribution to the study of the amyloid substance in the nervous system.'[3]

Although some researchers, especially Stürmer, initially questioned the validity of Lafora's findings, his contribution was finally recognised. Jakob highlighted the significance of Lafora's discovery and called the disorder 'Lafora disease'.

Lafora studied the clinical and anatomical correlations of the disease in great detail. He explained that, in his case and in those described by Westphal and Pilotti, intracellular 'amyloid' bodies were concomitant with myoclonia. This coincidence was not observed in the cases described by Spielmeyer, Bielschowsky, and Weimann. For this reason, Lafora stated that "...we can accept the possibility that myoclonus syndrome may depend on lesion location".[5]

Lafora's findings on myoclonus epilepsy are only an example of his many valuable contributions, such as research on clinical neurology and neuropathology, developing healthcare practices and a medical approach to sex education, education for people with intellectual disabilities, and topics in legal medicine.

Lafora studied neurosyphilis in depth and published several studies addressing juvenile general paresis. In 1917 and subsequent years, he investigated intrathecal treatment of neurosyphilis with bioiodide of mercury, bismuth, and neosalvarsan. Lafora used solutions prepared in vitro and employed an unusual therapeutic procedure: adding a drop of soluble bismuth to a recently extracted sample of CSF.

Lafora hypothesised that tabetic ataxia affected not only deep sensitivity but also the cerebellum, labyrinth, and second cranial nerves. He also postulated new theories on the aetiology of arthropathy caused by this disease. Another significant contribution was his study of the gastric or monosymptomatic forms of tabes dorsalis.

Lafora also studied forms of senile and pre-senile psychosis, including Alzheimer disease; in fact, he published the eighth case of Alzheimer disease ever documented.[6] He summarised his findings in the lecture that he presented at the first International Congress of Neuropathology, held in Rome in 1952, under the title '*Valorisation critique des découvertes histopathoIogiques dans sénilité*'. He highlighted the lesions in the small cerebral blood vessels present in the types of dementia described by Nissl and Alzheimer and the description of senile plaque formation. He also found that fibrillary degeneration in Alzheimer disease is more abundant in the parieto-occipital and the occipital regions. This loca-

tion explains the presence of aphasia, apraxia, and agnosia in patients with this disease. Lafora also highlighted works by Río-Hortega, who had described the fibrillary degeneration lesions typical of Alzheimer disease in astrocytes and ependymal cells. In one of his lectures, Lafora also presented a series of pathological concepts that often clashed with the ideas of his time.

The neuropathology of schizophrenia was another field to interest him due to the influence of Alzheimer and Nissl while he was in Munich. During his stay in Washington, D.C., he studied the brains of 60 schizophrenic patients. However, the scientific results they yielded were discouraging.

Lafora conducted neurophysiological studies in the laboratory which Cajal had arranged for him to direct. He explored the role of corpus callosum and the cause of motor and apraxic disorders in animal models. He was also interested in the physiology and pathology of sleep.

Throughout his clinical career, he published numerous case reports including myelographic studies, as well as articles on treatment and diagnosis. In 1915, Lafora described nose picking as a warning sign for cerebrospinal meningitis, which some authors later called the 'Lafora sign'.

Lafora addressed psychiatric and clinical care for mentally ill or intellectually disabled patients in many different published articles and conferences. He was also interested in mental hygiene and contributed to forensic reports both in Spain and in Mexico during his exile. His noteworthy articles on psychopathology include 'The born criminal', 'Psychopathology of crime', and 'Psychopathological study of Gregorio Cárdenas, strangler of women'.

Many doctors worked side by side with Lafora, first at the polyclinic in Calle de San Bartolomé, at Cajal's laboratory, and at Hospital Provincial. Their number included Rey Ardid, Valenciano, Obrador, and Fernández Armayor. However, these doctors were not Lafora's protegés but rather general physicians seeking to further their neurological training. This being the case, no school of neurology, strictly speaking, sprang up around Lafora.

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