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The letters of Pío del Río-Hortega

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ABSTRACT

Introduction: In 1918, Pío del Río-Hortega (1882-1945) developed a new staining technique using ammoniacal silver carbonate. It was with this technique that he discovered a new type of cell which he named microglia. In 1919, he published his study of microglia in four parts and described another type of cell that was later named oligodendroglia. He described their mesodermal origin and phagocytic roles in different pathological processes in 1921.
Material and methods: This article showcases a selection of letters and other documents that have been lent to the SEN's historical archive to be scanned. Dating from 1902 to 1945, the collected letters of Pío del Río-Hortega include 1036 items. Part of this collection (1902-1930) is already familiar, whereas content dated 1931 to 1945 has never before been published.
Results: Río-Hortega's collected letters include items documenting the start of his career as a professor and department head and his correspondence with scientific societies and well-known histologists, pathologists and neurosurgeons in the first half of the 20th century. As such, his letters can be divided into three large groups: 1) official documents, 2) correspondence with foreign scientists, and 3) correspondence with Spanish scientists and intellectuals.
Discussion: By examining Pío del Río-Hortega's collected letters, we can follow social and political events and the scientific career of one of the most distinguished figures in Spanish histology.

KEYWORDS:
Pío del Río-Hortega, correspondence, historical archive, Spanish school of histology.

Introduction

Pío del Río-Hortega was born in the town of Portillo in 1882 and earned his medical degree from the Faculty of Medicine in the neighbouring city of Valladolid. In 1910, he presented his doctoral thesis, titled "Nervous tissue changes and general symptoms in brain tumours". He began his career in 1911 as an interim lecturer of histology and anatomical pathology at the University of Valladolid's Faculty of Medicine. In 1913, thanks to a grant from the Board for Advanced Studies (*Junta para Ampliación de Estudios*), he furthered his training in Berlin (at the Koch Institute), London (at the Imperial Cancer Research Foundation), and Paris (where he studied histological techniques under Auguste Prenant and anatomical pathology under Letulle).[1]

He joined Achúcarro's team at the Nervous System Histopathology Laboratory in 1912. By 1918, he had developed a new staining method with ammoniacal silver carbonate and used that method to discover a new type of cell which he named 'microglia'. In 1919, he was made a laboratory assistant at Hospital Provincial, Madrid. He also published his study of microglia in four instalments and described another type of cell later named oligodendroglia. He presented his studies at the International Congress of Physiology in Paris. This step launched his international career, while at the same time, the Board for Advanced Studies outfitted him with his own laboratory in the student residence hall in Madrid.[2] (Figure 1)

He focused his efforts on microglia and in 1921 was able to describe their mesodermal origin and phagocytic functions in different pathological processes. In 1924, German scientists A. Metz and H. Spatz published a study on microglia in which they referred to these cells as 'Hortega cells'.[3]

Río-Hortega was named director of Spain's National Institute for Cancer Research in 1931. In 1933, he presented his

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Figure 1. Madrid, Residencia de Estudiantes, 1927. Pío del Río-Hortega (centre), shown with his colleagues.

pivotal study, "Microscopic study of the anatomy of central and peripheral nervous system tumours" at the International Congress on the Scientific and Social Struggle Against Cancer, held in Madrid.[1]

Not long after the outbreak of the Spanish Civil War in 1936, Río-Hortega went into exile in Paris. He worked at the histopathology laboratory at Hospital de La Pitié until his transfer to Oxford in 1938; that university awarded him an honorary doctorate.

Don Pío was invited by the Spanish Cultural Institute of Buenos Aires to present a course in 1940. That institute also promoted the creation of the Laboratory of Histological and Histopathological Research which Río-Hortega was to direct. His papers on peripheral nervous system pathology were published in *Archivos de Histología Normal y Patológica*, a journal founded by Río-Hortega in 1942.[1] (Figure 2)

Figure 2. Buenos Aires, ca. 1942. Don Pío with his colleagues in the Laboratory of Histological and Histopathological Research, Spanish Cultural Institution. From left to right, Buño, Río-Hortega, Polak, and Cross.

Don Pío died in Buenos Aires in 1945; his last three studies on staining methods, glial cells, and the classification of nervous system tumours were published in the same year.[1]

Material and methods

This article showcases a selection of letters and other documents that have been lent to the SEN's historical archive to be scanned. Dating from 1902 to 1945, the collected letters of Pío del Río-Hortega include 1036 items. The first part of his correspondence (1902-1930) has been published, while content dated 1931 to 1945 is being presented for the first time.

Results

1) Official documents.

One letter, issued by the Faculty of Medicine at University of Valladolid and dated 1 October 1904, certifies that Pío del Río-Hortega was admitted as a medical student under the departments of descriptive anatomy, embryology, and anatomical pathology.[4(p187)] Another letter dated the same day notified the student that he would receive a yearly scholarship of 500 pesetas.[4(p185-6)] Both letters were signed by the Chancellor, Antonio Alonso Cortés.

A later certificate, dated 16 November 1907, informs Río-Hortega that he had been named district physician of Portillo and the surrounding area.[4(p187-8)]

In another letter, dated 5 June 1911, confirms Río-Hortega's position as Interim Assistant to the practical and experimental departments at the Faculty of Medicine in Valladolid. The letter was signed by José María Zorita y Diez, Undersecretary of the Ministry of Public Education and Fine Arts.[4(p190)]

On 29 October 1917, Madrid's Central University (later known as Complutense University) named Don Pío interim assistant of the Department of Histology and Anatomical Pathology; the department head at that time was Santiago Ramón y Cajal.[4(p198)]

Río-Hortega's prestige was such that in December 1932 he became Director of the National Cancer Institute.[6] He was clearly awarded this honour based on his ground-breaking studies of tumours of the nervous system; in undertaking his projects, he received histological slides of tumours which neurosurgeons from many different countries sent him for

diagnosis. This earned him the nickname of "the tumour importer".

In 1937, while the Spanish Civil War was raging, Río-Hortega lived in France and worked as a pathologist alongside neurosurgeon Clovis Vincent in Hospital de la Pitié. He moved to England the same year after being invited by Hugh Cairns to work in Oxford's Nuffield Institute. On 25 February 1939, the University of Oxford conferred on Don Pío the degree of Doctor of Sciences *honoris causa* at the urging of Sir Charles Scott Sherrington.[7]

In 1940, at the end of his professional tour, Don Pío transferred to Buenos Aires. After spending some time pursuing his career in both Buenos Aires and Montevideo, he was to settle definitively in the capital. In 1942, the Spanish Cultural Institute of Buenos Aires created the Laboratory of Histological and Histopathological Research; Río-Hortega was named director.[8] He would continue his sterling work at that laboratory.

2) Correspondence with foreign scientists

The collection contains various letters from foreign scientists, most of whom wrote to request copies of his reports on glial cells and staining techniques.

One of these letters was written in Spanish by Percival Bailey of Hospital Peter Bent Brigham in Boston and dated 2 September 1922; in it, Bailey requests copies of Río-Hortega's articles on neuroglia and his staining methods. In the same letter, he also enquires about the address of the editors of *Archivos de Neurobiología* in order to take out a subscription.[4(p203-1)]

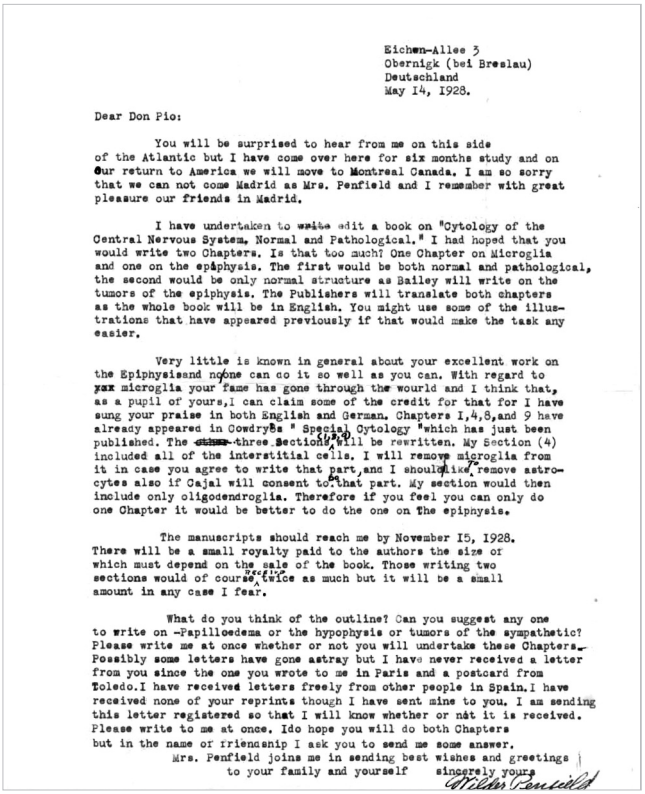
Another two letters of Bailey's, dated February and May 1923, mention the possibility of inviting Río-Hortega to give lectures in different hospitals. They also refer to one of Río-Hortega's collaborators, Dr Collado, who was to join the staff at Hospital Peter Bent Brigham.[4(p240-1)]

The collection even includes numerous letters from the prestigious neurosurgeon and physiologist Dr Penfield and his wife Helen. In addition to their professional subject matter, these letters all reveal indications of close friendship.

In a letter dated 13 November 1924, Río Hortega read that Adolf Meyer –the top psychiatrist in the United States, according to Penfield– had offered Penfield a job at Johns Hopkins Hospital in Baltimore. Penfield observes that they had an opening in neuropathology at that time. In that new location, he would also be able to study the work of Dandy the neurosurgeon, and even that of Cushing in Boston. Penfield describes Baltimore as a smaller and more economically feasible city to live in than New York, but he did not know what salary Meyer was prepared to offer him.[4(p253)]

In another letter dated 14 May 1928 (Figure 3), Penfield asks Río-Hortega to write two chapters of a book he was editing, titled *Cytology of the Nervous System: Normal and Pathological*. Penfield requested that Río-Hortega write the chapters on microglia and the epiphysis; the deadline for submitting the manuscripts was set for November of the same year.[4(p347-8)]

In a letter dated 16 April 1929, Penfield expresses concern about the lateness of Don Pío's chapters. He gently stresses the urgency of the project. On 25 May, Penfield increases the pressure on Río-Hortega by commenting that all the other authors had already submitted their sections. Finally, in a letter dated April



Eichen-Allee 3
Obernigk (bei Breslau)
Deutschland
May 14, 1928.

Dear Don Pio:

You will be surprised to hear from me on this side of the Atlantic but I have come over here for six monthe study and on our return to America we will move to Montreal Canada. I am so sorry that we can not come Madrid as Mrs. Penfield and I remember with great pleasure our friends in Madrid.

I have undertaken to ~~write~~ edit a book on "Cytology of the Central Nervous System, Normal and Pathological." I had hoped that you would write two Chapters. Is that too much? One Chapter on Microglia and one on the epiphysis. The first would be both normal and pathological, the second would be only normal structure as Bailey will write on the tumors of the epiphysis. The Publishers will translate both chapters as the whole book will be in English. You might use some of the illustrations that have appeared previously if that would make the task any easier.

Very little is known in general about your excellent work on the Epiphysisand no one can do it so well as you can. With regard to ~~xax~~ microglia your fame has gone through the wourld and I think that, as a pupil of yours, I can claim some of the credit for that for I have sung your praise in both English and German. Chapters I,4,8,and 9 have already appeared in Cowdry's " Special Cytology "which has just been published. The ~~three~~ three Sections will be rewritten. My Section (4) included all of the interstitial cells. I will remove microglia from it in case you agree to write that part, and I should like, ~~to~~ remove astrocytes also if Cajal will consent to that part. My section would then include only oligodendroglia. Therefore if you feel you can only do one Chapter it would be better to do the one on the epiphysis.

The manuscripts should reach me by November 15, 1928. There will be a small royalty paid to the authors the size of which must depend on the sale of the book. Those writing two sections would of course, ~~twice~~ twice as much but it will be a small amount in any case I fear.

What do you think of the outline? Can you suggest any one to write on -Papilloedema or the hypophysis or tumors of the sympathetic? Please write me at once whether or not you will undertake these Chapters. Possibly some letters have gone astray but I have never received a letter from you since the one you wrote to me in Paris and a postcard from Toledo. I have received letters freely from other people in Spain. I have received none of your reprints though I have sent mine to you. I am sending this letter registered so that I will know whether or nat it is received. Please write to me at once. Ido hope you will do both Chapters but in the name or rriendsnip I ask you to send me some answer.

Mrs. Penfield joins me in sending best wishes and greetings to your family and yourself sincerely yours

Wilder Penfield

Figure 3. Letter from Wilder Penfield to Pío del Río Hortega asking him to contribute two chapters to *Cytology of the Nervous System: Normal and Pathological*. 14 May 1928.

1930, Penfield thanks Río-Hortega for sending him the completed chapters. He also asks for permission to use images belonging to Río-Hortega in his chapter.[4(p372)]

After reading these letters, we calculated Río-Hortega's delay in sending the manuscripts, which were not received until April 1930 although the deadline had been set for November 1928. This is a sign of Don Pío's busy schedule, as well as a hallmark of the casualness characteristically displayed by authors of scientific studies.

Another letter that ties in with Penfield's was written on 20 November 1924 by Adolf Meyer, director of the psychiatry department at Johns Hopkins Hospital. After an exchange of ideas with Penfield, he offered Río-Hortega a position as the director of his hospital's neuropathology laboratory. He comments that Río-Hortega would be very well received because of his professional prestige, and that his yearly salary would fall between $2500 and $3000.[4(p255)]

Bernard J. Alpers of Philadelphia wrote a letter on 1 January 1929 in which he expressed an interest in travelling to Spain to further his knowledge of neuropathology in general, and brain tumours in particular.[4(p364)]

Gordon Holmes, editor of *Brain* at that time, sent a letter on 28 January 1927 acknowledging Río-Hortega's and Penfield's commitment to submit a study on changes in neuroglia in brain injuries.[4(p330)]

Río-Hortega's fame spread as far as Eastern Europe. On 13 November 1922, Marinescu in Bucarest asked Río-Hortega for reprints of his publications on microglia, which was one of his major interests.[4(p237)]

Knud H. Krabbe of Copenhagen sent a letter dated 3 January 1921 to Villaverde, a friend of Río-Hortega's. On the basis of this friendship, Krabbe asked for reprints of Río-Hortega's studies on the fibrillar structure of neuroglial protoplasm and his paper on nerve cell centrosomes. At the same time, Krabbe stated that a nervous system laboratory would shortly be created in his city, and expressed an interest in exchanging scientific projects with Cajal's laboratory.[4(p226)]

In July 1932, Egas Moniz of Portugal, who would go on to win the 1942 Nobel Prize in Medicine, wrote to ask Río-Hortega where he could find his studies on the structure and systematic classification of gliomas and paragliomas, and his 1930 paper on meningotheliomas.[9]

3) Correspondence with Spanish intellectuals and scientists

Río-Hortega received a letter from Lafora, dated 23 October 1923, informing him that Lucien Cornil had been made Chair of Anatomical Pathology in Nancy. Lafora mentions Cornil's request for copies of Cajal's and Río-Hortega's papers on neuroglia.[4(p244)]

While travelling through Argentina and Uruguay, and because of the success of his lectures in those countries, Río-Hortega received a congratulatory letter in 1925. It was from Jiménez Díaz, who was Chair of Internal Medicine at the University of Seville at that time.[4(p291)]

It is a sign of Río-Hortega's success in Argentina that B.A. Houssay also sent him a handwritten letter, signed in Buenos Aires on 9 January 1926. Years later, in 1947, Houssay too would win the Nobel Prize.[4(p302-3)]

Don Pío's scientific prestige is clearly illustrated by the letter dated 6 November 1931 and signed by Miguel de Unamuno, the President of the Board of Public Instruction. In this letter, Unamuno requested his assistance in drafting a new law to renew cultural institutions.[10]

J. Martínez Penas received a letter dated 29 July 1932 from leading endocrinologist Gregorio Marañón. This letter comments on Río-Hortega's refusal to be honoured and mentions the possibility of granting him an award despite his protests.[11]

This collection also includes four handwritten letters which Río-Hortega received from Cajal. On 9 May 1932, Cajal also thanked Don Pío for sending him his articles on gliomas and oligodendroglia. He also recognised Río-Hortega, and not the Scottish scientist Robertson, as the first to categorise glial cells by their distinct types.[12](Figure 4)

Cajal addressed another letter on 9 August 1932 to the committee entrusted with organising a banquet in Río-Hortega's honour. Here, he confirmed his appointment to the committee, but regretted that he would be unable to attend the event himself because of his advanced age. He indicated that his co-worker Fernando de Castro would attend as the representative of the Cajal Institute.[13]

Cajal's letter to Río-Hortega, signed in Madrid on 4 May 1933, expressed wishes for his full recovery from a bout of influenza.[14]

Cajal sent another letter, stamped with his home address and dated 12 May 1934, to the president of the committee formed to honour Río-Hortega. Here, Cajal confirms his endorsement of the ceremony titled "Dr del Río, illustrious histopathologist and tireless researcher".[15]

In October 1933, García del Real, one of the department chairs at the Faculty of Medicine in Valladolid, sent Río-Hortega a handwritten letter. In it, García del Real reveals that he had been appointed to the advisory committee for the Nobel Prize in Physiology and that he nominated Río-Hortega for that award.[16]

Discussion

Río-Hortega's collected letters document his career path from lecturer to department head and include professional correspondence with scientific societies and prominent histologists, pathologists, and neurosurgeons of the first half of the 20th century. Some of these letters simply request reprints or scientific information, but others are deeply personal and reflect the high esteem in which his contemporaries held him due to his concern for colleagues and students alike. Others illustrate his relationship with leading intellectuals in Spain, some of whom worked outside of the field of medicine.

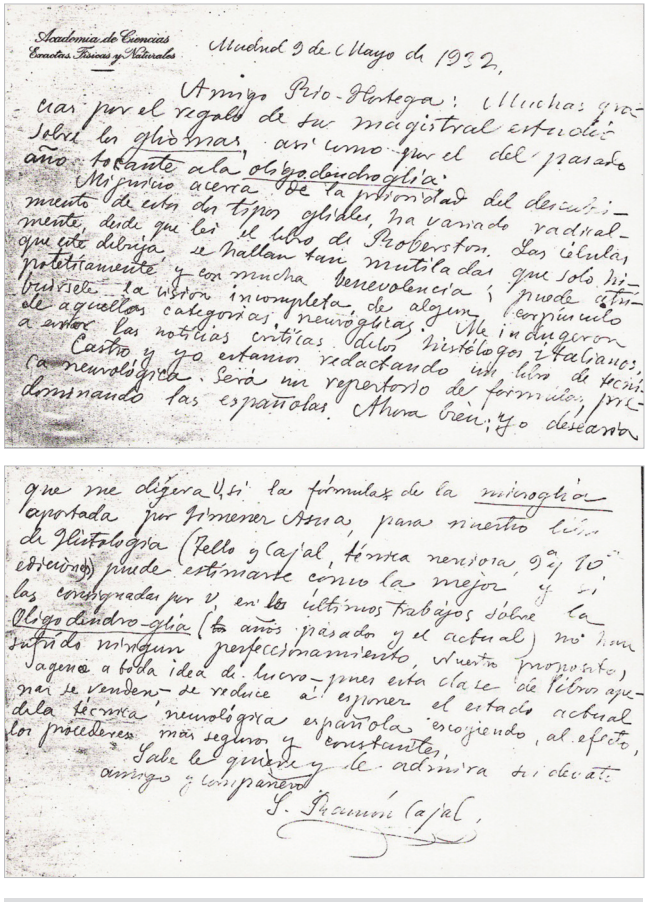


Figure 4. Letter from Santiago Ramón y Cajal to Pío del Río-Hortega, 8 May 1932. Photographs of the original letters taken by Pío del Río-Hortega.

As a result of his considerable prestige, Río-Hortega forged scientific and personal relationships with the most well-known names in medicine of his time. By examining Pío del Río-Hortega's collected letters, we can follow the scientific career and social and political events in the life of one of the most distinguished figures in Spanish histology.

Acknowledgements

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