Alejandro San Martín Satrústegui: a pioneer of Spanish neurology

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ABSTRACT

"Alejandro San Martín was the most capable master of our generation": this assertion of Cajal's is a good representation of the esteem with which Alejandro San Martín Satrústegui (1847-1908) was held both by Cajal himself and by those generations of physicians and scholars, and which led him, briefly, to sit in the government cabinet of Segismundo Moret. An important medical journalist, university professor, and a noteworthy surgeon in several areas, especially the nascent field of vascular surgery, San Martín has been said to have "put Spain back on the international surgical map," with his knowledge, proficiency in several languages, and relevant social skills and projection all playing a role. However, little attention has been paid to his achievements in the also nascent fields of neurology and neurosurgery. This study focuses on these specific aspects, and notes certain parallels with the life of Cajal.

KEYWORDS

Arteriovenous anastomosis, Cajal, history of neuroscience, lathyrism, neuroscience, neurosurgery, Simarro, trigeminal nerve, brain tumours.

Introduction

Alejandro San Martín (1847-1908) was a multifaceted physician from Navarre, who played a crucial historical role in Spain in the second half of the 19th and the early years of the 20th century. San Martín played an active role in medical education and journalism; his greatest achievements were related to his interest in vascular and brain surgery and in changing the education system, which led him briefly to sit as a government minister shortly before his death. In 1873, he described Azañón disease, at a time when lathyrism, a dietary neurotoxic process, had not yet been named. He also participated in one of the first brain tumour resections reported in Spain, and devised novel approaches for the surgical treatment of neuralgia of the trigeminal nerve or its branches, including extirpation of the Gasserian ganglion. This interest in the brain and its diseases was partly related to his contact with figures including Luis Simarro Lacabra (1851-1921) and especially Santiago Ramón y Cajal (1852-1934), the founder of modern neuroscience, with whom he shared certain relevant biographical parallels.

Material and methods

A systematic review was conducted to analyse the figure of Alejandro San Martín Satrústegui, both in his scientific and his cultural, teaching, and political activities. The search included different forms of his surname ("San Martín," "Sanmartín"), with and without the second surname (Satrústegui). The same approach was followed for

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Figure 1. Alejandro San Martín Satrústegui's origins in Navarre. A) His native Larráinzar (Navarre), with the parish church of Saint Peter, which was rebuilt with new plans between 1827 and 1830; barely two decades before Alejandro San Martín was baptised there in 1847. B) *El Zurriago* was the main publication that opposed the physician and eminent soldier José Martínez de San Martín, also known as "Tintín de Navarra" (in the bottom half of the page shown he is referred to as "the feeble brute Tintín"), great-uncle of Alejandro San Martín Satrústegui. C) A passport issued with the coat of arms of José Martínez de San Martín, who at the time was a captain general of the armies and kingdoms of Valencia and Murcia. D) A portrait of Basilio San Martín Olaechea, Alejandro's uncle, as president of the Real Academia Nacional de Medicina de España. The cloister (E) and historical laboratory (F) of the Instituto de Segunda Enseñanza San Isidro, in Madrid, where Alejandro San Martín completed his secondary education. Images taken from Wikipedia under the Creative Commons licence.

other members of his family, such as his father and uncle, Mariano and Basilio San Martín Olaechea, respectively. Particular attention is placed on his relationships with Luis Simarro and Santiago Ramón y Cajal. Documents were gathered from the Madrid Municipal Press Archive and the Centre for Historical Studies of the Spanish National Research Council (CSIC, for its Spanish initials). The documentary collections of the Cajal Legacy (listed as world heritage by UNESCO: Memory of the World Register, reference no. 2016-31) of the Instituto Cajal-CSIC were consulted, in addition to the collections of the National Library of Spain, the Archives of the Spanish Senate, the General Administrative Archives, and various archives of the Spanish National Royal Academy of Medicine (RANME, for its Spanish initials) and the Royal Academy of Exact, Physical and Natural Sciences. Unpublished documents and other relevant information were obtained by contacting distant relatives of San Martín (Dr Jorgina Satrústegui, a retired CSIC researcher); a call for information was also issued on social media (Twitter, LinkedIn), but yielded no results.

Results

Childhood and early education of Alejandro San Martín

Alejandro San Martín Satrústegui was born on 17 October 1847 in Larráinzar, Navarre (Figure 1A), the first son of the village's physician and second-class surgeon Mariano San Martín Olaechea, of a family of physicians; his uncle, José Martínez de San Martín, was a

well-known soldier and guerrilla (Figure 1B and C).[1] Mariano was a court physician for the royal family, as was his younger brother, Basilio (Figure 1D; see below).

Alejandro San Martín was raised in Larráinzar until the age of 10 years, and was educated at one of the village's two schools. In 1857 he moved to Pamplona, the region's capital, where he received secondary education at the Instituto de Pamplona, beside the cathedral: there, only humanities subjects could be studied. But in 1860, the stars aligned: Mariano's younger brother, the brilliant physician Basilio San Martín Olaechea (1821-1901; Figure 1D), was elected to the RANME (seat no. 18; he became president of the Academy from 1887 to 1891, and was appointed by the Academy to represent it in the Senate in the period 1893-1895).[2] This reaffirmed to Mariano San Martín the possibilities available to him in the capital of the kingdom; using some savings, he decided in 1860 to move to Madrid to study for two years for his degree in medicine. The family decided to join their first-born son in his move to Madrid, with father and son sharing a small flat at number 4, Calle de Gravina, very close to the San Antón church.[3] Alejandro San Martín enrolled at the San Isidro secondary school (Figure 1E and F), which was founded in 1845 and occupied part of the buildings that had previously housed the Colegio Imperial, and subsequently the Reales Estudios de San Isidro, adjoining the Real Basílica Colegiata de San Isidro (consecrated in 1651 and completed in 1664, this collegiate basilica was the provisional cathedral of the diocese of Madrid from the time of its creation, in 1885, until 1993, when the Cathedral of Santa María de la Almudena, beside the Royal Palace, was consecrated). This prestigious institution had a modern laboratory for practical teaching in scientific disciplines (Figure 1F), and particularly physics[4]; the building also housed the Faculty of Philosophy and Letters of the Universidad Central, the Diplomatic School, and (from the same year, 1860) the School of Stenography.[5] San Martín completed the final two years of the five required to earn the title of Baccalaureate of Arts in 1862, with a classification of outstanding. The influence of his uncle Basilio, who only had daughters, is undeniable: Alejandro San Martín considered him his "second father."[3,6]

On 23 November 1862, Alejandro San Martín decided to enrol in pre-medical training, in which he began studying physics, general chemistry, botany, and mineralogy, which were taught at the Faculty of Science. He obtained his bachelors in medicine in 1867, with a classification of outstanding. The same year, he joined Hospital de San Carlos as an intern (Figure 2A and B), showing a particular affinity for anatomy, which he studied under Juan Fourquet Muñóz (1807-1865, Figure 2C), a Madrid academic of French descent, and the European-style surgery taught by the Basque surgeon Melchor Sánchez de Toca y Sáenz de Lobera (1806-1880; Figure 2D), to whom San Martín would dedicate a heartfelt lecture years later at the Ateneo de Madrid.[7]

In 1867, San Martín founded *La Aspiración Médica*, a controversial and short-lived publication where he and other students manifested their opposition to changes made to teaching legislation at the time.[6,8,9] It should be noted that, for various reasons that will be addressed in this article, San Martín was in favour of revoking the titles of the so-called "second-class and authorised physicians," radically opposing the plans of the RANME, which proposed that their practice be limited to villages, and only where there was no licensed or "first-class" physician.[10] Though he passionately welcomed the "la Gloriosa" or "la Septembrina" revolution of 1868, which overthrew Queen Isabella II, he soon openly criticised the revolutionary excesses that led to the end of merit-based chairs, creating new positions for people with no merits besides their having participated in the revolution; or doing away with such bodies as the Beneficiencia Municipal (municipal health system), which had done so much for the underprivileged over its 10 years of existence, including the salvation of many lives in various cholera epidemics.[11] In December 1868, just three months after the outbreak of "la Gloriosa," the revolutionary government ordered the closure of *La Aspiración Médica* in another show of its sectarian zeal.

Alejandro San Martín the physician, and his description of neurolathyrism

San Martín took the opportunity of the convulsion of 1868 to complete two courses needed to receive his medical degree, which he obtained on 24 December 1868, with a classification of outstanding.[12] However, despite having passed all courses in his degree (with the exception of physiology) with a classification of outstanding, he did not receive the extraordinary academic awards for the degree of medicine, due to changes derived from that year's political revolution.[13] After a forced pause due to the Christmas holidays, on 28 December of the same year Alejandro San Martín was appointed physician and surgeon of the villages of Ituren (the largest of which had

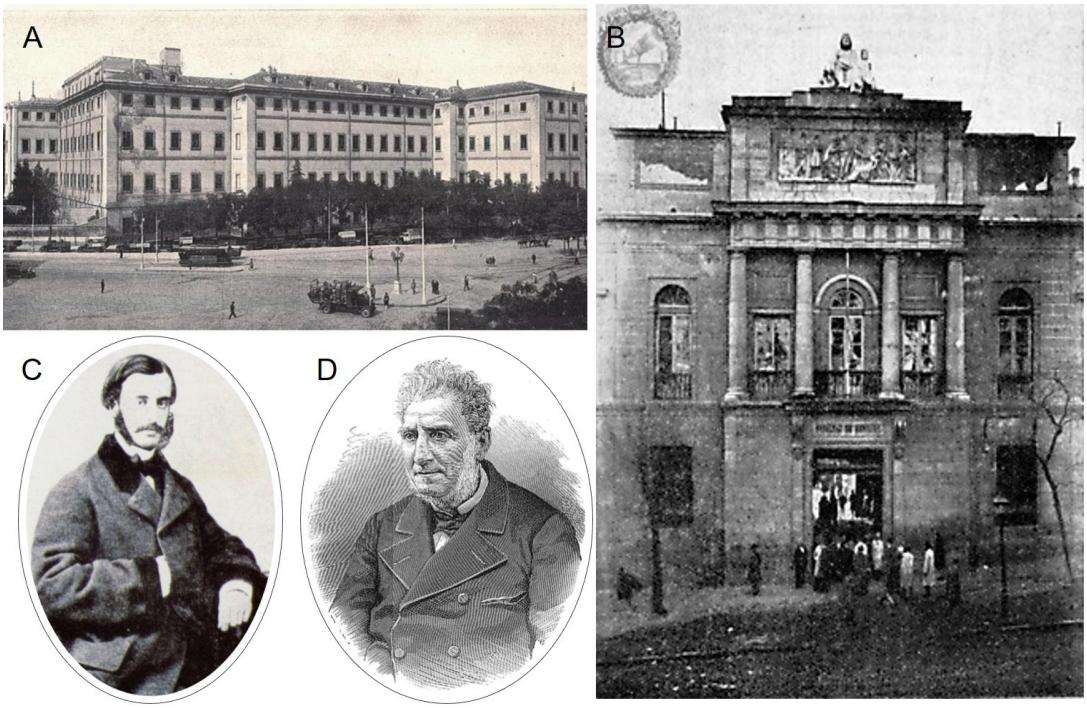

Figure 2. The Faculty of Medicine of Madrid and the professors who most influenced San Martín. A) Hospital de San Carlos ("old San Carlos"), belonging to the medical school of the Universidad Central de Madrid; the building now houses the Museo Nacional Centro de Arte Reina Sofía art museum. B) Entrance gate to the lecture hall of the Faculty of Medicine, on Calle Atocha. C) The surgeon and university professor José Fourquet Muñoz. D) The surgeon and university professor Melchor Sánchez de Toca y Sáenz de Lobera, first Marquess of Toca. Figures A-C were taken from Wikipedia under the Creative Commons licence.

a population of around 3000; Figure 3A and B), where he was a true rural doctor, travelling the district on horseback. He practised there for two years, "to the complete satisfaction" of the local population.[14] This timeline does not fit with the fact that in 1869, San Martín began collaborating with Francisco Giner de los Ríos (1839-1915), the thinker and essayist from Ronda, and the Institución Libre de Enseñanza,[3,6] specifically at the Centro Popular de San Carlos, which was opened at the Universidad Central, and offered evening classes to those who were unable to access formal education. San Martín taught anthropology, and other lecturers included Raimundo Fernández-Villaverde (theory of contributions) and Miguel Echegaray (responsible for political law; the director was Gonzalo Calvo Asensio). It appears likely that having received his medical degree, San Martín took the opportunity of his temporary return to rural Navarre to immediately enrol as a doctoral student (at the time, the curriculum included chemistry and history of medicine; histology was only incorporated into the doctoral curriculum in 1873, when Aureliano Maestre de San Juan became the first chair in the discipline in Spain, specifically at the Universidad Central, and into the undergraduate curriculum in 1886[15]); in 1870, he obtained his doctorate (with a classification of "pass") after defending a thesis entitled "Relaciones entre el sistema vascular y el nervioso" (Relationships between the vascular and nervous systems), the first known example of his interest in neurology.

Figure 3. San Martín: from an Ituren physician to *El Siglo Médico*. Ituren (Navarre) today (A), and the village's coat of arms (B), which shows Saint Martin, of French origin, riding a white horse, opening his red cape, alongside a crippled beggar leaning on a crutch. C) A portrait of Alejandro San Martín Satrústegui painted in 1910 by José Díaz Molina, commissioned by the Ministry of Public Instruction. Of the available images, this is the portrait in which San Martín appears youngest, hence its selection for this figure. D) Front page of an 1871 issue of *El Siglo Médico*, the year Alejandro San Martín joined the publication as an editor. Images taken from Wikipedia under the Creative Commons licence.

However, he outgrew his native Navarre. Thanks to his influential uncle Basilio, Alejandro San Martín (Figure 3C) was invited by Dr Francisco Méndez-Álvaro and Dr Matías Nieto Serrano, the founders and owners of *El Siglo Médico*, to join the publication as director; he assumed the role in 1871 (RANME archives, leg. 22/99). *El Siglo Médico* (Figure 3D), which resulted from the merger of several previous publications, was a prestigious medical journal in Spain at the time. After further mergers, it was renamed *Revista Clínica de Madrid* between 1915 and 1936.[16] Aureliano Maestre de San Juan (1828-1890), the first chair of histology in Spain and the author of the first Spanish-language histology manual,[17] had described in *El Siglo Médico* an association between loss of the sense of smell and genital atrophy, known today as Kallmann syndrome[18] (for a recent review of the subject, see De Castro et al.[19]). It was also the third and the most influential of the medical publications that Alejandro San Martín directed during his lifetime: *La Aspiración Médica* (for two years), *La Medicina* (for only four months), and *El Siglo Médico* (which he directed from 1871 to 1874), in which he wrote a total of 66 articles on medicine and related disciplines.[3] An important example is his description of a new disease that, finding no better eponym, he named "Azañón disease" after the village in which the first cases of a large outbreak of lathyrism were detected (Figure 4A-C).[20] San Martín describes how, in early 1872, five patients (including three from a single family) among the 120 inhabitants of the small village in La Alcarria (Figure 4D) presented

sudden onset of immobility of the legs ("nervous system lesions, predominantly locomotor ataxia"), although the patients themselves reported that "a considerable number were invaded by the same ailment, with some fortunate individuals who […] recovered their initial agility overnight." In fact, another seven patients, aged 10-42 years, were identified in neighbouring towns. San Martín includes the detailed medical histories collected by Dr Miguel Segura when, in autumn 1872, they were transferred to Hospital General de Madrid, and underscores the common features observed in all patients: no remarkable fever, minimal convulsive tremor (this symptom was, however, emphasised by another physician in a communication shortly thereafter[21]), noteworthy symptoms of "motor depression" (paresis of the lower limbs and, in some cases, the bladder sphincter) with appropriately coordinated movement, and tingling in the lower limbs with normal/preserved sensitivity sometimes accompanied by mild persistent pain in the sacral region. He also stresses "the most complete normality and even the most enviable robustness […] in all other acts in the lives of the exceptional paraplegics reported in this study." After a detailed discussion of the symptoms, he concludes that the neurological symptoms were caused by damage to the "anterior cords" of the lumbar spinal cord, although he emphasised in the conclusion that this could not be attributed to any type of "inflammatory, atrophic, or sclerotic origin, etc."[20] As a neurobiologist, I cannot resist mentioning one of San Martín's speculative explanations for Azañón disease: "Might it be explained by production of corpora amylacea in the spinal neuroglia?" Cerebral corpora amylacea were originally described by Jan Evangelista Purkinje in 1837 in patients affected by what we now know as neurodegenerative diseases (Alzheimer disease, Parkinson's disease, etc); this description was completed some years later by Rudolf Virchow.[22] They attracted the attention of Nicolás Achúcarro in his early studies on nervous tissue damage and the elimination of cell debris[23] (for a review on the subject, see Tremblay et al.[24]) and, though the terms "corpora amylacea" and "Lafora bodies" have often been treated as synonyms, the latter term should be restricted to bodies appearing in the context of progressive myoclonic epilepsy or Lafora disease.[25] Corpora amylacea are particularly abundant in subpial areas and/or near the cerebral ventricles; very recently, they were shown to act as containers, removing toxic metabolic waste products.[26] Curiously, the "neuroglia" initially described by Virchow,[27] known as astroglia or astrocytes since the late 19th century,[28] are now known to accumulate these corpora amylacea prior to their removal from the brain.[26]

In response to the appeal included in Alejandro San Martín's article, *El Siglo Médico* received various communications from its readers, reporting similar cases in different provinces of Castile that, analysed from this perspective, leave no room for doubt that the disease in question was that known today as lathyrism or neurolathyrism, although neither Alejandro San Martín nor any other of those Spanish physicians suspected the high intake of grasspeas (normally consumed as a gruel of grasspea flour) as the true aetiology of the disease.[29,30] In fact, Alejandro San Martín was unequivocal in the assertion that "no suspicious food had previously been noted in their diets, nor any unpleasant taste in their water or drinks": for him, this was a disease that involved "something new, very surprising, somewhat incomprehensible, and rather problematic, with considerable reason for it to be considered hereafter as one of the most challenging diseases to define."[20] Around the same time, Arnaldo Cantani (1837-1893; Figure 4E), an Italian researcher of Czech descent, coined the term lathyrism (or neurolathyrism), derived from the Latin name of the grasspea (*Lathyrus sativus*), and associated the appearance of spastic lower limb paraparesis/paraplegia with prolonged ingestion of large amounts of grasspea contaminated with the toxic subspecies *Lathyrus clymenum*.[31,32] Although the disease "described" by San Martín was reported in influential foreign publications (*The London Record*, Munich's Ärztliches Intelligenzblatt, etc), there is no evidence that the great Italian clinician would have been aware of this. The first official descriptions of lathyrism in Spain appeared over four decades later,[33-35] even after Pierre Marie, the renowned disciple of Charcot, had demonstrated the involvement of grasspeas.[36-38] The first description of an epidemic of neurolathyrism was in Spain,[39] with more than a thousand patients developing the disease due to nutritional deficits during the Spanish Civil War and immediate post-war period. However, it took some time before the connection was made with the disease described by San Martín in Azañón.[29,30] Since then, outbreaks of lathyrism have been reported on the Greek island of Santorini, in China, in Bangladesh, in India, and in Ethiopia.[30,40,41]

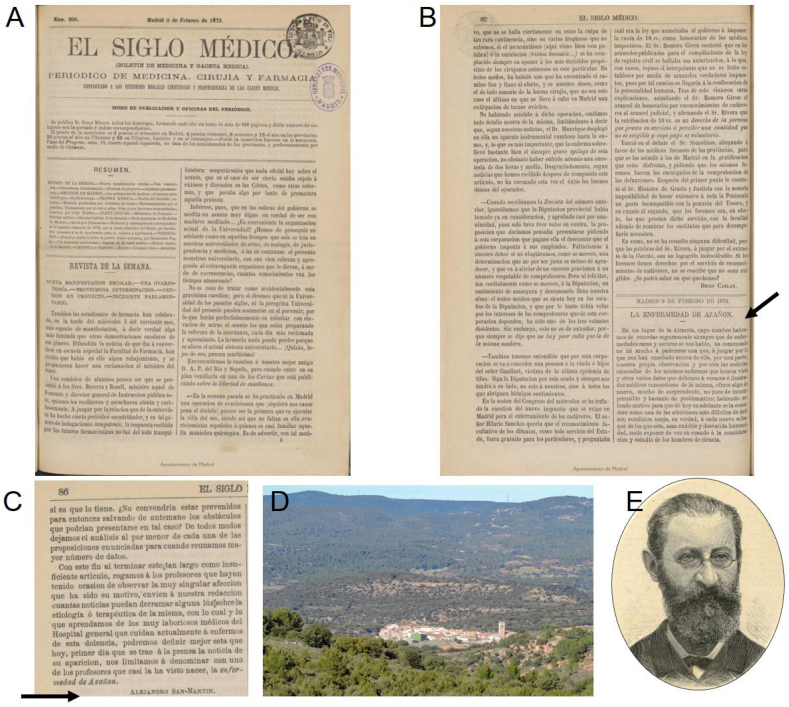

Figure 4. San Martín and Azañón disease or neurolathyrism. Reproductions of the front page (A) and second page (B) of the issue in which the description of Azañón disease begins, and detail from the final page (C), with Alejandro San Martín's signature, from the issue of *El Siglo Médico* in which he describes the disease known today as neurolathyrism. The arrows in images B and C indicate the beginning of the description and the author's signature, respectively. D) The idyllic view over Azañón today, taken from the Tetas de Viana mountain. E) Arnaldo Cantani, the Italian physician who described lathyrism, also in 1873, but associated it with excessive intake of grasspea. Images taken from Wikipedia under the Creative Commons licence.

During his time in Madrid, prior to the interesting episode of Azañón disease, San Martín, who was proficient in several foreign languages, translated Ernst Wagner's treatise *Manual on general pathology* from the original German; the work was published in Spanish in 1872 as a compendium with annotations by the translator.[42]

Triumph in academia: San Martín, a chair at 27 years of age

In 1874, Alejandro San Martín was appointed to the chair of physical therapy, at the Literary University of Seville's Faculty of Medicine in Cádiz (Figure 5A and B).[3] The faculty was founded in 1748 by Pedro Virgili Bellver as the Real Colegio de Cirugía de la Armada; after a brief spell as the Faculty of Medical Sciences of Cádiz (1844), in October 1845 it was incorporated into the Literary University of Seville, until, in 1979, it became part of the recently created University of Cádiz. San Martín inaugurated the academic year at the Royal Academy of Medicine of Cádiz,[43] and a few years later published a treatise of physical therapeutics, which he dedicated to his father (Figure 5C),[44,45] the first work of its kind in Spain.[3,6,46] One of the subjects addressed in the book is hydrotherapy: it is no coincidence that it was two Navarrans, San Martín and Antonio Simonena, who evaporated salts from the spa at Elgorriaga, demonstrating the medicinal relevance of these waters.

Francisco Giner de los Ríos (Figure 5D) came to Cádiz soon thereafter (1876), confined by the government of the conservative Cánovas del Castillo as a result of the "university problem." Besides their previous friendship (see above), San Martín personally attended Giner de los Ríos for various illnesses, strengthening their relationship. And when they coincided again in Madrid, from 1882, with San Martín being the chair of surgical pathology at the Universidad Central, he once more acted as

Figure 5. San Martín, chair in Cádiz. A) Alejandro San Martín Satrústegui as chair in the official photographs of the Cádiz Faculty of Medicine from 1881-1882. This is the earliest photograph found. B) Entrance of the Faculty of Medicine of the Literary University of Seville in Cádiz, where San Martín worked. C) A young Francisco Giner de los Ríos (ca. 1863), before his arrival in Cádiz. D) One of the illustrations from San Martín's treatise on therapeutics.[44] Figures A-C were taken from Wikipedia under a Creative Commons licence.

physician to the politician/pedagogist Giner. However, San Martín was far from radical in his liberalism, and by no means revolutionary. Rather, he was a moderate liberal.[3,47,48] Indeed, San Martín seems to have outgrown the city of Cádiz: in 1880, he requested a transfer to Zaragoza to occupy the chair of therapeutics; after the transfer had been approved, he requested that it be annulled due to "the harmful climate (of Zaragoza)" and, although in 1881 the competent authorities approved another transfer to the University of Barcelona (to occupy the vacant chair of general pathology, which included anatomy and general pathological histology), he barely occupied the chair, deciding to complete the academic year in Cádiz. Curiously, Cajal occupied the chair of histology and anatomical pathology at the University of Barcelona, but in 1888, the year he published his first original research article on the structure and organisation of the nervous system.[48,49]

However, in February 1882, San Martín applied to the vacant chair of surgical pathology of the Faculty of Medicine of the Universidad Central, in Madrid. The competitive examination was hard fought, but the examining board ruled in favour of Alejandro San Martín, who showed even better knowledge of and proficiency in surgical techniques than a chair from another university; his appointment was ratified on 6 May of the same year.[3,6] The university permitted him better access to international bibliographic sources and the opportunity to begin organising experimental studies. Just his presence in Madrid enabled him to participate in countless expert committees on the most varied of subjects.[3,50] Interested in the nascent field of bacteriology, in which he was viewed as an "expert" due to his very recent studies on the cause of cholera in Madrid, San Martín sat on the committee that assessed the true impact of attenuated bacteria inoculation, which Jaime Ferrán had trialled at the greatest focus of the 1885 Spanish cholera epidemic, Valencia. It is unclear whether San Martín and Cajal ever met in Valencia at that time: Cajal, who at that time was chair of anatomy of the University of Valencia, conducted a well-known study for the provincial government of Zaragoza, also evaluating Ferrán's attenuated bacterial vaccine against animal experiments with his own chemical vaccine.[51] The commission, chaired by Francisco Alonso and including F. Castellote (secretary), Aureliano Maestre de San Juan, Eduardo García de Sola, Alejandro San Martín, and Antonio Mendoza, published an overwritten and inconclusive report (with dissenting opinions from San Martín and Mendoza) exclusively authorising Ferrán to continue with the inoculations under his own full responsibility, although this report was more supportive of the innovation than had been the RANME. The full text of the report, the dissenting opinions of San Martín and Mendoza, the response of the RANME (which also included dissenting opinions), and the decision/order of the director general of the health system are available online in the *Gaceta de Madrid* (the equivalent of today's Official State Gazette) of 30 July 1885.[52] Thanks to this experience, San Martín was named as an official Spanish delegate at the 1893 International Sanitary Conference, held in Dresden (Germany), which focused on cholera.[50] Similarly, the Hospital General de Madrid

requested that Alejandro San Martín participate in a trip to Berlin in late 1890, alongside Luis Simarro Lacabra, Leopoldo López García, and Carlos María Cortezo, to visit Robert Koch (1843-1910), who had recently reported that tuberculin may be effective in treating tuberculosis, and to acquire from the German bacteriologist a tube of bacteria with which they could work in Madrid.[3,50,53-55] Robert Koch was awarded the Nobel Prize in Physiology or Medicine in 1905 "for his investigations and discoveries in relation to tuberculosis."[56]

Alejandro San Martín was admitted as a full member of the RANME on 28 January 1888, giving a speech entitled "Resultados en la cirugía experimental y clínica de las anastomosis arteriovenosas" (Results in experimental and clinical arteriovenous anastomosis surgery).[3] San Martín sought to ensure the implementation of Joseph Lister's (1827-1912) recommendations, and began advising students to study bacteriology before beginning their surgical training. Furthermore, he adopted aseptic and antiseptic methods, and methods to improve the posture of the surgeon in the operating theatre, suggesting that the theatre be adapted according to the type of intervention to ensure that the surgeon have optimal access to the surgical field and that the anaesthetic system be fully accessible to patients (see below). Alejandro San Martín was part of the select group of Spanish surgeons who personally met Lister (whom the former visited in Edinburgh and in London). He participated in international conferences between 1888 and 1898, arguing for the general implementation of Lister's antiseptic measures.[3] Furthermore, his uncle Basilio San Martín had introduced inhalation anaesthesia with ether in Spain (1847-1848), but Alejandro San Martín developed an anaesthesia method based on nasopharyngeal insufflation; once perfected, he published the technique in 1903.[57,58] As a surgeon, San Martín designed a method for valvular colostomy that maintained continence; performed osteoplasties after limb amputations (achieving a faster recovery); developed new forms of resection of tongue tumours, including removal of lymph nodes colonised by the tumour; and performed arteriovenous anastomosis procedures, which he had trialled experimentally and which were subsequently adopted by French surgeons, particularly Alexis Carrel (who was awarded the Nobel Prize in Physiology or Medicine in 1912 "in recognition of his work on vascular suture and the transplantation of blood vessels and organs"[59]) and the so-called Lyon School, as well as Spanish surgeons, particularly his former classmate Goyanes. According to several accounts, Cajal studied the histological aspects of his vascular anastomosis, although no articles were published on the subject.[3,60] In 1892, Alejandro San Martín, alongside Julián Calleja, Federico Olóriz, the Marquess del Busto, Mendoza, Cerrada, and Gil Saltor sat on the examining board for the competitive examinations to select a chair of histology at the Universidad Central; the board voted unanimously for Santiago Ramón y Cajal, who moved to Madrid, his last and longest destination. In Madrid, Cajal enjoyed access to a true, state-funded research laboratory, generating one of the most fruitful scientific schools of the history of biomedicine.[48,61-63] One of many curious anecdotes about Alejandro San Martín is the fact that, together with Cajal, José Gómez Ocaña, and Arturo Redondo, he sat on the committee that judged Pío Baroja's doctoral thesis "El dolor. Estudio de psicofísica" (Pain. A psychophysical study), which he defended on 27 May 1896.[64,65] Also in relation to neuroscience, Alejandro San Martín was a member of the committee that judged the thesis of Julio Perales García (a Valencian disciple of Luis Simarro[66,67]) in 1890; on 1906, he chaired the committee that judged the thesis of Nicolás Achúcarro Lund,[68] a distinguished member of the Cajal School.

San Martín, the neurosurgeon

As mentioned above, San Martín's first foray into the world of neurology was during his doctoral studies, dedicating his thesis to the relationship between the circulatory and nervous systems.[3,8] During his career, he particularly focused on such vascular problems as ischaemia and gangrene in the limbs, limb amputations, and arterial aneurysm surgery, always trialling surgical approaches before applying them in practice with his patients (this subject was recently reviewed by Vaquero et al.[69]). However, he sometimes treated neurosurgical problems, the main subject of interest for the present study.

San Martín was a pioneer in the detailed description of brain and ocular trauma, although this was included in the first volume of his unfinished work *Curso de patología quirúrgica* (Course on pathological surgery),[70] dedicated to traumatology. The same volume includes his innovative chapters on amputations, including his osteoplasty method, which consisted in covering the distal section of the sectioned diaphysis of long bones with a hard bone flap; this gives the resulting stump sufficient resistance to moderate or to completely eliminate pain,

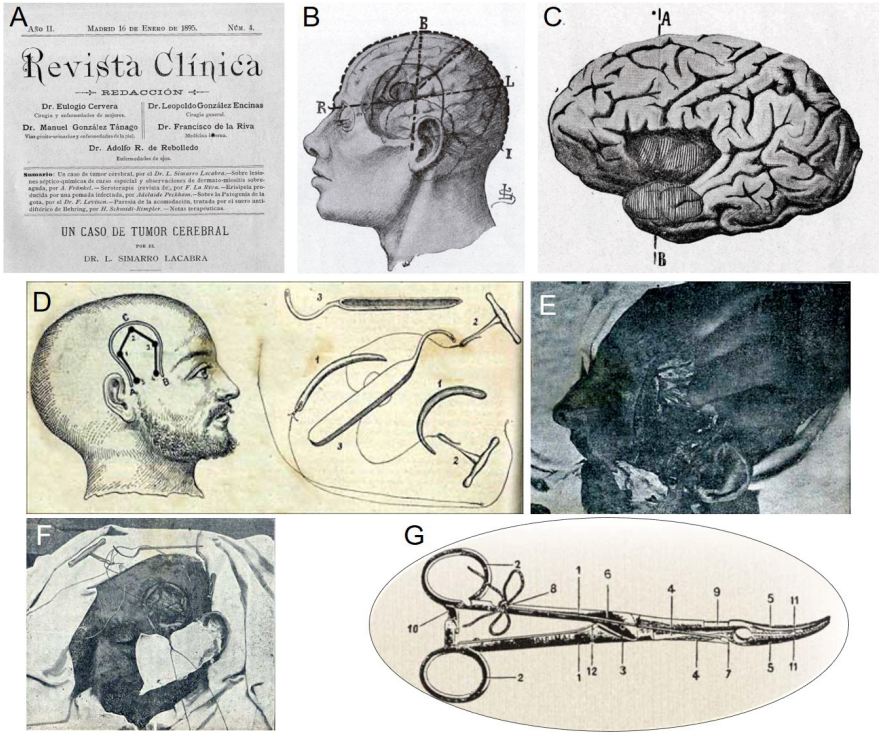

Figure 6. San Martín, the neurosurgeon. A) The issue of *Revista Clínica de Madrid* containing the title of the article by Luis Simarro, "Un caso de tumor cerebral" (A case of brain tumour), in which Alejandro San Martín performed the neurosurgical procedure. B) A drawing signed by Simarro (initials "LS," to the right), describing the location of the aforementioned tumour in the patient's head, shown in profile. C) The patient in fact had two brain tumours, as shown by the labels A and B. Images A-C are taken from the article by Simarro.[73] D) Diagram of the new "sphenoidal" approach proposed by San Martín for trigeminal neuralgia surgery, and the instruments used.[78] E) and F) Images from the interventions performed on cadavers. G) Drawing of a new model of surgical forceps designed by San Martín.[82]

prevents ulceration, and enables more stable placement of any necessary prostheses. San Martín reported that his method presented better outcomes in leg amputations than in forearm amputations; the technique was soon accepted by an international figure of the stature of Anton Freiherr von Eiselsberg, an Austrian surgeon living in Eiselsberg (Germany) and a leading disciple of Billroth.[3,50]

It was only a matter of time before San Martín became closer to Luis Simarro, with both men moving in the academic circles of Madrid. As noted above, they travelled together to Berlin in 1890, on the initiative of the government of Spain; San Martín was also a member of the thesis committee of one of Simarro's closest students. A work painted in 1897 by the master Joaquín Sorolla, *A research*, captures the laboratory that Simarro installed in his home, where he taught histological technique to selected guests and disciples. In the laboratory at his house on Calle del Arco de San Juan (today, Calle del Barquillo), in 1887, Simarro showed Cajal techniques including Golgi's *reazione nera*, a method that was fascinating and fickle in equal measures; Cajal soon mastered the technique and, thanks to his knowledge of photographic chemistry, was able to improve it, thus beginning his titanic work in neurohistology.[71] The scene would not have been very different from the one immortalised by Sorolla, although that was painted at Simarro's home laboratory at number 3, Calle del General Oráa, next-door to the home of Juan Madinaveitia Ortiz de Zárate (1861-1938)[72]: by the light of a table lamp, the neuropsychiatrist prepares a sample, surrounded by jars of different coloured reactants, watched by half a dozen interested spectators. Those standing closest to Simarro

are San Martín (in the background, nearly obscured by shadow) and Madinaveitia (in the foreground, wearing a black suit); the most distant, more rotund and shown in profile, is Miguel Gayarre y Espinal (1866-1936), a well-known member of the Spanish Neurological School from Pamplona.[63]

In 1894, Alejandro San Martín and Luis Simarro surgically treated a brain tumour in a 54-year-old man with complaints of vertigo that caused brief losses of consciousness, a condition that was subsequently complicated by postural and gait alterations, and aphasia (Figure 6A-C).[73,74] Although the patient was initially diagnosed with an atherosclerotic circulatory alteration, his sudden worsening and the onset of coma with severely impaired pupillary reflex led them to consider epileptic attacks secondary to a brain tumour. Given his general surgical experience, San Martín led the delicate procedure, as explained by Simarro in the article he published on the subject; the latter served as a secondary or assistant surgeon, although he participated in intraoperative decision-making. Following the previous description of Slocker de la Pola (1893), San Martín and Simarro carefully planned the anthropometric topography of the procedure, which Simarro illustrated by hand (Figure 6B)[73,74]: an initial trepanation through which they performed three punctures, which were unsuccessful, as they failed to locate the tumour. Several days later, they performed a second intervention with a thicker trocar, inserting it 6 cm and extracting approximately 15 mL of yellowish liquid, which was not found to be infectious; the patient improved, emerging from the coma and recovering the pupillary reflex, but died five days later after a second exacerbation. In the subsequent autopsy, the authors identified two tumours (Figure 6C): one below the insula lobe and the other in the temporal lobe, of which they also included a macroscopic illustration.[73] In a highly detailed study, Corral and Corral conclude that the tumours must be cerebral metastases with internal necrosis, as they are described as being well delimited to the brain parenchyma, and the patient's short survival time (barely four months) from the onset of symptoms clearly provoked by tumour growth "is consistent with what we would expect in brain metastases."[74] The fact that the autopsy was limited to the skull prevents us from identifying the primary tumour; we also lack any data from an anatomical pathology study, which would have been desirable and which Simarro probably intended to perform, as he announces in the published study that it is "to be continued."[73,74] As noted by these modern neurosurgeons, Luis Simarro never published any anatomical pathology results (if the study was ever performed), despite the fact that these studies were relatively frequent in the career of this neuropsychiatrist, who taught Cajal the Golgi method: he documented the procedures on at least two occasions.[55] Despite this, and more so than the clinical case in itself or the outcome of the intervention, the main interest of the report is probably the fact that it is one of the first published neurosurgical interventions performed in Spain.[74]

Alejandro San Martín is much better known for his novel methods for neurectomy of the trigeminal nerve (fifth cranial nerve) and Gasserian ganglion ("*ganglio de Gasserio*" was the antiquated nomenclature preferred by San Martín), published between 1900 and (posthumously) 1909.[75-78] In fact, these were a series of surgical cases and successive modifications that he published over the last years of his life. The first was a brief communication to the RANME, reporting a patient with trigeminal neuralgia, in whom he operated on the superior and inferior maxillary branches.[75]

From 23 to 30 April 1903, Madrid hosted the 14th International Congress of Medicine, where Cajal and Ivan Pavlov (who would win the Nobel Prize in Physiology or Medicine in 1904) were the stars of the show, a great recognition of the neurosciences.[79,80] Alejandro San Martín took the opportunity to present a communication, one of 1681 at the congress, reporting a novel surgical technique for treatment of facial neuralgia: in addition to the previous procedure, he resected the Gasserian ganglion with a new sphenoidal approach, a technique that he described in detail in an article published a couple of years later.[76] López Piñero identifies San Martín as a "typical follower of the pathophysiological mentality," as the surgeon from Navarre considered the purpose of surgery to be the restoration of function, where possible, not merely extirpation.[81] According to this view, given the pain normally caused by neuralgia of the fifth cranial nerve, and despite seeking where possible to follow his "pathophysiological" conception of surgery, San Martín proposed resection from the inside out, an improvement on the tympanic-zygomatic approach used at the time and which, in his opinion, offered six specific advantages over the surgery habitually used at the time: *1)* a larger hole in the bone prevented complications related to resection of the Gasserian ganglion and reduced the risk of compression due to accumulation of cerebrospinal

fluid; *2)* the surgeon had clear anatomical references available *de visu*, avoiding such complications as tears, damage to oculomotor nerves (and potentially muscles), and vascular lesions; *3)* the better surgical field also limited unnecessary bleeding, contributing to a better view of the Gasserian ganglion during the procedure; *4)* vascular compromise was reduced due to the lesser damage caused; furthermore, bleeding from affected vessels could be resolved through direct compression; *5)* the osteo-musculocutaneous flap could be placed with greater precision after completion of the resection; and *6)* subdural or subarachnoid drainage were possible, thus avoiding complications related to increased intracranial pressure.[76] It is perfectly possible to unify some of these conclusions under fewer headings.

His other two publications on neurectomies for the treatment of facial neuralgias appeared after his short-lived time as a government minister (see below): the first (a preliminary communication) was published in *El Siglo Médico*[77] and the second (somewhat more complete) appeared posthumously (Figure 6D-F).[78,82] In the latter publication, he describes how to apply gold to the foramen rotundum of the greater wing of the sphenoid bone, where the maxillary branch of the fifth cranial nerve exits the cranial fossa and enters the pterygopalatine fossa. This opening is secured with gold leaf, improving access for neurectomy of the second trigeminal branch.[78] This final publication is truly brief (just three pages long); it is unclear whether this is because the work was published posthumously and therefore was to some extent incomplete. Another posthumous work was even shorter: this publication described a new model of surgical forceps, and was included in the same issue of *Revista de Medicina y Cirugía Prácticas* (Figure 6G).[79]

There is no room for doubt of the recognition that San Martín enjoyed during his final years in Madrid, partly due to his studies related to neurology and neurosurgery, discussed here, despite his having been better known for his arteriovenous anastomoses (Figure 7A). Thanks to his great prestige, he was an official Spanish delegate at the 12th Congress of Surgery in Paris (1898), which influenced both his appointment to lead the Regional Ministry of Healthcare and Public Education in 1895, and to direct the Hospital Clínico of the Faculty of Medicine of Madrid (his beloved "old San Carlos") in 1900.[50] A remarkable group of students formed around San Martín, who were interested in pathophysiology, therapeutics, and, of course, surgery. Important members are Teófilo Hernando, Olivares, the Sánchez Covisa brothers, and Goyanes (Figure 7B), who was perhaps the closest to San Martín. The greatest disappointment in this period was probably the loss in 1902 of his revered uncle Basilio, who had opened so many doors for him in the medical and academic circles of Madrid (Figure 7C).

San Martín and Cajal… and San Martín, government minister

Given the neuroscientific focus of this study, and because the two men were contemporaries, we are obliged to review the relationship between San Martín and Cajal. As noted previously, Alejandro San Martín and Santiago Ramón y Cajal met during the competitive examination that led to the latter's selection for the chair in Madrid.[3,48] After moving to the capital, and at the pinnacle of academia in Spain at the time, Cajal decided to become closer to Alejandro San Martín, who presided over the famous Café Suizo group, where San Martín introduced the future Nobel laureate.[3,48] For both men, those gatherings were a distraction from the struggles of day-to-day life in the always difficult ecosystem of Spanish academia. Despite the great differences in their personalities, they became very close, largely due to the near-daily contact at the Faculty and in the restorative gatherings at Café Suizo. Without a doubt, Cajal admired the creativity and spiritual orientation of San Martín's ideas: ultimately, although they were dedicated to different disciplines, these were two points of connection for anybody interested in knowledge and research. However, Cajal also had great respect for the agreeableness and the manners of San Martín, from whom he said he had learnt some diplomacy over the years. Cajal was even sympathetic to the (apparently frequent) changes of mind and the doubts that San Martín raised on nearly all subjects: "He who doubts is not he who wishes to, but he who is able to."[48]

Alejandro San Martín always expressed clear views about university politics and education in general.[3] For instance, he was opposed to the dispersion of disciplines, the excessive atomisation of chairs that, alongside hyperspecialisation, also resulted in a loss of hierarchy and dispersion of power, with all the ensuing consequences. Due to his prestige and these clear ideas, he was elected to represent the Universidad Central in the Senate. He was first elected in 1898, and again in 1899 (both with relatively close results); in 1901, he won a landslide against his only opponent, Cajal, with 184 votes to 1 (188 electors), and also achieved very good results in 1905 and 1907.[83]

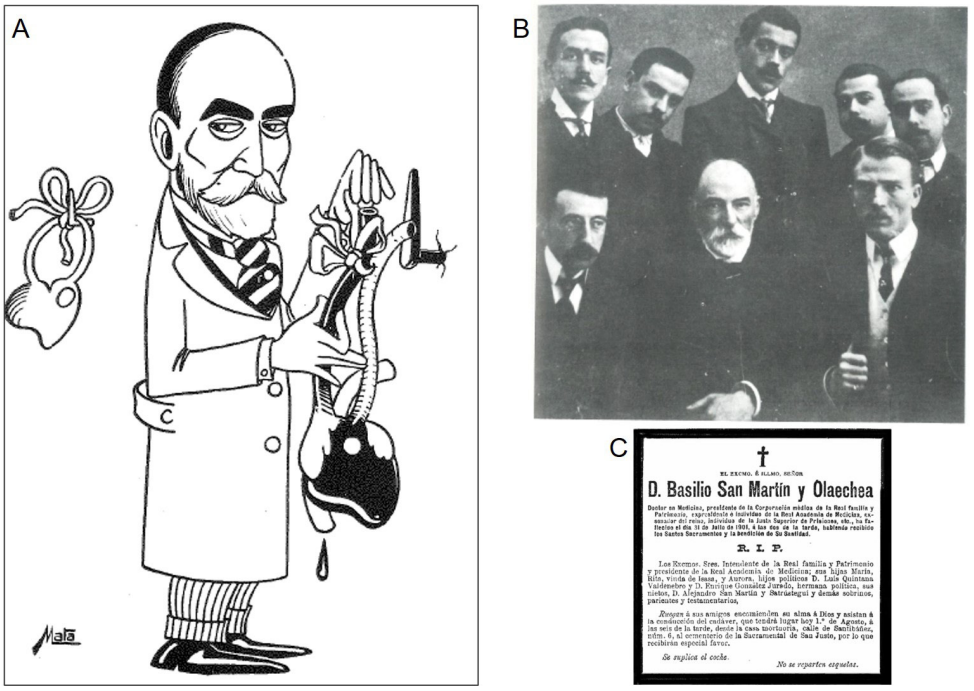

Figure 7. Alejandro San Martín, famous chair at the Universidad Central de Madrid. A) Caricature of San Martín as a pioneering vascular surgeon. B) San Martín with some of his disciples in the last medicine course. Back, from left to right: Teófilo Hernando, Laureano Olivares, unknown (centre), and the brothers José and Isidro Sánchez Covisa; front row, from left to right: Agustín del Cañizo García, Alejandro San Martín (now with very white hair and beard), and José Goyanes, without a doubt his closest disciple. C) Obituary of Basilio San Martín Olaechea, the uncle of Alejandro San Martín, who is listed among the former's nephews and other signatories.

As the Senate representative of the Universidad Central, San Martín was charged with delivering a speech when the institution decided to honour Cajal for winning the Moscow Prize, which he was awarded in 1900. No information is available on whether a similar session was held after Cajal was awarded the Helmholtz Gold Medal by the German National Academy of Sciences Leopoldina in 1905, despite the fact that, at the time, it was seen as the most distinguished scientific award, the most prestigious and elitist, a view also held by Cajal, at least until the First World War.[48] As senator, San Martín was once more charged by the faculty of "old San Carlos" with giving the official speech at the session honouring Cajal when he was awarded the Nobel Prize in Physiology or Medicine in 1906. San Martín advocated for Spain to follow the example of German universities, which did not limit the number of students in lectures; he cited the examples of Waldeyer and Helmholtz, who taught up to 300 or 700 students in a single course, or even the 200 per semester that Bergman received in his surgical clinic. He sought to reclaim for the Spanish universities of the day the same "universal" status of lecture theatres in the 16th and 17th centuries, the period of the greatest comparative development in the country's history.[84] San Martín argued that Spanish institutions should also follow the German example with respect to the organisation of universities ("teaching requires freedom in order that we may obtain the results achieved in Germany") and establish categories of universities ("but each university must be provided resources corresponding to its location, category, and mission […] in Germany there are modest universities, with faculties of 6 or 8 lecturers, whereas the university of Berlin has 14 chairs in the Faculty of Medicine and 12 in the Faculty of Law"), and thus progress beyond the

equally small number of chairs: "In Spain there are 500 university chairs. Can Spanish culture only produce 500 university masters? It appears to be so!"[84]

These ideas played a determinant (but indirect) role in the development of science in Spain. Because Cajal, when he was awarded the Nobel Prize, was also invited to join the government of Spain, by his friend and fellow member of the Ateneo de Madrid, Segismundo Moret (1833-1913), a liberal from Cádiz who on 1 December 1905 became Prime Minister, replacing Montero Ríos, also a liberal. Moret had initially appointed Vicente Santamaría de Paredes as Minister of Public Instruction and Fine Arts, but offered Cajal the position in an early reshuffle. The pair met and discussed the reforms that the country needed. They had known one another for years; the liberal politician was already a minister when, in 1899, Cajal was commissioned to create and direct the Instituto de Sueroterapia, Vacunación y Bacteriología de Alfonso XIII (renamed the Instituto Nacional de Higiene Alfonso XIII in 1908), "his [Cajal's] most direct intervention in Healthcare," in the words of the director general of healthcare at the time, Dr Carlos María Cortezo (these institutions also represent the true origin of the future Ministry of Health).[85,86] Cajal's apparent uncertainties dissipated after a congress in Lisbon: "Here you have San Martín, who is better prepared than I in matters of education."[48]

San Martín accepted the ministerial position, assuming the role on 6 June 1906 (Figure 8A and B). Even for a person with an undeniable political calling, such as San Martín, Cajal's suspicions were confirmed: Alejandro San Martín served only briefly as a minister, as exactly a month after his appointment, on 7 July 1906, the king accepted the resignation of the prime minister, Segismundo Moret, and the rest of the cabinet, including San Martín, writing that

> I hereby accept the resignation of Alejandro San Martín y Satrústegui as Minister of Public Instruction and Fine Arts, having been most satisfied with the zeal, intelligence, and loyalty with which he served.
>
> Issued by the Palace […] on the sixth of June, 1906.[87]

San Martín soon published a short book entitled *Mi paso por el Ministerio de Instrucción Pública* (My passage through the Ministry of Public Instruction), portraying his brief experience at the ministry, describing both the ideas that became orders and those that remained outstanding (Figure 8C).[88]

Cajal was notified on 25 October 1906 that he would be awarded the Nobel Prize, which he received personally from the king of Sweden at a ceremony in Stockholm on 10 December of the same year.[48,84] Cajal did not waste the occasion, and proposed the creation of the Junta para la Ampliación de Estudios e Investigaciones Científicas (JAE; Council for the Extension of Studies and Scientific Research); events moved rapidly and king Alfonso XIII signed the Royal Decree founding the JAE on 11 January 1907, which included a distinguished cast of personalities from all disciplines, including Cajal, Alejandro San Martín, and Luis Simarro.[89] The prime minister who worked that miracle was Marquess de la Vega de Armijo.[86] The latter, who led the last of the series of five short-lived liberal governments (Montero Ríos, Moret, López Domínguez, Moret once more, and Marquess de la Vega de Armijo), lasted only two months, but for the simple fact of having established the JAE in record time, he merits a place as one of the greatest (and most effective) politicians in the history of Spain. This clearly demonstrates how where there is a will, there is a way. Predictably, the members of the JAE selected Cajal to be president, and the body's decisions were guided by his judgement until 1934. Alejandro San Martín and Luis Simarro, the central figures in this work, were appointed members of the first JAE, alongside José Echegaray (winner of the Nobel Prize in Literature in 1904), Marcelino Menéndez Pelayo, Joaquín Sorolla, Joaquín Costa, Vicente Santamaría de Paredes, Julián Calleja, Eduardo Vincenti, Gumersindo de Azcárate, Ignacio Bolívar, Ramón Menéndez Pidal, José Casares Gil, Adolfo Álvarez-Buylla, José Rodríguez Carracido, Julián Ribera y Tarragó, Leonardo Torres-Quevedo, José Marvá, José Fernández Jiménez, and Victoriano Fernández Ascarza.[89] The JAE's main task was selecting the most promising representatives of the different scientific and technical disciplines and any area of human creativity in general, and to assist them in furthering their training in Spain and particularly at foreign centres at the leading edge of their respective branches.

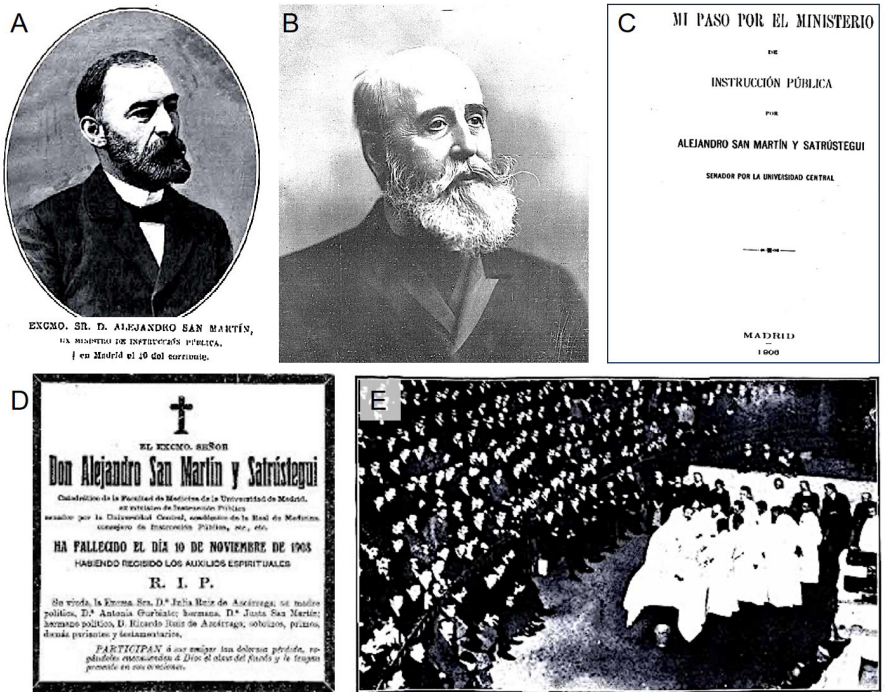

Figure 8. San Martín, minister and final years. A) Official portrait of Alejandro San Martín as Minister of Public Instruction, widely reproduced in the press at the time. B) Segismundo Moret, the liberal politician who included San Martín in his government. C) Front page of San Martín's book *Mi paso por el Ministerio de Instrucción Pública* (My passage through the Ministry of Public Instruction), which he signed as senator of the Universidad Central.[88] D) Press obituary of Alejandro San Martín. E) Autopsy room at the Faculty of Medicine, where Alejandro San Martín's autopsy is performed before a large audience.

After returning to Spain, they would implement their learnings at Spanish institutions, driving the development of Spanish society, which yearned to rise above the calamity of the 19th century, which had culminated with the so-called "disaster of 98." Resisting the temptation (which for him was never great) of taking an active role in politics, Cajal convinced the authorities to create two institutions through which he could have a decisive and active influence to improve Spanish society, the Instituto Nacional de Higiene Alfonso XIII and the JAE; these bodies showed a deep Cajalian imprint, and were directed by the founder of modern neuroscience until his retirement and death, respectively.

His health undermined by a case of tuberculosis that dragged on for decades, Alejandro San Martín died in November 1908 due to an intestinal problem that led to a disseminated infection, with the fatal outcome occurring a few days later (Figure 8D).[3,50] A passionate instructor, he requested that his body be donated to the university's chair of anatomy. His autopsy, really a mere formality, was performed by Florencio de Castro (1848-1928), chair of anatomical technique and author of a commendable manual on dissection,[90] the anatomist Julián Calleja (1836-1913, characterised by Cajal as "the dictator of San Carlos"), and, as an intern under that chair, Gregorio Marañón Posadillo (1887-1960); the brain was removed and given to Cajal for study (Figure 8E). In his will, he bequeathed different sums to the Instituto de Pamplona, the Instituto de San Isidro, and the Hospital of the Faculty of Medicine of Madrid, and left his significant library and surgical and scientific instruments to his

disciples (who, in turn, agreed that the library be moved to the Faculty of Medicine of the Universidad Central).[50]

Discussion

On his own merits, Alejandro San Martín was one of the physicians who developed the structure of Spanish academia in the final quarter of the 19th century, a process of modernisation that reached its zenith with Santiago Ramón y Cajal. The work of the JAE continued, with more or less steady growth, until the outbreak of the Spanish Civil War. San Martín is often cited alongside Cajal, the physiologist José Gómez Ocaña, Federico Olóriz, and a vague, indeterminate, and highly variable number of "others" in the generation of the 1880s, called "generation of the wise" by Laín Entralgo[91]; this grouping sometimes seems contrived, given the disparities in the different members' contributions to global knowledge, from the titanic contribution made by Cajal, who founded modern neuroscience, to others of which, with the passage of time, nothing remains. Alejandro San Martín Satrústegui specialised in surgery, influenced by the anatomist Juan Fourquet[7] and by Melchor Sánchez de Toca, physician-surgeon in the court of Isabella II and the first Marquess of Toca, and to a considerable extent by his own uncle, Basilio San Martín Olaechea. He was the first Spanish professor of surgery to include surgical pathophysiology in his courses.[3,8,50,60] Thus, not only did he form a surgical school including such highly distinguished names as José Goyanes and Laureano Olivares, but his pathophysiological approach to surgery left an imprint on clinicians of the stature of the internist Gregorio Marañón (who published his first work as a medical student: some 200 pages of notes on surgical pathology, taken during lectures by the chair, Dr San Martín, the same year that he died[92]), the dermatologist José Sánchez-Covisa, the psychiatrist César Juarros, and the influential pharmacologist Teófilo Hernando.[3,8,60,93] Part of this influence was due to his personality, which Cajal so admired: San Martín was a talented, brilliant, ingenious gentleman, who never missed an occasion, but was generally well-intentioned; as was so frequent in 19th-century Spain, he had great erudition, masterfully summarised by Cajal as "a man of many books" in an undated, handwritten letter conserved at the National Library of Spain under code MS/23308/63 in the General Catalogue, entitled "Some aspects of the psychology of Alejandro San Martín." Given the document's initial description, it was clearly written for some occasion honouring San Martín after his death, probably in 1908. The letter demonstrates Santiago Ramón y Cajal's affection for his friend San Martín.[48,93]

In fact, this admiration is largely responsible for San Martín's impact in the lasting 21st century. Several interesting parallels may be noted between the two men: both were born in towns in the kingdom of Navarre (San Martín in Larráinzar and Cajal in Petilla de Aragón); both were the sons of second-class surgeons who prospered and travelled throughout their lives, although Mariano San Martín arrived much earlier in a large city, Madrid, than Justo Ramón: this difference was doubtless related to the fact that San Martín had relatives who opened doors for him (his great-uncle José Martínez San Martín, who reached the rank of captain general in the army, and his uncle Basilio San Martín, who became president of the RANME), an advantage that Cajal did not enjoy. San Martín had an undeniable way with people that made him easily stand out in society, and was proficient in several languages, which facilitated relations with the great physicians of the day, such as Lister and Koch (from Britain and Germany, respectively), and repeatedly earned him positions in delegations officially representing Spanish institutions at congresses and other important meetings. Cajal, on the other hand, had barely conversational French, with which he dragged August Kölliker to his microscope to show him his revelatory histological preparations at the famous congress of the German Anatomical Society held in Berlin in 1889[48]: without the latter's conversion into little less than his prophet, the enthusiasm with which Cajal's studies were received may have taken longer to appear. This apparent coarseness and lack of sociability sometimes served as a shelter for the father of neurosciences, such as when San Martín entered the cabinet of the Moret government. Obviously, his great social skills, largely derived from having literally devoured the knowledge of others (normally abroad) until he dominated it, had to involve some negative consequences. It is logical that this form of dissipation, sometimes appearing febrile, so characteristic of those Spanish university professors throughout nearly the entirety of the 19th century, led the surgeon San Martín to touch on diverse areas, including neurosurgery, but meant that he was slow to publish his results (once more, we may cite the example of the neurosurgical techniques analysed above) and/or did so in ways that were already old-fashioned at the time, for example publishing articles in small Spanish journals or in books

printed in small runs, with practically no impact beyond Madrid's medical circles. Cajal, on the other hand, though he began publishing his results in even more modest outlets (*Revista Trimestral Micrográfica* was edited and distributed by Cajal himself, with his own funds), always made efforts to ensure they had the broadest reach within his limited possibilities. For instance, he forwarded the journal by post to the most relevant research institutions of the day; furthermore, the journal's resources and circulation grew in Madrid, and he was eventually able to secure its near-complete publication in French for over 20 years. This contributed decisively to increasing the international impact of the Spanish neurological school.[63]

Conflicts of interest

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References

1. Rodríguez de la Torre F. José Martínez de San Martín. In: Diccionario biográfico español, Vol. XXXIII: de "Martín Díez" a "Matos y Massieu". Madrid: Real Academia de la Historia; 2012.
2. Senado de España [Internet]. Madrid: Senado de España; 2020. San Martín y Olaechea, Basilio; [cited 3 Feb 2024]. Available from: https://www.senado.es/web/conocersenado/senadohistoria/senado18341923/senadores/fichasenador/index.html?id1=2640
3. Palma Rodríguez F. Vida y obra del doctor Alejandro San Martín Satrústegui. San Sebastián (ES): Sociedad Vasca de Historia de la Medicina; 1997.
4. González de la Lastra L. Instrumentos científicos antiguos en el Instituto San Isidro: recuperación y contextualización. Arbor. 2011;749:561-71.
5. Navarro Jurado A. Historia del Instituto de Segunda Enseñanza San Isidro de Madrid (1845-1936). Madrid: Universidad Complutense de Madrid; 1992.
6. Ribera Sans J. Biografía de Alejandro San Martín y Satrústegui. Madrid: Est. Tip. de la viuda e hijos de M. Tello; 1909.
7. San Martín Satrústegui A. El doctor Fourquet. In: La España del siglo XIX: colección de conferencias históricas celebradas durante el curso de 1885-86. Madrid: Librería de don Antonio San Martín; 1886.
8. Goyanes Capdevila J. El Dr. D. Alejandro San Martín. Rev Iberoam Cien Méd. 1908;20(51):321-6.
9. Goyanes Capdevila J. San Martín y su obra. Madrid: Artes Gráficas Plus-Ultra; 1920.
10. San Martín A. La Real Academia de Medicina y los facultativos de segunda clase. La Aspiración Médica. 1868 May 8.
11. San Martín A. El cuerpo de Beneficencia Municipal. La Aspiración Médica. 1868 Dec 23.
12. Archivo Histórico Nacional. Catalogue number: Universidades, file 1691/22.
13. Archivo de la Real Academia Nacional de Medicina de España. File 22/99.
14. Archivo General de la Administración. Box no. 16729.
15. López Piñero JM. Diccionario histórico de la ciencia moderna en España. Vol. II. Barcelona: Península; 1983. Aureliano Maestre de San Juan; p. 11-12.
16. Ossorio y Bernard M. Ensayo de un catálogo de periodistas españoles del siglo XIX. Madrid: Imprenta y Litografía de J. Palacios; 1903.
17. Espinosa-Sánchez JM, de Castro F. ¿Por qué Kallmann y no Maestre de San Juan? Historia y novedades de una enfermedad olfativa prototípica. Lecture presented at: VIII Jornadas Olfativas; 2022 May 4-7; La Franca, Spain.
18. Maestre de San Juan A. Teratología: falta total de los nervios olfatorios con anosmia en un individuo en quien existía una atrofia congénita de los testículos y miembro viril. El Siglo Médico (Madrid). 1856;3:211-21.
19. de Castro F, Seal R, Maggi R. ANOS1: a unified nomenclature for Kallmann syndrome 1 gene (*KAL1*) and anosmin-1. Brief Funct Genom. 2017;16:205-10.
20. San Martín A. Enfermedad de Azañón. El Siglo Médico. 1873;20:82-6.
21. Lázaro Adradas C. La enfermedad de Azañón. El Siglo Médico. 1873;20:231-2.
22. Virchow R. Ueber eine Gehirn und Rückenmark des Menschen aufgefundene Substanz mit der chemischen Reaction der Cellulose. Arch Pathol Anat Physiol Klin Med. 1854;6:135-8.
23. Catola G, Achúcarro N. Über die Entstehung de Amyloidkörperchen im Zentralnervensystem. Virchows Arch Path Anat. 1906;184:454-69.
24. Tremblay MÈ, Lecours C, Samson L, Sánchez-Zafra V, Sierra A. From the Cajal alumni Achúcarro and Río-Hortega to the rediscovery of never-resting microglia. Front Neuroanat. 2015;9:45. doi:10.3389/fnana.2015.00045.
25. Lafora GR, Gluck B. Beitrag zur Histopathologie der myoklonischen Epilepsie. Z Ges Neurol Psychiatr. 1911;6:1-14.
26. Riba M, Augé E, Campo-Sabariz J, Vilaplana J. *Corpora amylacea* act as containers that remove waste products from the brain. Proc Natl Acad Sci U S A. 2019;116(51):26038-48.
27. Virchow R. Die Cellularpathologie in ihrer Begründung auf physiologische und pathologische Gewebelehre. Berlin: August Hirschwald; 1858.
28. von Lenhossék M. Zur Kenntnis der Neuroglia des menschlichen Ruckenmarkes. Verh Anat Ges. 1891;5:193-221.
29. Giménez-Roldán S, Spencer PS. Azañón's disease. A 19th century epidemic of neurolathyrism in Spain. Rev Neurol (Paris). 2015;172(12):748-55.

30. Giménez-Roldán S, Palmer VS, Spencer PS. Lathyrism in Spain: lessons from 68 publications following the 1936-39 Civil War. J Hist Neurosci. 2023;32(4):423-55.
31. Cantani A. Latirismo. Lezione clinica. Morgagni. 1873;15:602.
32. Cantani A. Latirismo (lathyrismus) illustrate de tre casi clinici. II. Morgagni. 1873;15:754-65.
33. Fernández Sanz E. Dos casos de latirismo. An Real Acad Nac Med. 1916;36:238-9.
34. Fernández Sanz E. Contribución a la historia del latirismo en España. An Real Acad Nac Med. 1917;37:667-72.
35. García Izcara D. El latirismo de los animales domésticos. An Real Acad Nac Med. 1917;37:282-3.
36. Marie P. Des manifestations médullaires de l'ergotisme et du lathyrisme. Progr Méd. 1883;11:64-6.
37. Marie P. Lathyrisme et béribéri. Progr Méd. 1883;11:842-5.
38. Marie P, Londe P. Des manifestations médullaires de l'ergotisme et du lathyrisme. Progr Méd. 1883;11:83-7.
39. Ley E, Oliveras de la Riva C. Primera comunicación sobre una epidemia de latirismo. Rev Clin Esp. 1941;6:1-30.
40. Paissios CS, Demopoulos T. Human lathyrism. A clinical and skeletal study. Clin Orthop. 1962;23:236-49.
41. Getahun H, Lambein F, Vanhoorne M, Van der Stuyft P. Pattern and associated factors of the neurolathyrism epidemic in Ethiopia. Trop Med Int Health. 2002;7:118-24.
42. Wagner E. Compendio de patología general. Madrid: Librería Alfonso; 1872.
43. San Martín A. La terapéutica individual y social. Su pasado, su presente y su provenir. Discurso leído en la sesión inaugural de la Real Academia de Medicina de Cádiz. Madrid: Imprenta Suc. Rivadeneyra; 1875.
44. San Martín A. Estudios de materia física médica: ensayo de sistematización de las especialidades terapéuticas aeroterapia, hidroterapia, electroterapia, atmiátrica. Madrid: Imprenta, Estereotipia y Galvanoplástica de Aribau y C.ª (suc. De Rivadeneyra); 1880.
45. San Martín A. Valor curativo de la naturaleza en las enfermedades. Discurso leído en la Real Academia de Medicina para la recepción pública de Académico. Madrid: Tipografía de E. Teodoro; 1880.
46. López Rodríguez AF. Historia de la electroterapia: lección inaugural del curso académico 2022-2023. Ponferrada (ES): Universidad de León; 2023. Available from: https://buleria.unileon.es/bitstream/handle/10612/15209/Historia_Electroterapia.pdf?sequence=1&isAllowed=y
47. de Andrés Martín JR. Trayectoria política del doctor San Martín y Satrústegui. Príncipe de Viana. 2000;221:751-78.
48. Cajal SR. Recuerdos de mi vida. 3rd ed. Madrid: Imprenta Juan Pueyo; 1923.
49. Cajal SR. Sobre las fibras nerviosas de la capa molecular del cerebelo. Rev Trim Histol Norm Patol. 1888;1:33-49.
50. Merino Peinado A. A la memoria de D. Alejandro San Martín. Med Cir Guerra. 1959;1:35-40.
51. Cajal SR. Estudios sobre el microbio vírgula del cólera y las inoculaciones profilácticas. Zaragoza (ES): Tipografía Hospicio Provincial; 1885.
52. Gaceta de Madrid. 1885 Jul 30;211:299-318. Available from: https://www.boe.es/gazeta/dias/1885/07/30/pdfs/GMD-1885-211.pdf.
53. Cortezo CM. D. Alejandro San Martín. El Siglo Médico. 1908;59:273.
54. Cortezo CM. Cajal: su personalidad, su obra, su escuela. Madrid: Imp. Suc. Enrique Teodoro; 1922.
55. Campos-Bueno JJ. El encuentro de Cajal y Simarro en el Arco de Santa María. Neurosci Hist. 2021;9(4):174-96.
56. The Nobel Prize [Internet]. Stockholm: Nobel Prize Outreach; ©2025. Robert Koch - facts [cited 2 Feb 2024]. Available from: https://www.nobelprize.org/prizes/medicine/1905/koch/facts/.
57. San Martín A. La insuflación nasofaríngea en la anestesia general. Rev Med Cir Práct. 1903;76(863):1-17.
58. San Martín A. Las actitudes operatorias en relación con la anestesia. Rev Med Cir Práct. 1903;76(863):17-21.
59. The Nobel Prize [Internet]. Stockholm: Nobel Prize Outreach; ©2025. Nobel Prize in Physiology or Medicine 1912; [cited 2 Feb 2024]. Available from: https://www.nobelprize.org/prizes/medicine/1912/summary/.
60. Goyanes Capdevila J. Labor científica del Prof. San Martín. El Siglo Médico. 1925;76(3746):224-7.
61. de Castro F. Cajal y la Escuela Neurológica Española. Madrid: Complutense; 1981.
62. Andres-Barquin PJ. Santiago Ramón y Cajal and the Spanish School of Neurology. Lancet Neurol. 2002;1(7):445-52.
63. de Castro F. Cajal and the Spanish Neurological School: neuroscience would have been a different story without them. Front Cell Neurosci. 2019;13:187. doi:10.3389/fncel.2019.00187.
64. Baroja P. El dolor: estudio de psico-física. Salamanca (ES): Real Academia de Medicina de Salamanca; 1980.
65. Fernández Martínez MP. "El dolor" en Pío Baroja: análisis de una tesis. In: Actas del XIII Congreso de la Asociación Internacional de Hispanistas. Vol. II. 2000:170-6.
66. Campos Bueno JJ. Influencia de Simarro en la obra de Cajal: la tesis de Julio Perales y García. Rev Hist Psicol. 2004;25:23-30.
67. Vera Sempere F. Julio Perales García, un discípulo valenciano de Luis Simarro. Neurosci Hist. 2024;12(1):30-45.
68. Ezpeleta D, Morales F, Giménez-Roldán S. Nicolás Achúcarro y la histopatología de la rabia: una invitación histórica de Nissl y Alzheimer. Neurosci Hist. 2019:7(4):122-36.
69. Vaquero C, del Río L, García Rivera E, Brizuela JA, San Norberto E. Las curiosas aportaciones a la cirugía vascular de Alejandro San Martín y Satrústegui (1847-1908). Rev Iberoam Cir Vasc. 2020;8(3):145-50.
70. San Martín A. Curso de patología quirúrgica. T. I. Traumatología. Madrid: Estab. Tip. de los Sucesores de Rivadeneyra; 1893.
71. de Castro F. El arte que alumbró la moderna neurociencia: el dibujo científico de Cajal y sus discípulos. Kranion. 2021;16:146-58.
72. Campos-Bueno JJ. Art and science in Sorolla's painting *A research* in Dr. Simarro's lab. Psychol Latina. 2010;1:9-26.

73. Simarro Lacabra L. Un caso de tumor cerebral. Rev Clin (Madrid). 1895;2:49-56, 65-7.
74. Corral I, Corral C. Bibliografía clínica de Luis Simarro: un caso de tumor cerebral, 1895. Neurosci Hist. 2017;5(4):114-22.
75. San Martín A. Comunicación acerca de un caso de resección del nervio trigémino. An Real Acad Med. 1900;20:207-8.
76. San Martín A. Escisión esfenoidal de dentro afuera en la extirpación del ganglio de Gasserio. El Siglo Médico. 1905;52(2669):71-5.
77. San Martín A. Neurectomía del trigémino. El Siglo Médico. 1907;54:444-5.
78. San Martín A. Neurectomía de la segunda rama del trigémino con orificación del agujero redondo mayor. Nuevos datos anatómicos. Rev Med Cirug Práct. 1909;1097:172-5.
79. García-Albea Ristol E, García-Albea Martín J. El auge mundial de las neurociencias: XIV Congreso Internacional de Medicina (Madrid, 1903). Rev Neurol. 2010;50(9):551-7.
80. Campos-Bueno JJ, Martín-Araguz A. Neuron doctrine and conditional reflexes at the XIV International Medical Congress of Madrid of 1903. Psychol Latina. 2012;3(1):10-22.
81. López Piñero JM. Alejandro San Martín Satrústegui (1847-1908). Mente y Cerebro. 2006;19:7-10.
82. San Martín A. Nuevas pinzas quirúrgicas. Rev Med Cirug Práct. 1909;1097:175-81.
83. Archivo del Senado. Bundle 413, file no. 6-1 & 6-3; bundle 413, file no. 6-02 & 6-06; bundle 413, file no. 6:7; bundle 413, file no. 6:11; bundle 413, file no. 6:15; bundle 413, file no. 6:19.
84. Diario de Sesiones del Senado. 1903 Jun 22;467-8.
85. Cortezo CM. Cajal: su personalidad, su obra, su escuela. Madrid: Imp. Suc. Enrique Teodoro; 1922.
86. Serrano Sanz JM. Maduración y triunfos del "sabio popular". In: Jiménez Schumacher A, Serrano Sanz JM, eds. Santiago Ramón y Cajal: el hombre, el científico, el intelectual. Zaragoza (ES): Prensas de la Universidad de Zaragoza; 2023.
87. Gaceta de Madrid. 1906 Jul 7;188:93-108. Available from: https://www.boe.es/diario_gazeta/comun/pdf.php?p=1906/07/07/pdfs/GMD-1906-188.pdf
88. San Martín Satrústegui A. Mi paso por el Ministerio de lnstrucción Pública. Madrid: [s.n.]; 1906.
89. Gaceta de Madrid. 1907 Jan 15;15. Available from: https://boe.es/datos/pdfs/BOE//1907/015/A00167-00167.pdf
90. de Castro y Latorre F. Manual de disección. Madrid: Manuel Rodríguez; 1877.
91. Laín Entralgo P. Españoles de tres generaciones. Madrid: Real Academia de la Historia; 1998.
92. Marañón G. Lecciones de patología quirúrgica tomadas en la cátedra del Dr. Alejandro San Martín, curso 1907-1908. Madrid: Vidal; 1907.
93. Herrera Rodríguez F. Un cirujano y humanista singular: Alejandro San Martín y Satrústegui (1847-1908). Llull Rev Soc Esp Hist Cienc Tec. 2009;32:386-97.