

# Lafora and Trétiakoff: the naming of the inclusion bodies discovered by Lewy

Lafora e Trétiakoff: a denominação dos corpos de inclusão descobertos por Lewy

Elias Engelhardt

## ABSTRACT

Fritz Heinrich Jakob Lewy described, for the first time, in 1912, novel peculiar inclusions in neurons of certain brain nuclei in patients with Paralysis agitans, and compared his finding to the amyloid bodies described by Lafora one year before. Gonzalo Rodriguez Lafora studied one patient with Paralysis agitans, in 1913, and recognized, described, and depicted structures identical to those previously reported by Lewy. He was the first to acknowledge Lewy's finding, and also the first to name such inclusions after the discoverer – *cuerpos intracelulares de Lewy* (Lewy bodies). Konstantin Nikolaevich Trétiakoff named the inclusions he found in neurons of the substantia nigra of patients with Parkinson's disease as *corps de Lewy* (Lewy bodies), in 1919. Trétiakoff has unanimously received the credit for the eponym. However, Lafora's earlier description should make him deserving of the authorship of the eponym.

**Keywords:** Fritz Heinrich Jakob Lewy; Gonzalo Rodriguez Lafora; Konstantin Nikolaevich Trétiakoff; inclusion bodies; Lewy bodies; Paralysis agitans; Parkinson disease.

## RESUMO

Fritz Heinrich Jakob Lewy descreveu pela primeira vez, em 1912, inclusões singulares inéditas em neurônios de certos núcleos do cérebro em casos de Paralysis agitans e comparou seu achado aos corpos amilóides, como descrito por Lafora um ano antes. Gonzalo Rodriguez Lafora estudou um caso de Paralysis agitans, em 1913, e reconheceu, descreveu e representou estruturas idênticas às recentemente relatadas por Lewy. Foi o primeiro a reconhecer o achado de Lewy e também o primeiro a denominar tais inclusões segundo seu descobridor – *cuerpos intracelulares de Lewy* (corpos de Lewy). Konstantin Nikolaevich Trétiakoff designou as inclusões que encontrou em neurônios da substantia nigra em casos de doença de Parkinson de *corps de Lewy* (corpos de Lewy), em 1919. Ele recebeu o crédito pelo epônimo de modo unânime. Entretanto, a descrição anterior de Lafora deveria fazê-lo merecedor da autoria do epônimo.

**Palavras-chave:** Fritz Heinrich Jakob Lewy; Gonzalo Rodriguez Lafora; Konstantin Nikolaevich Trétiakoff; corpos de inclusão; corpos de Lewy; Paralysis agitans; doença de Parkinson.

Lewy discovered and described, in 1912, peculiar inclusions in neurons of certain nuclei of the brain in Paralysis agitans (Parkinson's disease)<sup>1</sup>. Lafora, in 1913, acknowledged Lewy's finding, and named the structure after him<sup>2,3</sup>. Trétiakoff, on investigating the pathology of the substantia nigra in Parkinson's disease<sup>4</sup>, named these inclusions after the discoverer, in 1919. Thus, these inclusions became known as Lewy bodies. It is common to credit Trétiakoff with the creation of the eponym. However, Lafora had already named the structure six years before.

Here, the research of the personalities related to this subject is outlined, aiming to authenticate the paternity of the eponym.

## THE PERSONALITIES AND THEIR RESEARCH

Fritz Heinrich Jakob Lewy (1885-1950), a German-American neuropathologist and neurologist<sup>5</sup>, identified novel inclusions

inside neurons of the vagus, Meynert's and paraventricular thalamic nuclei of the brain of patients with Paralysis agitans [Parkinson's disease]. He described his finding in the seminal 1912 publication in Lewandowsky's *Handbook of Neurology*. There he cited the 1911 paper by Lafora and Glueck among the references (Insert)<sup>1</sup>.

Gonzalo Rodriguez Lafora (1886-1971) was a Spanish neuropathologist and psychiatrist who, soon after graduating, left for the USA to replace Nicolás Achúcarro at the Mental Hospital in Washington<sup>6</sup>. There, together with Bernard Glueck, he was the first to recognize a new type of inclusion inside neurons in a case of supposed myoclonic epilepsy, the "amyloid bodies" (*Amyloidkörper*)<sup>7</sup>, published in 1911, in a renowned German journal<sup>7</sup>. The described illness was subsequently known as Lafora's disease<sup>6</sup>. Lafora reviewed the data in 1913, in a paper written in Spanish<sup>2</sup>. There he cited Lewy's 1912 publication, and stated: "Lewy was the first to find in the dorsal nucleus

Universidade Federal do Rio de Janeiro, Unidade de Neurologia Cognitiva e do Comportamento, Instituto de Neurologia/Centro para Doença de Alzheimer - Instituto de Psiquiatria, Rio de Janeiro RJ, Brasil.

**Correspondence:** Elias Engelhardt; Av Nossa Senhora de Copacabana, 749 / 708; 22050-002 Rio de Janeiro RJ, Brasil; E-mail: eliasz@centroin.net.br

**Conflict of interest:** There is no conflict of interest to declare.

Received 25 April 2017; Received in final form 16 June 2017; Accepted 04 July 2017.



of the vagus [and other nuclei] of some cases of Paralysis agitans... certain intracellular... formations, which he considered similar in their genesis to those we have described". Adding: "It is probable that there exist several classes of amylaceous bodies in the nervous system... and the intracellular bodies of Lewy (*cuerpos intracelulares de Lewy*) of Paralysis agitans have, without doubt, a genesis very similar to the intracellular amylaceous bodies described here, but diverge in their morphology and in their histochemical properties"<sup>2</sup>. Lafora also studied one case of typical Paralysis agitans [Parkinson's disease], and published, also in 1913, the results in the paper *Contribución á la histopatología de la parálisis agitante*, written in Spanish<sup>3</sup>. There, he described the inclusions in neurons of the vagus, facial, and oculomotor nuclei, and confirmed almost all Lewy's findings, despite divergence in some aspects. The paper was illustrated with figures clearly representing these formations, with shapes identical to those of Lewy's, labeling some as "Lewy's body with serpentine formations" (*cuerpo de Lewy con formaciones serpenteadas*) (depicted in his Figure 4), "elongated Lewy bodies" (*cuerpos alargados de Lewy*) (depicted in his Figure 9), among other labels<sup>3</sup>.

Konstantin Nikolaevich Tretiakoff (1892-1958), a Russian neuropathologist practicing at *La Salpêtrière*, mainly under Pierre Marie, and mentored by Georges Marinesco<sup>8</sup>, defended his doctoral thesis *Contribution a l'étude de l'anatomie pathologique du locus niger de Soemmering avec quelques déductions relatives à la pathogénie des troubles du tonus musculaire et de la maladie de Parkinson*, in 1919. He described the locus niger [substantia nigra] in his patients with typical Parkinson's disease, where he found an important loss of neurons, and mentioned the presence of intraneuronal eosinophilic inclusions, in many cases, designating them as *corps de Lewy* (Lewy bodies). The illustrations comprised two sketchy drawings of silver stained neurons, where the inclusions are poorly represented (Plate IV - Figures 9 and 10). The references included Lewy's 1912 and 1914 publications<sup>4</sup>.

## COMMENTS

Lewy described a novel inclusion, in 1912, and Lafora was the first to acknowledge Lewy's finding<sup>1,2,3</sup>, as well as being the first to name them, in 1913, as *cuerpos intracelulares de Lewy* (Lewy bodies)<sup>2,3</sup>. Trétiakoff mentioned the inclusions in his thesis<sup>4</sup>, and designated them as *corps de Lewy* (Lewy

bodies), in 1919. Trétiakoff has been unanimously credited for the eponym since then<sup>8</sup>.

Why did Trétiakoff, and not Lafora, gain paternity of the eponym? Explanations may be proposed, comparing similarities and differences between these brilliant researchers.

Trétiakoff worked in one of the most renowned European multidisciplinary neuroscientific centers, *La Salpêtrière*, surrounded by influential personalities (Pierre Marie, Babinski, Marinesco, Souques, Guillain, Foix, among others)<sup>9</sup>. Lafora worked mainly in Cajal's Institute, a flourishing world-recognized institution of neurohistology and neuropathology, surrounded by eminent researchers (besides Cajal, a Nobel prize winner, were Tello, Achúcarro, de Castro, Rio Hortega, Villaverde, Lorente de Nó, among others)<sup>6,10</sup>.

However, despite both having named the structure, and both having excellent credentials, some differential points must be underlined, as follows.

Trétiakoff was surrounded by personalities such as Marinesco, Souques, and Foix, who were interested in Parkinson's disease. Lafora, on the other hand, apparently had no researchers interested in the disease around him.

Trétiakoff wrote his thesis in French, one of the more accepted scientific languages at the time. Lafora's two papers mentioned were written in Spanish, which was poorly accepted internationally at the time. These papers were published in the *Trabajos del Laboratorio de Investigaciones Biológicas de la Universidad de Madrid*, a continuation of the *Revista Trimestral Micrográfica* founded by Cajal in 1896. This journal has changed its name and language from Spanish to French, several times since its founding. The language changes were attributed to the lack of knowledge of the Spanish language by most of the international scientific community at the time. Cajal even apologized for this in some of his papers, republished in French or German, years after having been published previously in Spanish<sup>10</sup>.

Trétiakoff's thesis, despite not being published, was cited many times in the following decades. There were no citations for Lafora's Spanish papers in the references of numerous publications related to the subject, apparently leaving Lafora ignored for almost a century.

It is possible that the exposure of their work in this field was the reason that awarded Trétiakoff with the paternity of the eponym. However, would it not be proper to give this primacy to Lafora? The historical evidence appears to point in this direction.

## References

1. Lewy FH. Paralysis agitans. 1. Pathologische Anatomie. In: Lewandowsky M, editor. *Handbuch der Neurologie*, Dritter Band, Spezielle Neurologie I. Berlin: Julius Springer; 1912. p. 920-33.
2. Lafora GR. Nuevas investigaciones sobre los cuerpos amiláceos del interior de las células nerviosas. *Trab Lab Invest Biol Univers Madrid*. 1913;11:29-42.
3. Lafora GR. Contribución á la histopatología de la parálisis agitante. *Trab Lab Invest Biol Univers Madrid*. 1913;11:43-54.
4. Tretiakoff C. Contribution a l'étude de l'anatomie pathologique du Locus Niger de Soemmering avec quelques déductions relative à la pathogénie des troubles du tonus musculaire et de la maladie de Parkinson. These de Paris, n. 293, 1919.

5. Holdorff B, Rodrigues e Silva AM, Dodel R. Centenary of Lewy bodies (1912-2012). J Neural Transm (Vienna). 2013;120(4):509-16. <https://doi.org/10.1007/s00702-013-0984-2>
6. De Carlos JA, Pedraza M. Santiago Ramón y Cajal: the Cajal Institute and the Spanish Histological School. Anat Rec (Hoboken). 2014;297(10):1785-802. <https://doi.org/10.1002/ar.23019>
7. Lafora GR, Glueck B. Beitrag zur Histopathologie der myoklonischen Epilepsie. Z Gesamte Neurol Psychiatr. 1911;6(1):1-14. <https://doi.org/10.1007/BF02863929>
8. Lees AJ, Selikhova M, Andrade LA, Duyckaerts C. The black stuff and Konstantin Nikolaevich Tretiakoff. Mov Disord. 2008;23(6):777-83. <https://doi.org/10.1002/mds.21855>
9. Broussolle E, Poirier J, Clarac F, Barbara J-G. Figures and institutions of the neurological sciences in Paris From 1800 to 1950. Part III: Neurology. Rev Neurol (Paris). 2012;168(4):301-20. <https://doi.org/10.1016/j.neurol.2011.10.006>
10. Gamundí A, Timoner G, Nicolau MC, Rial RV, Esteban S, Langa MA. [The Work of Santiago Ramón Y Cajal in the Revista Trimestral Micrográfica] (Trabajos Del Laboratorio De Investigaciones Biológicas). Rev Neurol. 2005;40(11):696-700. Spanish.

## APPENDIX

Lewy's findings published in 1912 in Lewandowsky's Handbook of Neurology (excerpts)<sup>1</sup>.

Lewy's seminal description in the vagus and Meynert's nuclei, in selected excerpts:

"These changes are characterized as inclusions, which partly in their genesis, apparently have to do with those depicted by Lafora, and by him assigned, not in a proper way as I believe, to the structure of the *Corpora amylacea*. They present, accordingly, some reactions of the *Corpora amylacea*, but are smaller, irregularly shaped, and do not have their typical glassy, onionskin-like appearance" (*Diese Veränderungen charakterisieren sich als Einlagerungen, die z.T. in ihrer Genese mit den von Lafora abgebildeten und von ihm, wie ich glaube nicht ganz mit Recht, den Corpora amylacea zugerechneten Gebilden zu tun zu haben scheinen. Sie geben demgemäss zunächst einige Reaktionen der Corpora amylacea, sind aber kleiner, unregelmässiger geformt, haben auch nicht das typische glasige, zwiebelschalen-artige Aussehen derselben (Taf. VIII, Abb. 1 u. 7).*

And then:

"On characteristic images it is possible to see, with Mann's stain, spherical, elongated, and serpiginous forms that stain bright red (Pl. VIII, Figs. 2-5)" (*An charakteristischen Bildern sehen wir mit Mannscher Färbung in einer blauen Plasmamasse Kugel-, strang- und schlangenförmige Gebilde, die sich leuchtend rot färben (Taf. VIII, Abb. 2-5).*