

# The scientific output of Pío del Río Hortega (1882-1945) and the laboratory of the Residencia de Estudiantes

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## ABSTRACT

This study analyses the scientific output of Pío del Río Hortega (1882-1945). A review was conducted of the content of his publications, articles he wrote in collaboration with other authors, and the profiles of the publications in which his work appeared.

Analysing the scientific oeuvre of Del Río Hortega necessarily also requires analysis of the laboratory at the Residencia de Estudiantes. It was at this laboratory that he developed his histological school, beginning in October 1920, and where his scientific work gained clear international recognition. To that end, this article offers an overview of Del Río Hortega's Spanish and foreign students at the laboratory of the Residencia de Estudiantes, shedding light on the relevance of the histological school he created.

This study is based on a detailed review of various primary sources (Del Río Hortega's doctoral thesis from the Universidad Central, annual reports of the Junta de Ampliación de Estudios [Board for Study Extensions], his autobiography, his correspondence, and the original documents of his publications), which are contrasted with the extensive literature on Del Río Hortega.

Publications and their contents are contextualised with information on Del Río Hortega's life, taking into account the immediate and lasting impact of his findings and the influence of the successive republication of English translations of his work (the majority of his work was originally printed in Spanish).

The sheer volume of publications, and especially their quality and the originality of his findings, solidify Del Río Hortega's status as one of the greatest ever microscopists in the medical sciences, becoming, after Cajal, the most distinguished member of what is universally recognised today as the Spanish histological school.

## KEYWORDS

Del Río Hortega, students, Residencia de Estudiantes, scientific publications, Spanish histological school

## Introduction

A century ago, in late October 1920, Pío del Río Hortega began his scientific activity at the laboratory of the Residencia de Estudiantes, belonging to the Junta de Ampliación de Estudios (Board for Study Extensions, JAE). It was at this laboratory that he developed his histological school, and where his scientific work gained clear international recognition.<sup>1,2</sup>

The laboratory at the Residencia de Estudiantes emerged from the nervous system histopathology laboratory, directed by Nicolás Achúcarro until his early death in 1918, and functioned as an annex to Cajal's Laboratorio de Investigaciones Biológicas. From the very beginning, Achúcarro's laboratory was conceived as a place to train young researchers, who would later receive grants from the JAE to complete their training abroad.<sup>3-5</sup>

The laboratory's move to the Residencia de Estudiantes in October 1920 was the solution proposed by Cajal to the well-known, unfortunate rift<sup>6</sup> that formed between him and Del Río Hortega, which the latter bitterly recalls in his autobiography.<sup>3</sup> At Del Río Hortega's request, the laboratory at the Residencia de Estudiantes was soon renamed the Laboratorio de Histología Normal y Patológica (Laboratory of Normal and Pathological Histology), as he sought to broaden the scope of its activities.<sup>3,7</sup>

It was at this laboratory, which largely inherited the work of Nicolás Achúcarro and, indirectly, the mastery of the Valencian Luis Simarro,<sup>8</sup> that Del Río Hortega formed a group of direct disciples in a situation of clear spatial and scientific separation from Cajal. It was also here that Del Río Hortega's work achieved its greatest impact in the scientific community, as demonstrated by the number of foreign visitors to the laboratory. This impact persists today, as demonstrated by the publication of new editions of works by Del Río Hortega, many of which have been translated into English,<sup>9-14</sup> with the great majority of his works having been written in Spanish.

In spite of this impact, as well as the vast literature on Del Río Hortega,<sup>15</sup> many specific details of his scientific output, with respect to the media in which his work appeared and the members of his histological school, are not well established. Without doubt, some of these problems were favoured by the complete disintegration of the Spanish Histological School and the scarce diffusion of the figure of Del Río Hortega and his students after the Spanish Civil War.

This study is based on a detailed review of the scientific work of Del Río Hortega, analysing the content of his publications, the works he produced through collaborations, the profiles of the publications in which his works appeared, and their scientific impact. It also presents an overview of the students who attended his laboratory at the Residencia de Estudiantes. The latter subject demonstrates the importance of the histological school that took shape there around the figure of Del Río Hortega.

Data were gathered from a review of various sources, including Del Río Hortega's doctoral thesis at the Universidad Central,<sup>16</sup> the annual reports of the JAE,<sup>17</sup> his own autobiography,<sup>3,18</sup> his correspondence,<sup>7,18</sup> made available digitally by the Spanish Society of Neurology,<sup>19,20</sup> various monographs on Del Río Hortega,<sup>1,21-23</sup> and the

original scientific works published by him and by several of his main disciples. Though his students merit detailed analysis, this should be the subject of a subsequent study, given the number of them and the great importance of several.

## Development

### *The scientific output of Del Río Hortega at the laboratory of the Residencia de Estudiantes*

A century after Del Río Hortega began working at the laboratory at the Residencia de Estudiantes, many of his disciples and their subsequent activity are not widely known. However, we do know that Del Río Hortega was able, in a short space of time, to bring together a significant number of collaborators at this laboratory: according to the annual reports of the JAE,<sup>17</sup> more than 60 Spanish collaborators and 30 foreign disciples spent time working at Del Río Hortega's laboratory.

The documentary evidence gathered was used to establish an incomplete summary of the disciples, both Spanish (Table 1) and foreign (Table 2), who worked at the laboratory to learn the techniques and procedures developed by Del Río Hortega, who at the time was becoming one of the best microscopists in the medical sciences internationally.

Some crucial aspects of Del Río Hortega's histological work began and developed in the three years prior to 1920. However, it was in 1920, at the Residencia de Estudiantes, that Del Río Hortega established and assembled the microscopy findings that definitively enabled him to describe the morphology and the origin and functions of two new nervous system cells; the laboratory became an international focus of scientific attention.

Scientific activity at the laboratory of the Residencia de Estudiantes was conducted from October 1920 until the Spanish Civil War. In 1937, on the instructions of Del Río Hortega, the laboratory was left under the directorship of his disciple Manuel López Enríquez, who had worked as a laboratory assistant and who ten years earlier had identified the two new cell types described by his master in the retina and optic pathway.<sup>24,25</sup> Due to records of the purge of staff of the JAE,<sup>26</sup> it is also known that, after the end of the war, the laboratory's staff included a total of six people, only two of whom were not purged within the following months.

Therefore, microscopy research was only conducted at the laboratory for 17 years. Research conducted in this period may be divided into two distinct phases: in the first, from 1920 to 1928, the work was focused on neurohistology, whereas in the second phase, from 1928 until the Spanish Civil War, there was a progressive move towards oncological research. This was due in part to the fact that Del Río Hortega was appointed as head of the experimental cancer research laboratory of the National Oncological Institute in 1928, and as its director three years later.<sup>27</sup>

Work at the laboratory ended with the Civil War. As occurred with the direct students of Cajal,<sup>28</sup> the immediate effect of the conflict was a process of total disintegration of Del Río Hortega's school of disciples.

Several disciples, as well as Del Río Hortega himself, were forced into exile; others were marginalised or in situations of self-exile within Spain, often dedicating their work to activities other than microscopy research (Table 1). The remaining disciples who did not face reprisals continued their research in the following years in conditions of scarcity and shortage, in a country that was socially and economically devastated and internationally isolated but which, at the same time, hoped to rebuild itself from the established power, breaking from everything related to its previous roots.

In this view of Del Río Hortega and the members of his school, it should be noted that, as López Piñero reminds us,<sup>1,29</sup> the figure and scientific work of Del Río Hortega have not been mythicised in Spain in the same way as those of Cajal. Some studies neglect to address not only the origins of his wonderful oeuvre, but also the roles and personalities of the different groups that arose from his work and formed the so-called Spanish histological school.<sup>1,29</sup>

At the time of its publication, the scientific work of Del Río Hortega did not achieve great popularity or dissemination among the general population in Spain, particularly when compared to Cajal's research. The mythicisation of Cajal, who had died in 1934, persisted or even intensified after the Civil War,<sup>30</sup> particularly from 1945, often with attempts to obscure any potentially inconvenient aspects of his thought, which was understood to be hegemonic at all times.

After the Civil War, knowledge of the scientific figure of Del Río Hortega, who was in exile, was soon limited

to the exclusive, restricted sphere of histology and histopathology, and did not translate to changes in the framework of public institutions; this situation persisted until the transition to democracy.

Two decades ago, López Piñero<sup>1</sup> noted, with foresight, that the time had come to analyse the importance of the work of Del Río Hortega and his disciples from solid documentary foundations, as well as the influence of their microscopy work on universal scientific knowledge.

In line with this, the following sections offer a summary of the publications of Del Río Hortega and of several of his students, contextualised against the biography of their master.

#### *The publications of Del Río Hortega*

Del Río Hortega's scientific oeuvre is very extensive. It is significant both for the sheer number of articles and for the technical quality and originality of his work. His scientific output extends chronologically from his student days to the time of his death in 1945, although new editions and translations of many of his works continued to appear thereafter.

Quantifying his scientific publications is a challenging task, for several reasons. Firstly, of the huge number of studies he conducted, many were disseminated not only through journals, but also as abstracts presented to different scientific societies, which also disseminated them in their own journals and gazettes.

As is also the case with Cajal, many of his studies appeared in several media or publications to broaden the reach of the reported results. The cited publications also include examples of microscopy contributions that were reported to scientific societies but were never printed as scientific articles.

These factors explain the differences observed between lists of the scientific publications of Del Río Hortega. For instance, his disciple Ortiz Picón<sup>31</sup> places the number of studies published at 200. In turn, López Piñero<sup>1</sup> lists a total of 126 publications from between 1909 and 1945, whereas the collection of his correspondence<sup>7</sup> mentions 144 works, with a similar number (140) in the list compiled by González Santander.<sup>21</sup>

With respect to his earliest publications, Del Río Hortega, still a medical student, published his first article<sup>7</sup> in 1903, a study describing clinical and histopathological findings from a patient with a tumour of the neck. It was published

**Table 1.** Disciples of Del Río Hortega at the laboratory of the Residencia de Estudiantes

| Name  | Time at the Laboratory      | Grant from the JAE                       | Subsequent profession   |
|---|-----------------------------|--|---|
| <b>A. Abaunza Fernández</b>                 | 1929-1930                   | 1930-31 (Germany, Austria)               | Psychiatry (*exile in Mexico)                                     |
| <b>R. Alberca Lorente</b> (1903-1967)       | 1922-1924 (s); 1924-1930    | 1926 (France, England)                   | Psychiatry in Murcia, Uni. Ch. in Valencia                        |
| <b>J.M. Aldama Truchuelo</b> (1900-1970)    | 1924-1930                   | 1928 (Austria)                           | Psychiatry  |
| <b>S. Alvarado Fernández</b> (1897-1981)    | 1922-1924                   | 1921-1923 (Germany)                      | Biologist, naturalist, professor                                  |
| <b>M. Álvarez Cascos</b> (1896-1988)        | 1922-1930                   | 1933 (Germany, Austria, France)          | Dermatology   |
| <b>J. Bejarano Lozano</b> (1893-1965)       | 1922-1924; 1933-1934        | ≠1930 (France)                           | Dermatology (*exile in Mexico)                                    |
| <b>J. Bofill Deulofeu</b> (1905-1995)       | 1926-1930                   | 1930-31 (Germany)                        | Histopathology, physiology (*exile in Venezuela)                  |
| <b>M. Cárdenas Pupo</b> (?-1963)            | 1931-1932                   |  | Neuropathology, internal medicine (Cuba, USA)                     |
| <b>C. Collado Aguirre</b>                   | 1920-1926                   |  | Neuropathology placement in Boston, which he rejected             |
| <b>I. Costero Tudanca</b> (1903-1979)       | 1922(s)-1934                | 1929-1930 (Germany)                      | Uni. Ch. of histology and anatomical pathology (*exile in Mexico) |
| <b>E. Escardo Peinador</b> (1907-?)         | 1933-1934                   | 1931 (Austria, Germany)                  | Psychiatry  |
| <b>A. Gallego Canel</b> (1879-1930)         | 1922-1930                   |  | Uni. Ch. of veterinary histology and anatomical pathology         |
| <b>A. Gallego García</b> (?-1937)           | 1929-1934                   |  | Histology†  |
| <b>F. Jiménez Asúa</b> (1892-1973)          | 1920-1928                   | 1917-1919 (Italy, Switzerland)           | Uni. Ch. of histology and haematology (*exile in Argentina)       |
| <b>A. Ley Gracia</b> (1908-1975)            | 1924-1926                   | ≠1931-1934 (Estonia, USA)                | Neurosurgery  |
| <b>M. López Enríquez</b> (1890-1968)        | 1920-1921 and 1924-1937     | 1915 and 1929 (Switzerland, Netherlands) | Ophthalmology#  |
| <b>A. Llombart Rodríguez</b> (1905-1997)    | 1922-1924 (s) and 1924-1930 | 1929 and 1930-1932 (France, Germany)     | Uni. Ch. of histology and anatomical pathology                    |
| <b>L. Mier Jadraque</b>                     | 1935                        | 1935 (England)                           | Ophthalmology, professor  |
| <b>A. Muniesa Belenguer</b> (1905-1936)     | 1926-1930                   |  | Medical analysis†   |
| <b>J.M. Muniesa Belenguer</b> (1895-1936)   | 1929-1930                   |  | Medical analysis†   |
| <b>J.M. Navaz y Sanz</b> (1897-1975)        | 1924-1928                   | 1927 (France)                            | Oceanography  |
| <b>D. Nieto Gómez</b> (1908-1985)           | 1929-1932                   | 1932-1933 (Germany)                      | Neuropathology, psychiatry (*exile in Mexico)                     |
| <b>S. Obrador Alcalde</b> (1911-1978)       | 1933                        | 1934-1935 (England)                      | Neurosurgery (*exile in Mexico until 1945)                        |
| <b>A. Peña Pineda</b> (1904-1971)           | 1922-1924 (s)               | 1931 (Germany)                           | Uni. Ch. of urology   |
| <b>J.M. Ortíz Picón</b> (1903-1995)         | 1929-32                     | 1932-1934 (Germany)                      | Uni. Ch. of histology and anatomical pathology                    |
| <b>M. Pérez Lista</b> (1901-1988)           | 1924-34                     | 1931 (Germany)                           | Pathology   |
| <b>J.M. Sacristán Gutiérrez</b> (1887-1957) | 1933-1934                   | 1912-1914 (Germany)                      | Neuropsychiatry#  |
| <b>E. Roda Pérez</b> (1906-1983)            | 1924-1934                   | 1933-34 (Germany)                        | Internal medicine (*exile in Peru)                                |
| <b>J. Sánchez Lucas</b> (1901-1969)         | 1924-1928 and 1931-1932     | 1926-29 (Germany)                        | Uni. Ch. of histology and anatomical pathology                    |
| <b>J. Sanchis Banús</b> (1893-1932)         | 1924-1926                   | 1917 (Germany, France)                   | Psychiatry  |
| <b>P. Toledo Moreno</b> (1893-1960)         | 1929-1930                   | 1930 (Germany)                           | Medical analysis, pathology                                       |
| <b>J. Torre Blanco</b> (1895-1987)          | 1922-1926                   | ≠(France, Switzerland, Germany)          | Gynaecology (*exile in Mexico)                                    |
| <b>R. Vara López</b> (1904-1982)            | 1920-1926                   | 1933-1934 (Germany)                      | Uni. Ch. surgery  |
| <b>E. Vázquez López</b> (1907-1951)         | 1929-1934                   | 1933-1934 (Germany)                      | Neuropathology (*exile in England)                                |

NOTE: A further 30 disciples of Del Río Hortega at the Laboratory of Normal and Pathological Histology could not be clearly identified, as only one surname is cited in the annual reports of the JAE<sup>12</sup>; this is not the case for those who received grants from the JAE.<sup>4</sup>

JAE: Junta para la Ampliación de Estudios (Board for Study Extensions); Uni. Ch.: university chair.

(s) placement at the laboratory as a student; †: died during the Civil War; #: purged after the Civil War; \*: exile abroad after the Civil War; ≠: placement abroad with no evidence of funding from the JAE

**Table 2.** Foreign visitors to the laboratory of the Residencia de Estudiantes (Laboratory of Normal and Pathological Histology)

| Name  | Institution/country of origin                 | Years spent at the laboratory | Subsequent profession/institution   |
|---|---|-------------------------------|---|
| <b>Alpers</b> , Bernard Jacob (1900-1981)     | Harvard Medical School (USA)                  | 1928-1930                     | Neurosurgery; University of Pennsylvania/Jefferson Medical College Philadelphia |
| <b>Brusco</b> , Gabriel                       | Argentina                                     | 1924-1928                     |   |
| <b>Cárdenas</b> , Pupo Mario (?-1963)         | Universidad de La Habana (Cuba)               | 1931-1924                     | Neuropathology/internal medicine; Hospital América Arias (Havana)/Miami         |
| <b>Da Fano</b> , Corrado Donato (1879-1927)   | University of Pavia (Italy)                   | 1922-1924                     | Histology/neuropathology; King's College London                                 |
| <b>D'Ancona</b> , Humberto (1896-1964)        | University of Rome (Italy)                    | 1922-1924                     | Naturalist/zoologist; University of Padua                                       |
| <b>Dubois</b>                                 | France  | 1933-1934                     |   |
| <b>Erausquin</b> , Jorge                      | University of Buenos Aires (Argentina)        | 1933-1934                     | Professor of histology; University of Buenos Aires                              |
| <b>Estable</b> , Clemente (1894-1976)         | University of Montevideo (Uruguay)            | 1922-1924                     | Neurobiology/histology; Faculty of Medicine, Montevideo                         |
| <b>Kubie</b> , Lawrence S (1896-1973)         | Johns Hopkins University (USA)                | 1924-1926                     | Neurology and psychiatry; New York  |
| <b>Laidlaw</b> , George Frederick (1871-1937) | New York Medical College (USA)                | 1926-1928                     |   |
| <b>León Blanco</b> , Pedro M. (1899-1958)     | University of Havana (Cuba)                   | 1931-1932                     | Director, pathology dept., Hospital Clínico Joaquín Albarrán (Havana)           |
| <b>Llinás Olarte</b> , Juan Pablo (1903-1982) | National University of Colombia               | 1933-1934                     | Chair of pathology; National University of Colombia                             |
| <b>Mir</b> , León                             | Cuba  | 1928-1930                     | Assistant at Hospital de la Pitié-Salpêtrière                                   |
| <b>Moyano</b>                                 | Argentina                                     | 1928-1932                     |   |
| <b>Neuhaus</b> , Karl                         | Munich Institute of Pathology (Germany)       | 1931-1932                     |   |
| <b>Norcross</b> , Nathan Crosby               | Harvard University (USA)                      | 1933-1934                     | Neurosurgery; University of California Medical School                           |
| <b>Ower</b> , John James (1885-1962)          | University of Alberta (Canada)                | 1933-1934                     | Professor and head of pathology, University of Alberta                          |
| <b>Penfield</b> , Wilder G. (1891-1976)       | John Hopkins University (USA)                 | 1922-1924                     | Neurosurgery; McGill University, Montreal                                       |
| <b>Ramírez Corría</b> , Carlos M. (1903-1977) | University of Havana (Cuba)                   | 1933-1934                     | Neurosurgery; Hospital Universitario General Calixto García (Havana)            |
| <b>Ros Grangel</b> , Arturo R.                | University of Havana (Cuba)                   | 1933-1934                     |   |
| <b>Santos</b>                                 | Manila (Philippines)                          | 1931-1932                     |   |
| <b>Stevenson</b> , Lewis D.                   | New York (USA)                                | 1924-1926                     | Neuropathology; Cornell Medical College (New York)                              |
| <b>Torreblanca</b> , Eugenio Díaz             | UCLA Los Angeles (USA)                        | 1931-1932                     | University Hospital of Munich; rural physician (Guadalajara)                    |
| <b>Turchini</b> , Jean (1894-1979)            | University of Montpellier (France)            | 1922-1924                     | Chair of histology; Montpellier Faculty of Medicine                             |
| <b>Villela</b> , Eudoro Libânio (1907-2001)   | Federal University of Rio de Janeiro (Brazil) | 1931-1932                     | National Cancer Institute and Fundación Oswaldo Cruz; businessman/banker        |
| <b>Weiss Harvey</b> , Pedro (1893-1985)       | National University of San Marcos (Perú)      | 1922-1924                     | Chair of anatomical pathology; director of the Institute of Pathology, Lima     |

**NOTE:** The years reported for visitors' time at the Laboratory of Normal and Pathological Histology are those for which the annual reports of the Board for Study Extensions report these placements. Some mentions of these visitors are very brief,<sup>15</sup> often mentioning only one surname or the country or institution of origin, preventing correct identification of the person in question.

in the *Boletín del Ateneo de Internos*, a fortnightly journal published by the athenaeum of interns of the Faculty of Medicine of Valladolid, which was established in 1898 and remained active for only six years.<sup>32</sup>

The next published results from his studies in Valladolid were linked to the preparation of his doctoral thesis (Figure 1), which he defended in Madrid in 1909,<sup>16</sup> entitled “Etiología y anatomía patológica de los tumores del encéfalo” (Aetiology and anatomical pathology of brain tumours). The thesis was based on the study of brain tumours in patients from the clinics of the medical faculty and of the provincial psychiatric hospital of Valladolid; the results were published in 1911-1912 in three articles in *La Clínica Castellana*,<sup>7,22,23</sup> a journal founded in 1910 by a group of physicians from the city, which was published without interruption until 1930. These articles, new editions of which were published in the early 1990s,<sup>22</sup> demonstrate Del Río Hortega’s interest in lesions and tumours of the brain.

In 1912, Del Río Hortega transferred to Madrid to work at the laboratory of Nicolás Achúcarro; from 1913 to 1915, he received grants to work in Paris, Berlin, and London. His scientific activity in this period centred around a range of histological subjects; without yet showing a clear preference for neurohistology, he displayed great precision in his microscopy observations, great skills with staining techniques, and significant talent as a draughtsman.<sup>31,33,34</sup> In 1913, he published a study of the histological structure of the ovary<sup>35</sup> and another analysing smooth muscle tissue<sup>36</sup>; in the latter article, he noted that some techniques were performed at M. Prenant’s laboratory in Paris.

With the outbreak of the First World War, Del Río Hortega returned to Achúcarro’s laboratory. There, he focused on the tannin–ammoniacal silver oxide technique, described by his master in 1911,<sup>37</sup> and published some of his results from work performed in Paris and Berlin. In 1915, he published only one article,<sup>38</sup> coinciding with the outbreak of the First World War and the completion of his placements in France, Germany, and later England.

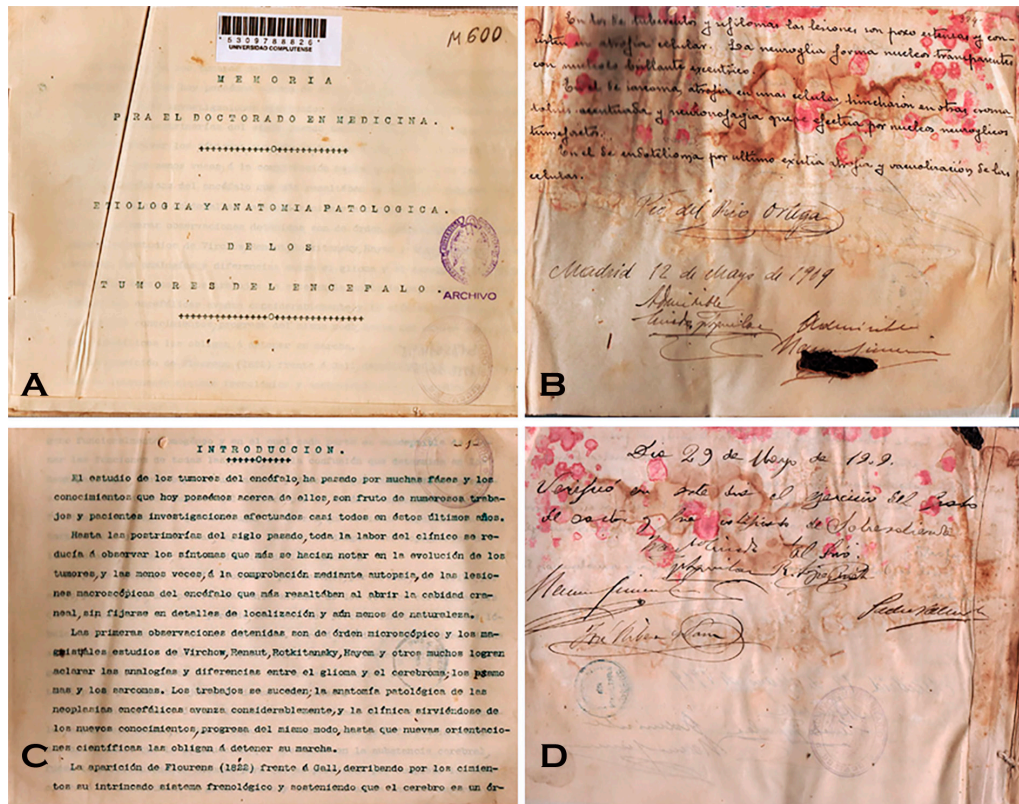
The period from 1916-1917 until 1927 was the beginning of what López Piñero<sup>1</sup> characterises as “Del Río Hortega’s great creative period.” During this stage of his scientific career, he dedicated his work mainly to studying the neuroglia, as well as analysing the structure of the pineal gland.

During this period, Del Río Hortega described four modifications or variants<sup>39-41</sup> of Achúcarro’s tannin–ammoniacal silver method, with a specific application for each. Through these modifications, he demonstrated that he was the histologist with the best understanding and mastery of Achúcarro’s method and all the opportunities it offered, to the extent that it was suggested that the figures of Achúcarro and Del Río Hortega seemed in reality to be a single person incarnated in two successive lives.<sup>42</sup> Of these works, the most important is probably the one addressing the centrosome of neurons and neuroglial cells,<sup>43</sup> using the first variant of Achúcarro’s method. His disciple Ortiz Picón points to this study as the clearest demonstration of Del Río Hortega’s technical prowess, analysing and producing gouache drawings of an organelle whose dimensions are at the limit of the resolution of optical microscopy.<sup>33</sup>

With Achúcarro’s death in April 1918, Del Río Hortega was made provisional director of the laboratory of histopathology. A month earlier, he reported a new technique, staining samples with an ammoniacal solution of silver carbonate.<sup>44</sup> This technique became the most powerful instrument he used in his subsequent research.

In November 1918, he used the technique to describe the significance of the neuroglial cells known as amoeboid cells.<sup>45</sup> This began the path to his discovery of a new type of cell, named microglia, which was first reported in 1919 in a series of four communications to the Spanish Society of Biology (SEB, for its Spanish initials) and which he referred to as a “third element of the nervous system”; new editions and English translations of these communications have since been published.<sup>12</sup> In 1920, nine months before moving to the laboratory at the Residencia de Estudiantes, he compiled his results (Figure 2) for an article in Cajal’s journal, asserting that “the microglia is capable, particularly, of phagocytising the products of disintegration of the nervous system” and that “having begun phagocytic activity, it changes shape and forms rod-like cells and granuloadipose bodies.”<sup>46</sup> This article, which was also republished the same year in *Archivos de Neurobiología*, offered a preliminary idea of what was known at the time as the interfascicular glia of the white matter.<sup>47</sup>

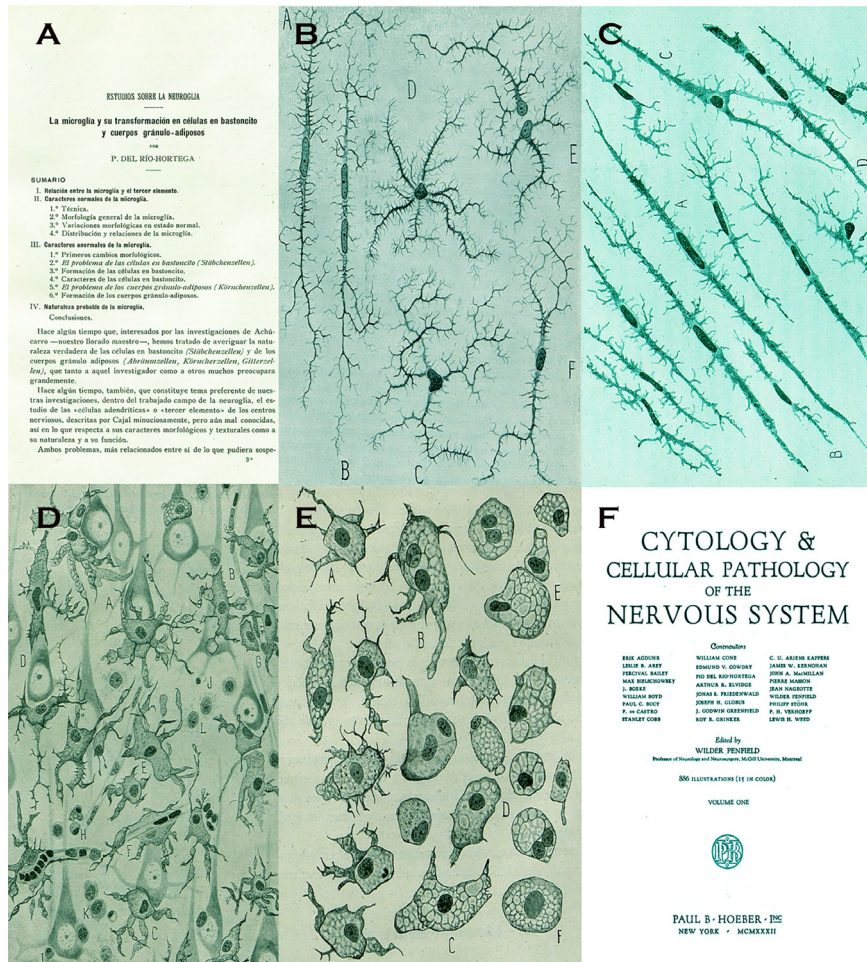
In 1921, now at the laboratory at the Residencia de Estudiantes, Del Río Hortega made his second great contribution: the description of oligodendroglia or sparsely branched glial cells,<sup>48</sup> and establishing the



**Figure 1.** The current state of Pío del Río Hortega's doctoral thesis, entitled "Etiología y anatomía patológica de los tumores del encéfalo" (Aetiology and anatomical pathology of brain tumours), which is preserved at the Complutense University of Madrid's Marqués de Valdecilla historical library. The thesis was typed on loose sheets in a landscape orientation (A,C), although the conclusions are handwritten and signed by the author (B); curiously, he signs his surname Ortega, without the H. The thesis was admitted to the repository of the Universidad Central on 12 May 1909 (C), and he defended it on 29 May, receiving a distinction (D) (Biblioteca Histórica Marqués de Valdecilla, signature no. M600; Universidad Complutense de Madrid, Madrid). The signatures on the evaluation report include those of José Ribera y Sans (chair of clinical surgery) and Ramón López Prieto, of Valladolid (tenured assistant professor in anatomy), a fellow student and old friend of Del Río Hortega.

similarity between this new cell type and Schwann cells.<sup>49</sup> Ninety years later, new editions and English translations of both contributions have been published.<sup>9,10</sup> His findings about the oligodendroglia were also compiled in 1928, in an extensive, 117-page monograph<sup>50</sup> with 79 figures (Figure 3), including many photomicrographs; he described the four varieties of cells and reaffirmed their functional and morphological similarities with Schwann cells. This text was also translated into English in 2013. The monograph, entitled *Third contribution to the morphological knowledge and functional interpretation of the oligodendroglia*, is, in the words of Ortiz Picón, the most original and best executed of all his master's works.<sup>33</sup>

Among Del Río Hortega's great microscopy contributions, we should also note his work on the pineal gland. Between 1916 and 1932, Del Río Hortega published a total of five articles on the histological structure of the pineal gland, which together represented the most complete study to date of this structure. In 1922, he characterised pineal parenchymal cells, identifying what are today known as pinealocytes and establishing that the gland includes "only two kinds of cells, parenchymal cells and neuroglial cells." He submitted the study for publication in a book honouring Cajal in 1922, and in Cajal's journal in 1923.<sup>51</sup> Six years later, he published his analysis of the neuroglial component of the pineal gland, this time in a book published in honour of Gregorio Marañón, as



**Figure 2.** An article published by Del Río Hortega<sup>47</sup> in Cajal’s journal in 1920 (A), months before his transfer to the laboratory at the Residencia de Estudiantes, addressing the microglia (B) and its transformation into rod-like cells (C) and granulo-adipose bodies (D,E), compiling his findings on what was known until then as the “third element” of the nervous system. These findings had previously been presented as four communications to the Spanish Society of Biology. This highly significant publication is frequently cited in the scientific literature, particularly citing Del Río Hortega’s English-language article on the microglia from 1932 (F), in volume II of the book edited by his disciple Wilder Penfield,<sup>55</sup> whose front page is shown.

well as in the journal *Archivos de Neurobiología*,<sup>52</sup> where he also reported his findings on the secretory activity of the pineal gland,<sup>53</sup> a function that had previously been proposed by his master Achúcarro.<sup>54</sup>

These studies demonstrate the value of the silver carbonate technique and its multiple variants as the most relevant technical contribution to the study of the pineal gland in the first half of the 20th century; his results were frequently cited, as (like his study of the microglia)

they were translated into English and published in 1932 in a three-volume treatise edited by his student Wilder Penfield (Figure 2).<sup>55</sup>(p481-534,635-703) In this treatise, Del Río Hortega definitively concludes that “the pineal is a gland in which the secretory phenomenon is located in parenchymal cells, without ruling out secondary secretory activity by the neuroglial cells”; thus, it is “[...] an endocrine gland hormonally connected with the testes, ovaries, thyroid, pituitary, and adrenal glands. Its activity regulates, reduces, or inhibits general somatic





**Figure 3.** A monograph (117 pages with 79 figures, including some photomicrographs) published in 1928 in *Memorias de la Sociedad Española de Historia Natural*,<sup>50</sup> in which Del Río Hortega compiles his findings on the oligodendroglia, describing its four variants and reasserting its functional and morphological similarities with Schwann cells. This was one of Del Río Hortega's most significant publications; a new edition and English translation was recently published.<sup>78</sup>

development and, in particular, the development of the sex organs"; these statements were eventually confirmed 27 years later with the isolation of the indolamine hormone melatonin.<sup>54</sup>

From 1928, with Del Río Hortega's incorporation into the National Cancer Institute, his scientific activity and publications took a new direction. He conducted this activity in parallel with his work at the Residencia

de Estudiantes, and several of his disciples (Abelardo Gallego, Isaac Costero, Ortiz Picón, Pérez Lista) also transferred to the Institute as collaborators. From that time, research work shifted towards the study of cancer, and the main journal in which he published was *Archivos Españoles de Oncología* (AEO). In this journal, he published two extensive monographs, one on meningeal tumours<sup>56</sup> and one on gliomas and paragliomas,<sup>57</sup> which served as the basis for a monumental lecture ("The microscopic anatomy of tumours of the central and peripheral nervous system") to the International Cancer Congress in 1933; the lecture was translated into English 30 years later.<sup>14</sup> In addition to these two great monographs, he and his disciples published a number of other studies in AEO, addressing oncological subjects unrelated to the nervous system.<sup>58,59</sup>

Later, between 1935 and 1938, his scientific output dramatically decreased, with only one article published in 1937, in *Cuadernos de la Casa de la Cultura de Valencia*,<sup>60</sup> at a time when the city of Valencia was the capital of the Spanish republic. This text, written shortly before his exile and republished two decades ago by López Piñero,<sup>1</sup> presents Del Río Hortega's thought on science and the use of language, taking a position clearly opposed to that of Cajal.

Del Río Hortega took exile, initially in Paris and subsequently in Oxford and finally, from August 1940, in Argentina, where he published his final works, some of which represent an attempt to systematically organise his oeuvre.<sup>1</sup> In 1945, the year of his death, he published two works in Argentina<sup>1,7,21</sup>: one in the journal *Archivos de Histología Normal y Patológica*, which he had founded himself three years earlier, and the other in a monograph published in Buenos Aires, addressing the nomenclature and classification of nervous system tumours. He also systematised all the modifications he had made to the silver carbonate technique, which he disseminated in an article published in four submissions,<sup>61</sup> the last of which was published several months before his death.

During his five years in exile in Argentina, and especially after the foundation of the laboratory of the Spanish Cultural Institution of Buenos Aires, he also published several works on tumours of the nervous system (neuroblastoma, angioglioma, neuroglioma, schwannoma, neurofibroma, and tumours of the optic nerve and chiasm), although the most important and original studies in this period were those addressing

the so-called peripheral neuroglia, the sympathetic<sup>62</sup> and sensory ganglia,<sup>63</sup> in which he demonstrates the neuroglial nature of the satellite cells ensheathing neurons of the ganglia. He had previously conducted preliminary research on these questions in Spain with his student Ortiz Picón,<sup>33</sup> which he completed with his Argentinian disciples: as we shall see, many works were published in collaboration with these authors.

#### *The collaborative publications of Del Río Hortega*

A striking feature of all available lists of Del Río Hortega's publications<sup>1,7,21,23,33</sup> is the fact that he appears as the sole author of the majority of these works; only 20 (approximately 13%) of all his publications were written in collaboration with any of his disciples. Of these 20 collaborative articles, all but two are signed by Del Río Hortega as the lead author, demonstrating the importance of his personal role in all of these works. With respect to this exclusive authorship, we may define three different periods. The first encompasses the time from his student days to the beginning of his activities at the laboratory of the Residencia de Estudiantes (ie, 1903-1920); in this period, Del Río Hortega published 43 articles, working practically alone, with only two of these being written with a collaborator.

The first of these collaborative works is an extensive article that appeared in 1917, addressing the histological structure of sponges,<sup>64</sup> which Del Río Hortega signed alongside the naturalist Francisco Ferrer Hernández (Figure 4).<sup>65</sup> The authors reported a histological study of a series of sponges preserved in alcohol from the Museum of Natural History, provided by Ferrer, which Del Río Hortega studied with three of his variants of Achúcarro's staining method, often referred to as the Achúcarro-Del Río Hortega method. This was Del Río Hortega's first article in the gazette of the Spanish Society of Natural History (RSEHN, for its Spanish initials), which he had recently joined; years later, after being forbidden from publishing in Cajal's journal, the gazette would become one of his main outlets for publishing his microscopy findings.

The second collaborative work is particularly meaningful. The study, published in 1919,<sup>66</sup> identified cytoplasmic inclusion bodies in rabies, which had been described 15 years earlier by Adelchi Negri, an assistant pathologist at Golgi's laboratory. The authors used Del Río Hortega's first modification of Achúcarro's method (Figure 5),

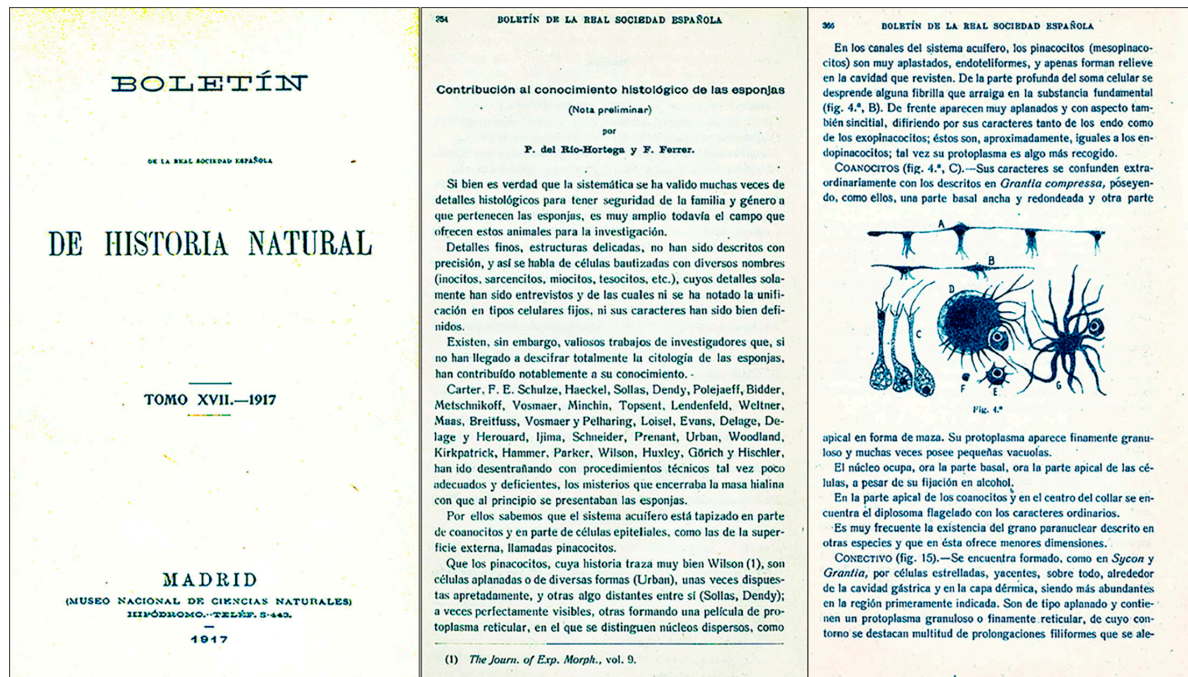
demonstrating its greater efficacy as compared to other procedures.

This study is one of the two collaborative articles in which Del Río Hortega does not appear as the lead author. The first signature is that of Cajal's son Jorge Ramón Fañanás, although Del Río Hortega is known to have been fully responsible for the work.<sup>3</sup> In his autobiography, Del Río Hortega<sup>3</sup> refers to this publication with bitterness and regret, explaining that he included Cajal's son as the lead author in order to ingratiate himself with him, despite the fact that Del Río Hortega had drafted the entire article himself, and that the second part of the work, which they had mutually agreed would be conducted by Ramón Fañanás, was never completed.

There is a degree of uncertainty regarding this article. It was published in the *Boletín de la Sociedad Española de Biología* in 1919.<sup>66</sup> González Santander<sup>21</sup> notes that it also appeared in *Trabajos del Laboratorio de Investigaciones Biológicas*, Cajal's journal, although a search of articles published in the journal did not confirm this. It has also been suggested<sup>17,23</sup> that the article was also published in 1918 in the journal *Laboratorio*; it has also not been possible to locate this journal. Several other authors<sup>1,7,23</sup> list the publication date as 1918. The study was indeed presented to the SEB on 3 May 1918. However, the print publication appeared in volume 8 of the society's *Boletín* in 1919 (Figure 5).<sup>66</sup> It was also referred to in the 1917 annual report of the JAE,<sup>17(p80)</sup> which lists Del Río Hortega as the lead author and Jorge Ramón Fañanás as the second author. The entry in the 1917 report of the JAE was probably written by Del Río Hortega himself, expressing his most private thoughts: at the time (with Achúcarro being sick), he was taking on numerous administrative duties at the laboratory, and the study in question was probably already underway by 1917.

This situation of shared authorship, with Del Río Hortega not appearing as the lead author, was not repeated until December 1930, when he published an article in collaboration with the surgeon José Goyanes Capdevila, the first director of the National Cancer Institute, in *Archivos Españoles de Oncología*. The circumstances surrounding the study on Negri bodies was probably a factor in Del Río Hortega's decision always to sign his articles as the lead author.

The second phase of Del Río Hortega's scientific activities, which merits consideration in the analysis of his collaborative works, comprises the period from 1920,

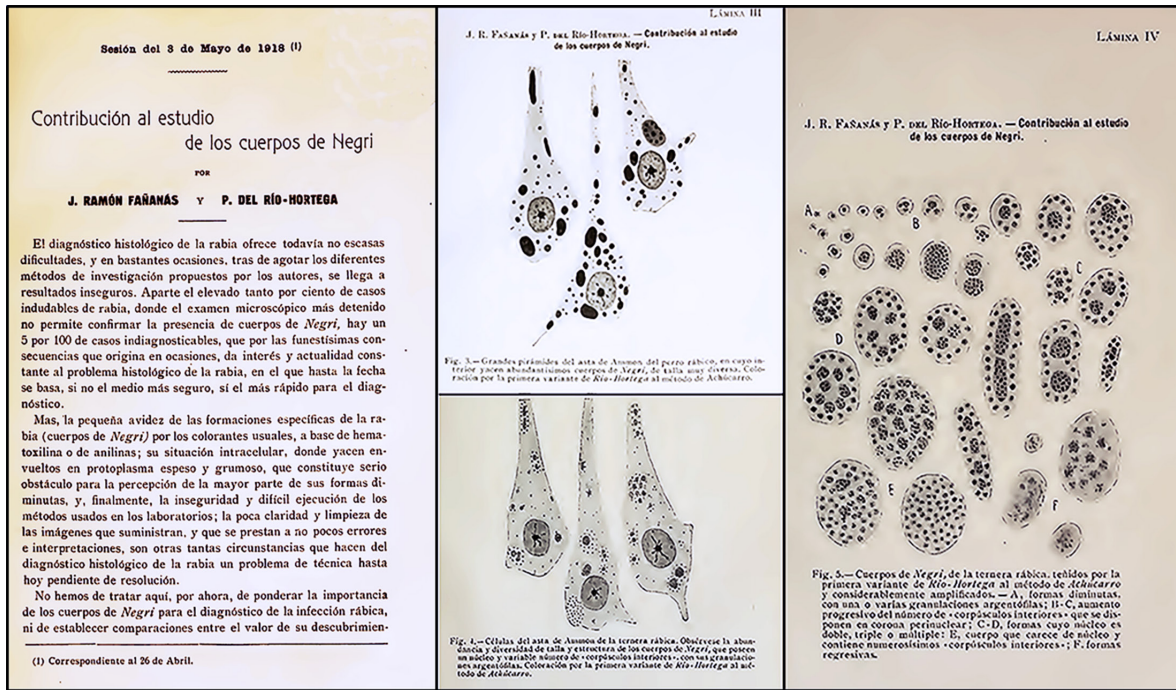


**Figure 4.** The article published in 1917 by Del Río Hortega and Francisco Ferrer Hernández in the *Boletín de la Sociedad Española de Historia Natural*, addressing the histology of sponges.<sup>64</sup> The article reports a study conducted with sponges preserved for a long time in alcohol at the Museum of Natural History, using Del Río Hortega's three variants of Achúcarro's tannin–ammoniacal silver method. This was Del Río Hortega's first collaborative study. His co-author, the naturalist Francisco Ferrer Hernández, was a distinguished expert in sponges, who identified a considerable number of new species at the Museum of Natural History.<sup>65</sup>

the year he joined the laboratory at the Residencia de Estudiantes, until the end of the Spanish Civil War in 1939, by which time he was working at Oxford. In this period, he published a total of 77 studies. The number of collaborative works was somewhat greater, with a total of 11; Del Río Hortega appears as the lead author in all cases. In the final years of this period (1935–1938), as noted above, Del Río Hortega published only one article, in *Cuadernos de la Casa de la Cultura de Valencia*.<sup>60</sup> Similarly, in 1939 he published only two articles, one of which was published in English in *The Lancet* and addressed the microglia<sup>67</sup>; this article reproduced a lecture given on 2 November 1938 at the Nuffield Institute of the Radcliffe Infirmary in Oxford. In the article, Del Río Hortega mentions his esteemed disciple Felipe Jiménez Asúa, noting that, in the light of the demonstrated role

of the microglia in erythrocytrophagosis, it would be plausible to suggest that the same cells may represent Aschoff's reticulo-endothelial system in the central nervous system.

The 11 collaborative works produced in this period (1920–1939) were developed with some of his disciples and collaborators from the laboratory of the Residencia de Estudiantes and at the National Cancer Institute. These included five articles published in collaboration with Felipe Jiménez Asúa, four with Isaac Costero Tudanca, one with Manuel Álvarez Cascos, one with José Goyanes Capdevila, and one with Wilder Penfield; the latter was published in English in the *Bulletin of the John Hopkins Hospital* in 1927, and analysed the participation of the neuroglia and microglia in cerebral cicatrix.<sup>68</sup>



**Figure 5.** A study produced by Del Río Hortega in collaboration with Cajal's son Jorge Ramón Fañanás, presented to the Spanish Society of Biology in May 1918 and published in the *Boletín de la Sociedad Española de Biología* in 1919.<sup>66</sup> This was the first collaborative article in which Del Río Hortega does not appear as the lead author, despite the fact that, as described in his autobiography,<sup>3</sup> the entire text was his own work. In the study (nine pages with four gouache drawings by Del Río Hortega), he identifies Negri bodies in rabies using the first variant of the Achúcarro-Del Río Hortega tannin-ammoniacal silver method, comparing the results against those previously obtained with other methods (the methods developed by Mann, Lentz, and Romanowsky; Heidenhain's iron-haematoxylin method, Bielschowsky staining).

The third period of Del Río Hortega's scientific work, with respect to collaborative studies, lasted just five years (1940-1945), and corresponds to his exile in Argentina: on 3 August 1940, he set sail from Liverpool for Buenos Aires, where he remained in exile until his death on 1 June 1945.<sup>1,7</sup>

In 1940, two short works by Del Río Hortega were published in England, both in English and printed in the *Proceedings of the Royal Society of Medicine*, reproducing his contribution in a session of the society on tumours of the optic nerve and chiasm,<sup>69</sup> and another article in *The Lancet*, reporting and synthesising three of his lectures at the Nuffield Institute.<sup>70</sup>

Including these two brief reviews published before he left England, a total of 32 works were published in this period, including seven in collaboration with his new

disciples in Argentina. Therefore, this was the period in which he produced the greatest number of collaborative works: of the seven, three were written in collaboration with Julián Prado, three with Julián Prado and Moisés Polack, and one with Manuel Ojea and León Zimman; most of these studies were published in the journal *Archivos de Histología Normal y Patológica*, founded in 1942. Once more, Del Río Hortega appears as the lead author in all of these studies.

#### Outlets for Del Río Hortega's publications

The journals in which Del Río Hortega published his research (Figure 6) are worth reviewing, as they shed light on many of the circumstances in which his scientific activity took place.

The main outlet for his work was the *Boletín de la Sociedad Española de Biología*, the official publication of the SEB. This society and its journal were founded in early 1911, with Ramón y Cajal as president. The society's membership was small (only 69 members, according to the *Boletín* of 1915, and a total of 78 in 1932).<sup>21</sup> This society was the natural extension of the laboratories and research centres inspired by Cajal,<sup>3,21</sup> and its *Boletín* was their means of disseminating the discoveries of the Cajal school.

Though irregularly, the sessions of the SEB were held at six o'clock in the evening on the last Friday of each month. They initially took place at the San Carlos Faculty of Medicine, and later at the College of Physicians of Madrid. Participants at the sessions presented short scientific communications, which had to be submitted in writing to the secretary of the society. The first secretary was Francisco Tello (1911), who was succeeded by Gonzalo Rodríguez Lafora (1913), Domingo Sánchez (1915) and, from 1919, Del Río Hortega. In 1932, the *Boletín* was renamed *Revista Española de Biología*; its first honorary president was Ramón y Cajal, the editor-in-chief was Del Río Hortega and the editorial secretaries were two of his disciples, Isaac Costero Tudanca and Juan Manuel Ortiz Picón. This gives an idea of the influence of Del Río Hortega and his students over the development of the journal. *Revista Española de Biología* was only active for five years, until 1936, at which time it was under the patronage of the RSEHN, as the SEB had been dissolved in May 1932, two years prior to the death of Cajal; the society's 78 members were incorporated into the RSEHN.<sup>21</sup>

The second outlet for Del Río Hortega's work, by number of publications, was the *Boletín de la Real Sociedad Española de Historia Natural (Bol. R. Soc. Esp. Hist. Nat.)*. The RSEHN was the leading scientific institution in Spain, with a solid organisational structure including delegated sections in various regional capitals. The society was founded in 1871, and created numerous publications from 1872, among them the aforementioned *Bol. R. Soc. Esp. Hist. Nat.*, which first appeared in 1903 and became an important medium for the dissemination of the works of Del Río Hortega, especially from 1921.

In 1917, Del Río Hortega joined the RSEHN, publishing an article the same year in *Bol. R. Soc. Esp. Hist. Nat.*, the text mentioned above on the histology of sponges.<sup>64</sup> However, it was in the period from 1921 to 1927 that he

published the most articles in this journal, surely because he had been forbidden from publishing in Cajal's own journal. Between 1917 and 1929, Del Río Hortega published a total of 20 articles in the journal; he became vice-president of the RSEHN in 1925 and president in 1926, though he only stayed in this position for a year, in accordance with the society's statutes.<sup>21</sup> From 1932, when the SEB merged with the RSEHN, the *Revista Española de Biología* was founded, as mentioned above, with Del Río Hortega as editor-in-chief and two of his disciples as editorial secretaries.

In turn, Cajal's journal, *Trabajos del Laboratorio de Investigaciones Biológicas (TLIB)*, was founded in 1901 as a successor to the *Revista Trimestral Micrográfica*, becoming the main medium through which Cajal disseminated his own research and that of his school.<sup>71</sup> This was indisputably the main publication of the Spanish histological school. The journal's editorial and manufacturing quality were outstanding, particularly compared to other publications of the day. Del Río Hortega published a total of 19 studies in the journal between 1913 and 1923.

His last article in Cajal's journal, written in French,<sup>53</sup> was published in 1923, after his transfer to the laboratory at the Residencia de Estudiantes. As mentioned above, it was an extensive study on the parenchymal component of the pineal gland, and was also submitted for a book honouring Cajal.

After 1923, neither Del Río Hortega nor any of his direct disciples published any further publications in Cajal's journal, with the only exception being a work published by Wilder Penfield in *TLIB* in 1924, analysing the microglia in a glioma he brought from the New York Presbyterian Hospital.<sup>72</sup> In that study, Penfield used the silver carbonate technique, and defended the hypotheses of his master. Regarding the question of how the study came to be published in Cajal's journal, a typewritten letter by Penfield himself, of significant historical value, was provided by Sixto Obrador; it is included in the Horacio Oliva documentary archive of the Spanish Society of Anatomical Pathology.<sup>73</sup> Penfield visited Cajal on 1 May 1924. He was not accompanied by Del Río Hortega, who charged Jiménez Asúa with introducing Penfield to the *Maestro*. However, Penfield's article was based on work conducted at the laboratory of the Residencia de Estudiantes, and Del Río Hortega was aware of the article being translated into French and

accepted by Cajal for publication in *TLIB*. Most probably, the fact of Penfield's being a foreign scientist who had come to Spain to learn Del Río Hortega's techniques played a role in Cajal's decision to accept the article.

Essentially, Cajal's journal was published in French between 1923 and 1937, as had also intermittently been the case in the past, under the name *Travaux de Laboratoire de Recherches Biologiques de l'Université de Madrid*. Del Río Hortega always took issue with this decision, calling it a "glaring mistake" of the *Maestro* to consent to his journal's publication in a foreign language.<sup>3,74</sup>

In 1937, publication of *TLIB* was interrupted due to the Spanish Civil War; in its last two years, after the death of Cajal, it was directed by Francisco Tello. The last volume of *TLIB* from 1937 is particularly relevant; it concludes with a study by Fernando de Castro,<sup>75</sup> whose introduction notes that the article was drafted in Madrid in the autumn of 1937, explaining "the fact that the references included in the bibliography are probably incomplete."

As mentioned above, Del Río Hortega never published in *TLIB* after 1923, with his article on the histology of the pineal gland<sup>51</sup> being the last to appear in Cajal's journal. It appears to be the case, as noted by González Santander,<sup>21</sup> that Cajal allowed the publication of that article because it had been included in a book written by various disciples to honour him on the occasion of his retirement as a university chair in 1922.

At that time, publishing in Cajal's journal had several significant advantages. The quality of the printing and the richness of the images were far superior to those of the *Bol. R. Soc. Esp. Hist. Nat.* and especially the *Boletín de la Sociedad Española de Biología*. Dissemination of the journal through exchange with other publications and Spanish and foreign libraries and institutions was also superior, unquestionably due to the influence of Cajal's standing as a scientist. In any case, lacking the option of publishing in Cajal's journal,<sup>3</sup> Del Río Hortega published the majority of his work in *Bol. R. Soc. Esp. Hist. Nat.* and *Archivos de Neurobiología*, in which several of his most important works on the microglia and oligodendroglia appeared.

*Archivos de Neurobiología* was founded in 1920 by Gonzalo Rodríguez Lafora, Sacristán, and Ortega y Gasset. Following the scientific renewal started by Achúcarro, the founders of the journal sought to

establish close ties between the clinical and laboratory settings.<sup>21</sup> It was published without interruption from 1920 to 1936, and was published once more from 1954, again due to the efforts of Lafora, who had returned from exile. From its early days, Del Río Hortega showed his support for the development of the journal, appearing as a collaborator in its first issue, although he notes in his autobiography<sup>3</sup> that it had "poor typographic conditions" and that the "figures were often disastrous," particularly in comparison with those of *Bol. R. Soc. Esp. Hist. Nat.* In volume I (June 1920) of *Archivos de Neurobiología*, months before he transferred to the laboratory of the Residencia de Estudiantes, Del Río Hortega reproduced his important study of the microglia and their transformation into rod-like cells and granulo adipose bodies,<sup>47</sup> which also appeared in Cajal's journal<sup>46</sup> and in an offprint published by the JAE.

In the article, Del Río Hortega elegantly demarcates the meaning of what Cajal called the "third element," clearly reporting the concept of microglia/mesoglia and putting forward a preliminary conception of his idea of the interfascicular glia of the white matter, which "is also mixed up in the concept of the third element," and "which we will characterise at a later time."<sup>46,47</sup>

Del Río Hortega later published a further six articles in *Archivos de Neurobiología*, with the last appearing in 1929, as his work after 1930 was published in *AEO*, the new journal developed by the National Cancer Institute.

*AEO* was a journal founded in 1930 by the surgeon José Goyanes Capdevila, still director of the National Cancer Institute at the time, and was published every four months. To date, no detailed bibliometric analysis had addressed the journal, although the works it published were of great quality and had a significant impact in the field of oncology.

In the first volume of *AEO* (1930), Del Río Hortega is listed as editor-in-chief, although he became the director of the journal from 1931. The journal, which is rarely discussed, was the first publication in Spain to focus exclusively on oncology. Its content encompassed subjects related to cancer research, both in humans and in experimental studies, and articles included photomicrography images. Unfortunately, the journal was very short-lived, with publication ceasing in 1933, surely due to political issues affecting the National Cancer Institute.



**Figure 6.** Front pages of the main journals in which Del Río Hortega published his extensive research. The journal in which he published the most articles was the *Boletín de la Sociedad Española de Biología* (A), whose publication continued after 1932 as the *Revista Española de Biología*. The publication in which the second greatest number of articles appeared was the *Boletín de la Real Sociedad Española de Historia Natural* (C), in which he published a total of 20 articles between 1917 and 1929, particularly after 1920, when he was forbidden from publishing in Cajal's journal, *Trabajos del Laboratorio de Investigaciones Biológicas* (B), in which he published 19 studies between 1913 and 1923. Many of his most significant contributions were republished in the journal *Archivos de Neurobiología* (D), which was founded in 1920 and supported by Del Río Hortega since its early days. From 1930, Del Río Hortega, as well as his disciples, mainly published in the journal *Archivos Españoles de Oncología* (E), contributing articles on oncology. Finally, the main outlet for his work was *Archivos de Histología Normal y Patológica* (F), which he founded in 1942 and in which he published the majority of the articles he wrote in exile in Argentina.

Most of the articles published in AEO were written by direct disciples of Del Río Hortega, including Álvarez Cascos, Abelardo Gallego, Pérez Lista, Bernard Alpers, Ortiz Picón, Vara López, Isaac Costero, Sánchez Lucas, Cárdenas Pupo, and Urtubey Rebollo.

Del Río Hortega published a total of six articles in AEO between 1930 and 1932, two in collaboration with other authors: one with Álvarez Cascos, addressing the histopathology of skin cancer,<sup>58</sup> and another with

the journal's founder, the surgeon Goyanes Capdevila, on Recklinghausen disease<sup>59</sup>; the latter was the second and final article that Del Río Hortega signed as second author.

However, the most significant of his works published in AEO were in the area of neuro-oncology, with the two monographs mentioned previously being particularly influential. The first, published in 1930, is an extensive article (93 pages with 78 photomicrographs) addressing

the classification of meningeal tumours.<sup>56</sup> In this article, he demarcates the complex terminology used for these tumours, and argues against the term endothelioma, proposing the term meningoexothelioma and describing the xanthomatous and fascicular variants; he also proposes four patterns of growth and differentiation of these tumours.

The second monograph appeared two years later, in 1932.<sup>57</sup> This is another extensive work, 206 pages long with 201 figures (all photomicrographs), in which the author systematises and classifies embryonal tumours of the nervous system. The study is based on data from 60 brain tumours, many of which were sent from abroad; all samples were studied with his silver carbonate technique. This monograph was recently described as a visionary work in the pathology study of nervous system tumours.<sup>76</sup> In terms of its content, it was at the time one of the most comprehensive histological works addressing tumours of the nervous system; together with the previous study,<sup>56</sup> it formed a solid basis for Del Río Hortega's monumental lecture at the International Cancer Congress in 1933, which was published as a book and translated into English 30 years later.<sup>14</sup>

Finally, in the last 5 years of his life, Del Río Hortega published most of his work in the journal *Archivos de Histología Normal y Patológica*, in which a total of 14 articles appeared. The journal was founded by Del Río Hortega on 1 August 1942, and was funded by the Spanish Cultural Institution of Buenos Aires<sup>1</sup>; this was the journal in which he published the greatest number of collaborative works, including the aforementioned studies of the peripheral neuroglia,<sup>62,63</sup> in which he collaborated with disciples in South America. In the first issue of the journal, Del Río Hortega described its objectives,<sup>77</sup> indicating that he would prioritise "studies presenting the analytical methods of the Spanish histological school, with objective results based on extensive images." After Del Río Hortega's death, the journal continued to be published until 1965, and later continued under the name *Archivos de la Fundación Roux-Ocefa*, after an Argentinian pharmaceutical institution; publication ceased in 1977.

### Conclusions

Having reviewed the different media through which Del Río Hortega disseminated his vast scientific output, we may comment on which of his publications had the

greatest impact in the international scientific literature. A bibliometric study by López Piñero,<sup>1</sup> in which only the literature from the 1980s was searched, found a total of 97 references to works by Del Río Hortega in the Science Citation Index; the author comments that, due to the status of English as the lingua franca of the scientific community, the most frequently cited works were his chapter on the microglia<sup>55(p635-703)</sup> in Wilder Penfield's three-volume treatise published in 1932 (Figure 2), and his book on nervous system tumours, presented as a lecture at the 1933 International Cancer Congress in Madrid, which was mainly cited via the English translation, published 30 years later.<sup>14</sup>

Del Río Hortega's microscopy contributions remain relevant today, as demonstrated by the successive English translations of his works. For instance, a total of five new editions and English translations of his works have been published,<sup>9-12,78</sup> as well as studies reinterpreting the validity of his findings<sup>79</sup> and his masterful illustrations of the oligodendroglia in the light of current morphological techniques, combining the high resolution of electron microscopy and the specificity of antibody staining.<sup>80</sup>

To conclude, it should be noted that the lasting impact and relevance of Del Río Hortega's microscopy findings recall a comment he wrote in Valencia in 1937,<sup>60</sup> shortly before leaving for exile: "A good product sells itself, and there can be no doubt that, sooner or later, all quality work will receive international recognition in spite of the language of publication."

### Conflicts of interest

The author has no conflicts of interest to declare.

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