### Dr Enrique de Areilza, a protoneurosurgeon in Bilbao

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#### ABSTRACT

Dr Enrique de Areilza was highly influential in Bilbao at the turn of the 20th century, as he participated in the development of several relevant institutions.

He spent most of his career at the Miners' Hospital of Triano, where he displayed not only exceptional surgical skills but also a strong inclination for science, making very early contributions in the fields of traumatic brain injury and epilepsy surgery.

This article addresses Areilza's pioneering contributions to neurology and neurosurgery; at that time, no neurosurgical interventions had yet been performed in the main Spanish hospitals. He was well informed about the novel interventions performed in Great Britain, France, and Germany. He had considerable neurological expertise and performed meticulous neurological examinations of his patients. He was fervently dedicated to advancing the theory of cerebral and spinal localisation, with a view to applying it to surgery. He achieved little success in the study of clinical-anatomical correlations in traumatic injuries; this, together with the poor outcomes of the first epilepsy surgeries, might explain why Areilza did not operate on tumours or other brain lesions.

#### **KEYWORDS**

Areilza, Bilbao Academy of Medical Sciences, cerebral localisation, neurosurgery, spinal cord localisation

#### Introduction

The figure of Dr Areilza has been explored in a number of articles.<sup>1-5</sup> Two of these<sup>1.5</sup> provide a brief summary of some of his articles. García-Molina and Enseñat-Cantallops<sup>6</sup> published in this journal an extensive study on one of Areilza's works on post-traumatic delirium and its potential association with frontal lobe functioning and injury. Another recent study<sup>7</sup> listed all of Areilza's articles and written works that are accessible today, and also provides an overview of his life and a brief analysis of his personality. Apart from the articles mentioned previously by other authors,<sup>1,5,8,9</sup> this study analyses other works found during a comprehensive review of all issues

Corresponding author: Dr Juan José Zarranz E-mail: jj.zarranz@hotmail.com of *Gaceta Médica del Norte* (*GMN*) (between 1881 and 1926), the official publication of the Bilbao Academy of Medical Sciences (ACMB, for its Spanish initials), an institution with which Areilza cooperated at the time.

The purpose of this article is to provide a more detailed analysis of Areilza's contributions to the fields of neurology and neurosurgery, based on his experience in the most inconceivable setting, the miners' hospital in the small village of Triano in the Basque Country.<sup>10</sup> In fact, it is this neurosurgical interest, forged very soon after Areilza performed his first intervention according to the novel procedure developed in other countries, that best reflects the striking precocity and peculiar personality of this Spanish protoneurosurgeon.

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#### Material and methods

The information used in this article was gathered from the works cited in the references section. The author also reviewed all issues of *GMN* (later called *Revista Clínica de Bilbao*), the official publication of the ACMB, from 1895 (first volume) to 1926, the year that Areilza died, to collect scientific articles published by Enrique de Areilza as well as his oral presentations at conferences. Regrettably, *GMN* ceased publication between the second semester of 1896 and 1899 "due to a lack of resources"; this period coincides precisely with Areilza's time as president of the ACMB.

The companion article<sup>7</sup> lists all of Dr Areilza's written works, as well as his most relevant oral presentations at the sessions of the ACMB, combining the articles cited by Guimón,<sup>1</sup> Vitoria,<sup>5</sup> Alegría,<sup>8</sup> and Díaz-Rubio<sup>9</sup> with those found after a review of all issues of *GMN*.<sup>7</sup> Some of his most relevant works were published in Barcelona, although Areilza is not known to have had any special connection with Catalan institutions.

#### Results

#### Brief biography of Dr Areilza

Enrique de Areilza (Figure 1) was born in 1860 on Calle San Francisco, in the village of Abando, a few years before it was absorbed by Bilbao. His father, Julián, was an *albaitari* ("veterinarian" in Basque) and was from the rural Carlist aristocracy of the villages of Zeanuri and Zeberio. He had moved to Bilbao to manage a hardware store. Areilza's mother, Ramona Arregui, was a strict Catholic. Enrique spent his childhood and adolescence in a suburb near the mines, located uphill from Bilbao's old town, which was next to the estuary. Julián died when Enrique was six years old, but the family managed to carry on with the help of Miguel de Areilza, one of Enrique's uncles, a Carlist marshal who was exiled in France.

After finishing school, Enrique moved to Valladolid to study medicine. These years of his life were analysed in detail in a recent study.<sup>11</sup> He stood out from an early age. Between 1876 and 1879, after passing a competitive examination, he practised as a clinical clerk at the surgical department of Prof. Nicolás de la Fuente Arrimadas, who exerted a fundamental influence on Areilza's medical training, and later directed his doctoral thesis. Judging by the outstanding surgical skills he displayed soon after completing his medical degree, we may assume that



Figure 1. Portrait of Dr Areilza in adulthood. Source: Banco de Imágenes de la Medicina Española. Real Academia Nacional de la Medicina Española.

he made good use of his clinical clerkship. A brilliant student, Areilza was awarded his medical degree with special distinction. He furthered his training for a little over a year, attending courses taught by Joseph François Polaillon (1837-1902) and Léon Athanase Gosselin (1815-1887) at the hospitals of La Pitié and La Charité, in Paris. This period was crucial in opening Areilza's mind to European liberal trends and in his decision to break away from his mother's religious beliefs. He began to show an interest in other disciplines, including oriental religions and Charcot's use of hypnosis.

In 1880, he earned his doctorate with special distinction at Universidad Central with his thesis "Valor de la cura de Lister en las heridas contusas" (Usefulness of Lister's method for concussive wounds). That same year, at just 20 years of age, he won a competitive examination and became director of the Miners' Hospital of Triano.<sup>10</sup> He initially moved to a guest house near the hospital, and subsequently lived in the hospital premises,<sup>1</sup> being readily available for work at all times.

Due to the lack of safety measures against explosions, roof collapses, and the traffic of minecarts, the mines were beset by carnage, with hundreds of miners affected by accidents. Using this huge amount of clinical material, and mainly through self-teaching, Areilza developed an astonishing surgical dexterity, which is reflected in the works he published during his time at the miners' hospital (1880-1900). At the Miners' Hospital of Triano, Areilza had to deal not only with all kinds of traumatic injuries but also with other diseases, such as terrible outbreaks of cholera and smallpox. He also engaged in a crusade to implement health and safety measures in mines and to improve miners' diets, insurance, and living conditions.<sup>1,2,5</sup>

He was very interested in the rehabilitation of the injured, especially of those with neurological sequelae, and worked tirelessly to create a school for the rehabilitation and instruction of the lame and crippled (language at the time was far from subtle).

Areilza opened a consultation in Bilbao in 1898 and a private clinic in 1900 (currently known as Sanatorio Bilbaíno). In 1905, he put an end to his long bachelorhood, marrying in the Catholic church. He had two children, Eloísa and José María; the latter edited a collection of his father's letters,<sup>12</sup> an indispensable source for understanding Areilza's personality and ideology.

These two decisions (opening a private clinic and getting married) represent a radical break from his former life and his well-earned fame as a bohemian bachelor who enjoyed a solitary life near the mines. This rupture was further consolidated in 1909, when he moved to the lux-urious mansion "El Salto," which his wife had inherited.

In 1904, Areilza was appointed head of ward at the old hospital of Bilbao in Achuri. He accepted the position, and requested dismissal from the Miners' Hospital of Triano, as the two positions were incompatible; however, his request was denied and Areilza had to resign from his appointment at the Achuri hospital.

In 1909, he promoted the creation of the Marine Sanatorium in Gorliz with the aim of fighting against the scourge of paediatric tuberculosis. The College of Physicians of Biscay (CMB, for its Spanish initials) was created in 1917 and Areilza was elected its first president, which gives an idea of the great prestige he enjoyed in the medical community. In 1918, he was appointed director of the new hospital of Bilbao, in Basurto (he renounced his honoraria). He made tremendous efforts to reform and modernise all hospital departments. His interest in teaching led him to create a body of medical interns to ensure postgraduate training. The hospital also offered paid theoretical and practical training to the students, who could subsequently sit open examinations at a medical school, frequently in Valladolid. Areilza's ultimate intention was to create a school of medicine, but the project failed.<sup>1</sup> He came up against the centralism of the Primo de Rivera dictatorship.<sup>5</sup>

In 1926, quite unexpectedly given his good health, Areilza died at the age of 66 years due to possible glomerulonephritis. His funeral was attended by an impressive number of people, including thousands of miners, and Areilza was buried in the cemetery of Portugalete. Many towns named streets and squares after him, and commemorative busts were erected in the hospitals of Gorliz and Basurto (one of the buildings at the later hospital of Basurto also bears his name) and in the Hospital-Asylum of Portugalete; the latter was funded by his widow.

He was admitted as a full member of the Spanish National Royal Academy of Medicine and the academies of medicine of Barcelona, Rome, Paris, London, and Lisbon, which gives an idea of the scientific and professional prestige he achieved.

#### The personality of Dr Areilza

At the young age of 20 years, Areilza assumed a position as physician/surgeon and the management of a hospital next to the mines, in a place where asking for help was not an option; this reveals that he was far from timorous and that he had an unwavering self-confidence. Dr Areilza soon consolidated his surgical skills, which further strengthened his self-sufficiency. A polyglot with an insatiable curiosity, Areilza read scientific journals in several languages. He also travelled regularly across Europe and bought books about novel surgical procedures (his medical library, containing around 1500 books, is held at the Basque Museum of the History of Medicine; another small part is held at the Museo de la Mineria del Pais Vasco, in Gallarta); his surgical expertise was undoubtedly far superior to that of his contemporaries. During his presentations at the sessions of the ACMB, Areilza always congratulated the speakers and used restrained language, although he frequently boasted about his vast surgical experience. Furthermore, in some private documents, he spared no criticism of his colleagues at the ACMB; these comments probably came to light and earned him some enemies. His colleagues at the ACMB were probably not the only ones to be criticised by Areilza, who is described by his own son, in the epilogue to Dr Vitoria's doctoral thesis,<sup>5</sup> as "sometimes surly and cold, of curt and mocking manners." Even with his patients, whom he normally treated with the utmost interest and care, he was occasionally blunt and distant. The collection of Areilza's letters compiled by his son<sup>12</sup> includes many other instances of the sharp, even offensive, criticism made by Areilza of his contemporaries, for example the abbot of the monastery of Silos. In a 1902 letter to Pedro Giménez, Areilza spared nobody, targeting the rich, the socialists, and the government alike. Even his long-term friend Miguel de Unamuno received harsh criticism.

We may hypothesise that, despite Areilza's unanimous prestige in the medical field, he was not held in great esteem by his colleagues due to his haughtiness. In fact, upon his death, he did not receive any tribute from either the ACMB or the CMB, two institutions that he had helped to establish and had presided over. A review of the minutes of all the meetings of the executive board of the CMB held in 1926, the year of Areilza's death, only yielded a succinct, conventional obituary. The *GMN*, official journal of the *ACMB*, limited the announcement of his passing to couple of lines. In contrast, the press in Bilbao and Madrid was flooded with eulogistic articles and laudatory obituaries.

Dr Areilza has been described in contradictory terms, as have some of his acts. Though he was openly anticlerical, his private clinic was managed by a community of nuns, he married according to the Catholic rite, he baptised his children, and he was buried according to the Catholic rite.

The information available on Dr Areilza suggests that he was a difficult person, with a strong and fascinating character.

#### The works of Dr Areilza

A thorough review of Dr Areilza's complete scientific output is beyond the scope of this article; rather, I will focus on articles published in different journals and oral presentations at the ACMB that are relevant from a neurological or neurosurgical viewpoint, providing a more detailed analysis than in a previous article.<sup>7</sup>

Most of Areilza's works addressed surgery and traumatology, and reveal the precariousness, even heroism, of surgical interventions at a time when anaesthesia and operating theatres were rudimentary, before the existence of antibiotics and postoperative care. Dr Guimón,<sup>1</sup> a renowned surgeon and urologist who studied the history of the Miners' Hospital of Triano and even knew Dr Areilza personally, gave a written account of the great efforts made by Areilza to provide the hospital with the best equipment, turning it into "the first great traumatology clinic in Spain."

Most of Dr Areilza's written works were published over a span of little more than two decades, between 1887 and 1909, with the exception of a few articles published between 1909 and his death. His participation in the activities of the ACMB also ceased around that time.

## *Articles of neurological and neurosurgical interest written by Dr Areilza*

This review analyses seven articles on neurology or neurosurgery.<sup>13-19</sup> It should be noted that Areilza showed an interest in these fields from a very young age; these topics were addressed in his first two monographs, published in Barcelona in 1887 and 1888. The text of the communication on head trauma presented at the ACMB in May 1921 could not be obtained.

1. De las fracturas de cráneo y de la trepanación. Estudio clínico<sup>13</sup> [On skull fractures and trepanation. Clinical study] (Figure 2)

This extensive study has two parts. The first part explores the environmental factors promoting head trauma in mines, particularly the lack of preventive measures. Areilza provides a detailed description of 27 cases of head trauma treated surgically. He did not include mild cases or cases of immediately fatal trauma. He exhibited an excellent knowledge of skull and brain topography, which he used to identify the gyri involved based on the area of the skull that was injured. In many cases, Areilza did not indicate surgery immediately, but rather on the second day, based on the appearance of progressive symptoms of compression.

He meticulously described a number of surgical techniques, including bone flap or craniectomy, surgical repair of depressed skull fractures, removal of foreign



**Figure 2.** Photograph of Dr Areilza and his colleagues performing trepanation at the Miners' Hospital of Triano. Source: Enfermería Avanza [Internet]. Los hospitales mineros de Triano, Vizcaya; 29 Jan 2017 [cited 24 Apr 2024]. Available from: https://enfeps.blogspot.com/2017/01/los-hospitales-mineros-de-triano-vizcaya.html

bodies, haemostasis, disinfection with antiseptic solutions, draining, etc.

In many cases, he took daily notes on post-surgery progression, a remarkable effort considering his circumstances, which reveals his great methodological rigour. He gave detailed descriptions of some surgical complications, including rupture of the dural sinuses or progressive oedema with brain herniation through the craniotomy opening, giving it the appearance of a mushroom cap. In case 7, Areilza notes that oedema was associated with pupillary dilation, which is now known to be the first sign of medial temporal lobe herniation. He performed autopsy studies of patients showing poor prognosis and drew practical conclusions.

The descriptions of the cases are replete with "neurological gems." Case 1, reported in 1881, presented a parietal lesion that left the brain covered only by a thin membrane, allowing Areilza to feel the pulsation of the brain; furthermore, compression of adjacent cortical areas caused vertigo in this patient. The patient also presented migraine and vomiting.

Case 2 had experienced left frontal trauma and, as expected, presented right hemiplegia with aphasia, which

Areilza analysed in detail, even going so far as to describe it as amnestic (forgetting words), ataxic (difficulty articulating words), and paraphasic, with preserved comprehension.

Areilza described the cases of three patients who did not undergo surgery and progressed poorly, dying due to brain abscesses. In two cases of epidural haematoma secondary to rupture of the middle meningeal artery, he identified the free interval between the injury and the onset of coma.

The second part of the monograph, which he called "deductive," had two purposes. On the one hand, he discussed the theory of cerebral localisation, demonstrating exceptional neurological knowledge, and, on the other, he established the indications for trepanation in cases of brain trauma; both topics were highly controversial at the time.

Regarding localisation, and aiming to determine what his cases may contribute to the topic, he divided his patients into two groups. The smaller group included four cases with marked motor and language symptoms, consistent with left frontal lobe injury, which enabled him to conclude that "none of the symptoms of paralysis or aphasia observed in our cases disproves the theory of cerebral localisation." The rest are classified according to skull and brain topography: motor region, parietal region, angular gyrus, occipital lobe, and temporal lobe.

He was well informed about, and even argued against, the theories of such relevant authors as Charcot, Ferrier, Duret, and Broca. He gave a detailed definition of the gyri forming the motor area, and reported that he had examined patients with lesions in those gyri who "did not present the corresponding functional symptoms. Although we do not wish to challenge the well-founded and proven theory of cerebral localisation, we faithfully describe our findings, which do not confirm the claims of these wise men." Case 5 was the most evident example of this clinical-pathological discrepancy.

Areilza also defined the prefrontal lobes as the "special seat of the highest mental faculties," asserting that injury to the region causes "imbecility and atrophy of intellectual functions" (although he believed this only to be true for bilateral lesions). He rightly hypothesised that his patients did not develop these symptoms because they were attended during the acute stage of injury. He concluded that the consequences of concussion and compression may resemble those of epileptic seizures "due to propagation to the bulbomedullary centres," obscuring any possible focal manifestations of trauma. Areilza further stated that "the cases of brain trauma observed in our hospital do not give much credit to the theory of cerebral localisation."

Patient 6 had acute delirium with bilateral prefrontal lesions. In the discussion of the case, Areilza speculated that delirium might represent "pre-paralytic excitation," some sort of exaggerated neuronal release before the functional abolition caused by the lesion. He was particularly interested in the association between frontal lobe trauma and acute delirium, and even published a monograph on the topic.<sup>15</sup>

He made two final remarks. The first concerns the brain's capacity to recover volume, a hypothesis that some authors rejected. Areilza described how the brain could expand even in cases where the cortex was compressed several centimetres below the trepanation hole; this corroborated some of Luys' experiments. He also commented on the possible explanation for neurological recovery over time, offering three hypotheses: 1) compensation by the homologous region on the contralateral side; 2) activation of the centres located in the subcortical ganglia (although this would only explain the recovery of automatic movement); and 3) compensation by new centres located in neighbouring areas.

The second objective of this monograph was to discuss the indications for trepanation in cases of head trauma. After a historical review of trepanation across cultures and the motivations for the procedure (eg, fabricating amulets, freeing the sick from evil spirits, relieving pain and seizures, etc), Areilza made a critical assessment between "those who have spread it without foundation and those who have condemned it."

He suggested that the presence of foreign bodies at the fracture site represents an absolute indication for trepanation as the technique may prevent undesired effects, which he flawlessly classifies as: 1) immediate, due to brain compression; 2) secondary, such as inflammation and abscesses; and 3) delayed, such as epilepsy and organic or functional atrophy. He described each one of these, and gave a particularly long description of abscesses. He recommended actively screening for these undesired effects by performing several punctures, as they may go unnoticed at first sight. He also paid particular attention to post-trauma epilepsy. He made interesting observations, such as the long symptom-free period before seizure onset, which lasted up to 16 years. Areilza was also in favour of operating on patients with post-trauma epilepsy, and cites a work by Walsham, a surgeon at St. Bartholomew's Hospital in London, who operated on 82 patients, 65 of whom recovered ("radically" in 48 cases). He was surprised at the recovery of nine of 16 patients presenting no observable macroscopic lesion. He was also informed about Horsley's experiences operating on motor regions, "a most daring practice," which, though successful on three occasions, "is not recommended as it is too risky."

The section focusing on the indications for trepanation concludes with an extensive review of the tools used, antisepsis, anaesthesia with chloroform, etc. Areilza emphasised that mortality is linked with lesion severity rather than with the intervention itself.

This monographic work includes an appendix with two additional cases. The first case is an example of post-traumatic epilepsy surgery, whereas the second report describes the recovery of a compressed brain, a topic discussed previously.

In the first case, trauma had been caused by a rifle bolt, resulting in a fracture with frontal compression; symptoms did not manifest immediately, and the patient received only basic care. Ten days later, he presented an episode of severe furious delirium, fever, and seizures, and received conservative treatment. Since then, he continued to present convulsive seizures over the course of 10 years, predominantly at night; seizures were not very frequent (monthly) and were of variable periodicity. In the past two years, however, seizure frequency had increased, with seizures presenting weekly or even daily. The patient was attended for the first time in 1886. Dr Areilza meticulously described the seizures: prodromal symptoms were followed by focal onset, with convulsive symptoms affecting the right side, and subsequent generalisation. Areilza operated on the patient with the help of Dr Llano, removing bone fragments that were compressing the meninges and frontal gyri. Surgery resulted in a marked reduction in seizure frequency: the patient presented "a few [seizures] in the following four months" and Areilza was hopeful that he would experience "fewer and fewer seizures." Anaesthesia with chloroform had been difficult to perform. This had previously been observed in other patients with epilepsy, which led Areilza to hypothesise that epilepsy "hinders anaesthesia as it causes an irritative state of the sensorimotor centres of the pons, where anaesthesia acts." He made an analogy to tolerance to morphine or chloral hydrate. Based on this idea, he discussed the pathophysiology of epileptic seizures, and concluded by supporting the notion that "the cause [of seizures] would be located in the meninges and cerebral cortex, but the mechanism underlying the discharge would reside in the pons, influenced and excited by these locations according to the laws of diffusion and reflection of nervous tissue."

It should be noted that this monograph is richly illustrated with photographs of many of his patients. Areilza must have brought all his photography equipment (cameras, plates, developing tools, etc) from Paris when he returned to Spain in 1880 (commercial film did not yet exist), as his first photograph of a patient was taken in 1881. Once more, this reveals Areilza's intention to make top-quality observations of his patients. He may have been inspired by *Iconographie photographique de la Salpêtriére* (Bourneville and P. Regnard, 1878), one of the first texts illustrated with photographs.

# 2. *La trepanación en la epilepsia*<sup>14</sup> [Trepanation in epilepsy] (Figure 3)

As an anecdote, it should be mentioned that the copy of this monograph consulted by the author is dedicated to Dr Lereboullet. The signature appears to be the autograph of Dr Areilza (based on comparison with other manuscripts of his). No additional data are provided about this physician; judging by the year, it might be Léon Lereboullet, whom Areilza met during his stay in Paris.

In the introduction to this monograph, published only a year after the previous one, he argued that the controversy around trepanation for traumatic injuries was a thing of the past. He also expressed concern that trepanation might be trivialised and begin to be performed "by charlatans for the relief of chronic headaches." In contrast, he asserted that the procedure is "highly interesting for epilepsy treatment." He made reference to recent studies by Horsley and Macewen, which had impressed him greatly. He wrote with excitement: "The sanctum sanctorum of all organs, the brain, is now under the dominion of the scalpel." This was as early as 1888! He cited his own previous work, referring to the case described in the appendix, and contributed several additional cases.

The first case was a patient with focal motor-onset seizures in the forearm, with secondary generalisation. He had no relevant medical history. The procedure was justified by the disabling frequency of the seizures, which occurred over 30 times per day. Areilza did not find macroscopic cortical lesions, despite which he resected part of the motor region, which he believed was the origin of the seizures (some four grams of brain tissue from the middle-superior third of the Rolandic fissure). According to Areilza, all the interventions for the treatment of epilepsy conducted to date had resected visibly abnormal tissue, but no one had ever dared to remove apparently normal brain tissue. He justified his decision by explaining that the brain may present "more intimate, molecular lesions." He argued that the localisation of the resected tissue was correct, as the procedure was followed by complete brachial paralysis and partial paralysis of the leg, with transient facial paresis. However, the patient's progression was paradoxical, in Areilza's view: a) while the resection of the suspected epileptogenic region was correct, seizures subsided only transiently and then reappeared with even greater frequency; and b) paralysis, which was expected to be irreversible due to the nature and amount of motor cortex tissue resected, was surprisingly brief, and the patient recovered nearly completely. Areilza referred to several previous experiences, such as one of his own cases published in 1881, a patient who had lost brain mass through a hole in the skull, leaving a cavity; the patient fully recovered and returned to work.

According to Areilza, these experiences contradicted the observations made by Macewen, who, in a brilliant presentation on brain surgery at the latest medical congress in Glasgow (we may wonder whether Areilza was present), warned that surgical resection of a tumour located in the motor region involved a high risk of permanent hemiplegia. Areilza considered this view to be exaggerated: surgery on the motor region should not be ruled out, given that hemiplegia could be treated with rehabilitation therapy, electrotherapy, etc.

3. El delirio en las fracturas de la base del cráneo, 1898 (Congreso Hispano-Portugués de Cirugía, Madrid, 1899<sup>15</sup> [Delirium in basilar skull fractures] (Figure 4)

This work was extensively reviewed in a previous article published in this journal.<sup>6</sup> It describes a series of five patients diagnosed with basilar skull fractures based on clinical data (radiology was not yet available). All patients presented delirium or a prolonged acute confusional state, which Areilza attributed to concussion of the inferior aspect of the frontal and temporal lobes. Areilza had already established an association between these brain regions and mental functions. He drew a distinction between these symptoms and those caused by cortical lesions secondary to trauma to the cranial vault. In one of the patients, Areilza conducted an experiment that tested the boundaries of ethics. He introduced tools through the craniectomy opening to progressively compress the orbital aspect of the frontal lobes in an attempt to gain a better understanding of their function. He interrupted the experiment when the patient began to develop a convulsive seizure, but did not observe neurological defects that may localise lesions to that area, which was his true obsession.

#### 4. Localizaciones medulares<sup>16</sup> [Spinal cord localisation]

This article is based on the observation of a patient with severe trauma to the thoracic and lumbar spine, which resulted in a fracture of vertebrae L1 and L2, causing paraplegia. Areilza operated on the patient 48 hours after the incident, without much conviction. His spinal cord was crushed; Dr Areilza enlarged the spinal canal to decompress it. The immediate postoperative progression was good; however, the patient died 48 hours after the intervention due to circulatory failure as a result of massive bleeding. Before surgery, Areilza had examined the patient thoroughly and found that sensitivity was preserved in the external aspect of both legs and two-thirds of the feet. He concluded that the only explanation for the preserved sensitivity in those distal areas was the extension of dermatome L2 (as the lower spinal segments had been destroyed), despite the anatomical distance. He explains that his motivation for publishing this case was to discuss spinal cord localisation, which was as complex as cerebral localisation.

5. Análisis y crítica de los fenómenos sensorio-motrices de una fractura del parietal derecho con absceso consecutivo de la zona rolándica<sup>17</sup> [Analysis and critical appraisal of sensorimotor phenomena of a fracture of the right parietal bone with an abscess in the Rolandic area]

This article describes the case of a patient with right parietal trauma who presented left-sided hemiplegia starting immediately following the injury. When Areilza attended him, several days later, the wound was infected and the skull was depressed. He operated on the patient, and found an intracerebral abscess, which he drained, releasing a large amount of pus. He hypothesised that the gyri



Figure 3. Covers of Dr Areilza's first two monographic works of neurosurgical interest.

Publicaciones Españolas
EL DELIRIO EN LAS FRACTURAS DE LA BASE (DEL CRANEO (1)
POR EL DR. D. ENRIQUE AREILZA
Hemos vacilado repetidas veces antes de presentar este trabajo porque resulta una labor inacabable é incapaz de ofrecer conclusio nes positivas ante vuestra consideración. Los hechos clínicos que le sirven de base parecían, más de una vez, arrojar alguna luz en el obscuro problema de las localizaciones psiquicas más elevadas; pero, como veremos, datos sucesivos de orden clínico y experimental han venido á destruir nuestras espe- ranzas.
Son estos desengaños propios de toda investigación en el campo de la Medicina, y sería bien lamentable perder el tiempo siguiendo una falsa pista si, por otra parte, no resultara cierta compensación
(1) Comunicación al Congreso Hispano-Portugués de Cirugia.

**Figure 4.** Cover of Dr Areilza's monographic work on basilar skull fractures secondary to head trauma, where he expresses his disappointment at his inability to advance the theory of cerebral localisation.

compressed by the bone fragments were the upper third of the ascending frontal gyrus and the lower portion of the first and second frontal gyri, whereas the destruction and loss of brain mass caused by the abscess involved the middle third of the ascending frontal gyrus and the middle superior third of the ascending parietal gyrus. Progression was excellent, with the patient recovering fully. The purpose of the article was to provide a comprehensive description and discussion of the patient's motor and sensory deficits, which may well have been made by the most skilled of neurologists. He tried to differentiate the signs and symptoms attributable to the compression of the bone fragments from those caused by the abscess.

A. Sensory findings. Dr Areilza signalled that thepatient felt as if their left limbs were dead. He performed an excellent preoperative sensory examination, including touch, temperature, pain, Weber's compass, somatic localisation, pressure (tested by placing the arm in water), joint position, location of the limb in space with the patient's eyes closed, assessment of weight, and object recognition. Areilza described the defects found on the left side of the body and indicated that he had found sensory alterations in areas of the ipsilesional side of the body.

B. Motor findings. The patient presented complete hemiplegia for all voluntary, associated, synergistic, and reflex movements (including the plantar reflex). He did not present paresis of the face, tongue, pharynx, rectum, or bladder. Interestingly, the patient presented a tendency to opisthotonos, which Areilza attributed to brainstem excitation and which disappeared within days after surgery. The patient improved gradually over the following months, with sensory symptoms improving faster than motor symptoms. Dr Areilza was particularly thorough in his assessment of muscle strength, which he tested muscle by muscle, nearly every day, as the patient gradually recovered his strength, and documented how the patient finally was able to move the hand or walk with a cane, the equinus position of his feet, etc.

C. Discussion. Dr Areilza not only described the case but also delved into the then-controversial issue of cortical localisation of sensory and motor functions in humans. He mentioned that Ferrier had suggested, in 1875, that sensory function was located in the limbic lobe, but that the most recent studies by Hornslet, Bastian, and Bechterew reported that lesions posterior to the Rolandic area cause "sensory and motor disorders at the same time." He gave a detailed account of the complex sensations of movement, space, body position, etc, concluding that astereognosis must be linked to "a lesion to the ascending parietal gyrus," in line with the cases published by Reignier, Dublens, and Bonhôffer.

He pointed out that motor recovery had followed "a regional, rather than functional, order; thus, the hand and forearm recovered, nearly in unison, the movements of extension and flexion, of pronation and supination, without a clear preference for one or the other." He underscored that paralysis was flaccid, which he interpreted as an "abolition of spinal reflexes," contradicting the hypothesis of the moderating role of the cortex.

6. Fractura de la clavícula derecha con parálisis del brazo derecho y lesión de la arteria subclavia. Presentación del paciente<sup>18</sup> [Fracture of the right clavicle with paralysis of the right arm and lesion to the subclavian artery. Presentation of a patient]

This work was bassed on an oral presentation to the ACMB. Dr Areilza had visited the patient that same day; he proposed bringing him to the ACMB to present his case. Due to an accident several months earlier, the patient presented head trauma and a fracture to the right clavicle, which was followed by right arm paralvsis. Areilza thoroughly described the characteristics of paralysis: amyotrophy, claw hand, and causalgia. He ruled out the hypothesis that paralysis was secondary to a brain lesion, given that the trauma had affected the right occipital region. The motor deficits in the arm were also incompatible with a spinal cord lesion; furthermore, there was "absence of pupillary symptoms inherent to a lesion to the ciliospinal centres." Therefore, he issued a diagnosis of a lesion to the plexus as a result of the clavicle fracture, which had also caused thrombosis of the subclavian artery. He proposed operating on the patient, a suggestion that was supported by other physicians.

7. *Hematomas intracerebrales retardados posttrauma*. *Discusión*<sup>19</sup> [Post-traumatic, delayed-onset intracerebral haematomas. A discussion]

This presentation took place as the result of a previous debate on head trauma at the congress of the ACMB. Areilza underscored the complexity of the topic and described the cases of two patients who, after moderately severe trauma and without immediate onset of symptoms, presented hemiplegia a few hours after the event and eventually died. In both cases, post mortem studies revealed haematoma in deep structures (striatum, centrum semiovale). He referred to these cases in relation to the concept of "late-onset traumatic apoplexy," highlighting its potential consequences for legal medicine and labour laws.

#### Comments

A previous article<sup>7</sup> analysed the fascinating personality of Dr Areilza and explored the reasons that may have led a young physician with an outstanding academic

record and a doctorate with honours, who would have been welcomed into the most prestigious hospitals and universities in Spain, to choose a position as a physician at a remote hospital for miners in the middle of nowhere. There is evidence that he had planned to sit the competitive examinations for the chair of surgery at the University of Cádiz, but eventually opted not to participate, preferring to stay in Triano.<sup>11</sup> In any case, two facts are clear. Firstly, at 21 years of age, Areilza had an almost insolent self-confidence. This may explain why he dared to perform neurosurgical interventions at a miners' hospital when such procedures were not yet being performed at university hospitals in Madrid or Barcelona, nor at the best private clinics, which would later become renowned centres, such as the Instituto Rubio in Madrid or the Clínica Corachán in Barcelona.<sup>20</sup> And secondly, Areilza took his new position at Triano very seriously from the beginning. He had received strict university training and began to apply it immediately. Case 1 of his first monograph on trepanation was attended in 1881, when he had only recently arrived at the hospital, despite which he gave a detailed description of the patient's clinical history, the surgery protocol, and postoperative progression. This strict methodology reveals scientific inclinations that went beyond his surgical activity. He wished toreport his observations systematically. He was determined to make a significant contribution to surgery with his work and a rigorous analysis of his observations.

It should be noted that Areilza's first two monographs on trepanations and epilepsy surgery were published in 1887 and 1888, and condense his experiences from the previous six or seven years. To better comprehend Areilza's surgical precocity, it should be noted that Broca's first published account of an operation on a brain abscess was in 1876,<sup>21</sup> and Macewen first performed a surgical resection of a meningioma in a patient with epilepsy in 1879.<sup>22</sup> The definitive articles by Horsley, the father of neurosurgery in Great Britain, were published in 1886 and 1887,<sup>23,24</sup> and Macewen's<sup>25</sup> were published in 1888, that is, simultaneously with Areilza's early monographs.

The incipient specialty of neurosurgery was based on three pillars, which had only recently been established: anaesthesia (chloroform in most cases), antisepsis (following in the footsteps of Lister), and the theory of cerebral localisation (with Broca as the leading exponent), which fascinated the young Areilza.<sup>24-27</sup> At that time, injuries to the left frontal area causing right hemiplegia and aphasia were practically the only lesions that could

be localised with certainty. Areilza, who was well versed in skull and brain topography and had demonstrated excellent neurological knowledge, was very disappointed to find that the study of patients with traumatic brain lesions did not enable him, or other authors, to advance the theory and practice of cerebral localisation to manage other pathologies. However, he was also well-informed about the advances made by the pioneers in brain surgery in other countries<sup>28-30</sup>; in fact, in his library he kept a copy of the 1911 edition of Krause's Chirurgie des Gehirns und Rückenmarks. Nach eigenen Erfahrungen, a seminal text on neurosurgery<sup>31</sup> written by one of the field's foremost pioneers (Figure 5).<sup>32</sup> In any case, Dr Areilza did not transition from traumatology to the surgical treatment of brain tumours or other brain lesions, or at least there is no evidence of his having done so, despite his early interest in neurosurgery.

As mentioned previously, Areilza's articles provide numerous "neurological gems." In the first case report in his monograph on trepanation,<sup>13</sup> a patient attended in 1881, Areilza made an extremely interesting observation. The patient had undergone right parietal craniectomy, leaving the brain covered only by a soft, thin membrane; Areilza found that pressure applied over the cortex triggered vertigo, probably a pioneering observation of the cortical projections of the vestibular system.<sup>33</sup> That patient had also begun to present migraine after the trauma; this association, widely recognised today, was probably unknown at the time.<sup>34,35</sup> In the second case, a patient with a left frontal lesion, Areilza described the aphasia in the technical terminology of neurology, reporting the three main clinical features of the condition: forgetting words (amnesia or anomia), dysarthria or ataxic speech, and paraphasia, with preserved comprehension. There is no doubt that Dr Areilza was well informed about the clinical characteristics of the types of aphasia described by Broca, Wernicke, and other classic authors<sup>A</sup>.

In his monograph on trepanation,<sup>13</sup> Areilza makes another two relevant contributions. Firstly, he reported brain abscesses in three patients with contaminated wounds who had not been treated surgically; this was a powerful argument in favour of trepanation, a highly controversial procedure with very few advocates at the time.<sup>36-39</sup> Secondly, in two cases of epidural haematoma secondary to rupture of the middle meningeal artery, he described a "free interval" between the trauma and the onset of coma, which is currently well established. Both this first monograph<sup>13</sup> and another article<sup>15</sup> clearly demonstrate that Dr Areilza knew that the frontal lobes constitute the seat of the "psychic faculties of the highest order," a notion already proposed by phrenologists and subsequently confirmed in other studies.<sup>39</sup> Strikingly, as early as in his 1887 article, Areilza asserts that bilateral frontal lobe lesions cause "imbecility and atrophy of intellectual functions"; Pick's first work on the association between cognitive impairment (language, behaviour) and frontal lobe atrophy was not published until 1892.<sup>40</sup> Unfortunately, Dr Areilza did not report the references from which he had drawn such accurate information on the effects of frontal lobe lesions.

Areilza was also knowledgeable about the hypothesis that focal epileptic seizures originate in the cortex, which he believed to be true, and that generalisation results from "propagation to the bulbomedullary centres," a hypothesis linked to Penfield's concept of the "centrencephalic system," developed several decades later and which encompassed mesodiencephalic structures.

He defended the brain's ability to recover volume following compression, another controversial issue, and also speculated about the neurophysiological basis of functional recovery following a brain lesion, using a terminology that remains valid today. Likewise, his comments on the topic of trepanation resembled a neurological lecture: he defends its indication in cases of head trauma, classifying its undesired effects as immediate (by compression), secondary (inflammation [oedema], abscesses), and delayed (epilepsy, organic or functional atrophy). His technical comments constitute a model for rigour, common sense, experience, and innovation.

A few comments should be made regarding epilepsy surgery.<sup>13,14</sup> It is very likely that Areilza indicated surgery for post-trauma epilepsy inspired by Walsham's overly optimistic results, even in patients without macroscopic lesions, a particularly controversial indication. Areilza described Horsley's operations on motor regions as a "reckless practice that cannot be recommended as it is too risky"; however, he acknowledges in his second monograph<sup>14</sup> that he decided to operate on a patient and resect tissue at the level of the Rolandic fissure to alleviate his focal motor seizures. This case is of particular interest given that the patient had no relevant aetiological history or macroscopic lesions; justifying the resection of apparently healthy cortical tissue, Dr Areilza cited the extremely high seizure frequency and his belief that the patient may have lesions at a molecular level. Areilza's surgical curiosity knew few bounds. He was probably one of the first physicians to resect macroscopically normal tissue from the motor cortex to treat focal epilepsy, despite his initial reservations ("a reckless practice") even in patients with visible lesions. The procedure was a complete failure, either because there was a hidden lesion (eg, focal dysplasia at the bottom of a sulcus that was not resected) or because the epileptogenic zone was larger than initially thought. It is now well established that epilepsy surgery in patients with macroscopically normal tissue and no imaging evidence of lesions is associated with poor outcomes, even in spite of modern technological advances.41,42 This failed intervention was extremely frustrating for Areilza, and he was not consoled by the fact that his patient recovered from hemiplegia despite the resection of motor cortical tissue. However, this observation allowed him to contradict the views of none other than Macewen, who had recently warned about the risk of definitive hemiplegia following surgical resection of tumours located in the motor region.

Areilza's interest in the consequences of lesions near the Rolandic fissure was even more evident in the discussion of the case of a patient with an abscess in that location.<sup>17</sup> As mentioned earlier, Areilza displayed extraordinary knowledge of brain topography and anatomy, and was remarkably skilled in the motor and, especially, sensory examination of patients, making observations that were comparable to those of an experienced neurologist. It is praiseworthy that a surgeon working at a remote miners' hospital would conclude, after an expert discussion of the case, that astereognosis must be linked to "a lesion to the ascending parietal gyrus [...] according to the

<sup>&</sup>lt;sup>A</sup>It should be noted that Areilza's knowledge of neurological semiology, and probably many other fields, was largely self-taught. The Museo de la Minería in Ortuella holds several neurological textbooks (such those of Joanny Roux, Bechterew, Purves Stewart, and Lewandovsky) that are full of handwritten notes, showing that Dr. Areilza read and studied them with the utmost interest. It is unlikely that he would have received specific neurological training during his years in Valladolid. During the year he spent in Paris (1880), his main focus was on surgery. He is also known to have attended Charcot's famous lessons, which at the time already revolved around hysteria and hypnosis; the master of La Salpêtrière would soon thereafter reach the pinnacle of his career with the chair of diseases of the nervous system in 1882. However, the careers of Charcot's most prominent students were yet to reach their peak, bringing about the blossoming of the field of neurology (in 1881, Dejerine was 32 years old, Pierre Marie was 28, and Babinski was 24). Dr Areilza was undoubtedly familiar with the advances in German neurology, which at the time was at a similar stage in its development as French neurology: in 1881, Wernicke was 33 years old, Oppenheim was 23, and Erb had just inaugurated his polyclinic, and Westphal described the absent patellar reflex in tabes dorsalis in 1878.



Figure 5. Cover of Krause's wonderful treatise on brain and spinal cord surgery, and a figure illustrating brain metastasis. This is one of the books that Dr Areilza's widow donated to Hospital de Basurto.

cases published by Reignier, Dublens, and Bonhôffer." Unfortunately, Dr Areilza did not cite the exact references for these cases, which would have enabled better understanding of his sources of information.

Another fact demonstrating Areilza's command of neurological semiology is the discussion of a case of traumatic brachial plexus injury.<sup>18</sup> In the differential diagnosis, he rightly noted that the patient did not present sympathetic ocular syndrome (Horner syndrome, in today's terminology) secondary to a lesion to the ciliospinal centres, which ruled out the hypothesis of a spinal root lesion. This case was presented at a session of the ACMB; Areilza had attended the patient earlier that same day and brought him to the meeting to illustrate the case. It is worth noting that the atmosphere at these sessions, attended by no more than a dozen people, was rather informal and relaxed. Areilza's presentation of the case to the ACMB is reminiscent of Charcot's famous

*leçons du mardi*, where the master would present a patient he had attended at his consultation that same day to discuss their case.

Another relevant contribution to neurosurgery is his description of delayed post-traumatic cerebral haematoma,<sup>19</sup> a well-known complication,<sup>43,44</sup> which he illustrated with two cases, providing autopsy data from both patients; once more, this reflects his inclination toward empirical evidence, from which he would draw practical conclusions.

We may conclude this short article on Dr Areilza with two reflections: one is a certainty and the other is a question.

The certainty is that Areilza was an extraordinary physician and surgeon, an autodidact, with remarkable determination and self-confidence. In fact, he practised at the level of the European pioneers in neurosurgery for epilepsy and head trauma. He may be considered a protoneurosurgeon in late 19th-century Spain.

The question, on the other hand, is why he should choose to devote most of his career to a miners' hospital, rather than a general or university hospital, where he would have had the opportunity to create a school of followers and make advances in the surgery of tumours and other pathological processes of the brain. His individualism probably influenced many of his decisions. Unfortunately, his appointment as head of ward at the old hospital of Bilbao in Achuri did not come to fruition, and he was not included on the staff of the new hospital, in Basurto, despite serving as its director for nearly a decade.

Areilza made it clear in his writings that he was greatly disappointed with both his inability to advance the theory of cerebral localisation (where he had detected many clinical-pathological discrepancies) and the uncertain outcomes of epilepsy surgery, as he was eager to obtain positive results that may guide his surgical practice. This disappointment may partly explain why his interest in neurosurgery faded over time. In 1915, Dr López-Albo arrived in Bilbao; this was an extraordinary neuropsychiatrist who displayed great interest in neurology45,46 and neurosurgery. He was authorised to open a neurology clinic within the internal medicine department at Hospital de Basurto, but was never officially considered a member of the medical staff of said hospital. Despite this lack of official recognition in neurology and neurosurgery, it seems natural to assume that Dr López-Albo and Dr Areilza would have had some kind of professional, if not personal, relationship. However, there is no written evidence of any collaboration between the two. Two of Dr López-Albo's first contributions to the sessions of the ACMB were subsequently published in the academy's official journal<sup>47,48</sup>; we may deduce from both articles that there was no professional relationship between López-Albo and Areilza, and that Areilza was not a reference in the field of brain tumour surgery. The first case was a patient with a frontal lobe tumour; Dr López-Albo operated on the patient, presenting the specimen and patient in person at one of the academy's sessions. The second case was a possible tumour of the posterior fossa; diagnosis was clinical, and no surgery was performed. Dr López-Albo was also unable to progress in neurosurgery, a specialty that was not officially recognised at Hospital de Basurto until the arrival of Dr Ramón Jacas, in 1960. Neurology started over two decades later, after overcoming the traditional resistance to change: specialisation in medicine, in this case. But that is another story.

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#### References

- 1. Guimón J. El doctor Areilza, precursor de la universidad de Bilbao. Bilbao (ES): Real Academia de Medicina Distrito de Bilbao; 1971.
- Montalban J. El Dr. Areilza, médico de los mineros. Bilbao (ES): Muelle de Uribitarte Editorial; 2008.
- 3. La memoria de los días olvidados: el blog de Josu Montalbán [Internet]. [s.l.]: Josu Montalbán; [s.d.]. Areilza y Unamuno en el ágora bilbaína; 24 Mar 2012 [cited 10 Mar 2024]. Available from: https://josumontalban.blogspot.com/2012/03/areilzay-unamuno-en-la-agora-bilbaina.html
- Blog de Iñaki Anasagasti. [s.l.]: [s.n.]; [s.d.]. Montero T. Enrique de Areilza, doctor, testigo y heraldo. Cited: 11 Mar 2024. Available from: https://ianasagasti.blogs.com/mi\_ blog/2012/03/enrique-de-areilza-doctor-testigo-y-heraldo. html.
- 5. Vitoria Ortiz M. Vida y obra del Dr. Areilza. Bilbao (ES): La Gran Enciclopedia Vasca; 1975.
- García-Molina A, Enseñar-Cantallops A. Lesiones cerebrales traumáticas frontales en la cuenca minera de los Montes de Triano (1881-1898). Neurosci Hist. 2017;5:52-7.
- 7. Zarranz JJ, Areitio E. Breve semblanza del Dr. Areilza y sus obras de interés neurológico o neuroquirúrgico. Gac Med Bilbao. Forthcoming 2024.
- 8. Alegría Mendialdua F. Bibliografía del Dr. D. Enrique Areilza y Arregui. Trabajos de la Cátedra de Historia Crítica de la Medicina. 1934-1935;V:99-105.
- Real Academia de la Historia [Internet]. Madrid: Real Academia de la Historia; © 2018. Enrique Areilza Arregui; [cited 2 Feb 2024]. Available from: https://dbe.rah.es/ biografias/18200/enrique-areilza-arregui
- 10. Vitoria Ortiz M. Los hospitales mineros de Triano. Bilbao (ES): La Gran Enciclopedia Vasca; 1978.

- Gilsanz Rodríguez F, Guasch Arévalo E. Enrique Areilza Arregui (1860-1926). Un ilustre licenciado de la facultad de medicina de Valladolid. Arch Fac Med Valladolid. 2023;5:12-7.
- 12. Areilza E. Epistolario. Areilza JM, ed. Bilbao (ES): Librería Arturo; 1964.
- 13. Areilza E. De las fracturas de cráneo y de la trepanación. Barcelona: La Academia; 1887.
- 14. Areilza E. La trepanación en la epilepsia. Barcelona: La Academia; 1888.
- Areilza E. El delirio en las fracturas de la base del cráneo. (Congreso Hispano-Portugués de Cirugía, Madrid, 1899). Revista de Ciencias Médicas de Barcelona. 1899;8:292-307.
- 16. Areilza E. Localizaciones medulares. Gac Med Norte. 1899;5:497-504.
- Areilza E. Análisis y crítica de los fenómenos sensoriomotrices de una fractura del parietal derecho con absceso consecutivo de la zona rolándica. Gac Med Norte. 1900;6:228-50.
- Areilza E. Fractura de la clavícula derecha con parálisis del brazo derecho y lesión de la arteria subclavia (presentación). Gac Med Norte. 1902;8:711-4.
- 19. Areilza E. Hematomas intracerebrales retardados posttrauma. Discusión. Gac Med Norte. 1908;14:54-6.
- 20. Izquierdo JM. Historia de la neurocirugía española (1950). Neurocirugía. 1993;4:164-71.
- Broca P. Diagnostic d'un abcés situé au niveau de la région du langage; trépanation de cet abcés. Rev Anthropol. 1876;5:244-8.
- 22. Macewen W. Tumour of the dura mater removed during life in a person affected with epilepsy. Glasg Med J. 1879;12:210-3.
- 23. Horsley V. Brain surgery. BMJ. 1886;2:670-5.
- 24. Horsley V. A note on the means of topographical diagnosis of focal disease affecting the so-called motor region of the cerebral cortex. Am J Med Sci. 1887;96:342-69.
- 25. Macewen W. An address on the surgery of the brain and spinal cord. Br Med J. 1888;2:302-9.
- Macewen W. Intra-cranial lesions, illustrating some points in connexion with localization of cerebral affections and the advantages of antiseptic trephining. Lancet. 1881;2:541-3.
- 27. Finger S. The birth of localization theory. Hand Clin Neurol. 2010;95:117-27.
- Finger S, Stone JL. Landmarks of surgical neurology and the interplay of disciplines. Hand Clin Neurol. 2010;95:189-202.
- 29. Ormond DR, Hadjipanayis CG. The history of neurosurgery and its relation to the development and refinement of the frontotemporal craniotomy. Neurosurg Focus. 2014;36:1-11.

- Shen E, Terai H, Ben Haj Frej K, Dean J, Chozick B, Bulsara KR. Sir Rickman John Godlee—Contributions in addition to his 1884 tumor resection, a review. World Neurosurg. 2024;183:187-91.
- Krause F. Chirurgie des Gehirns und Rückenmarks. Nach eigenen Erfahrungen. Berlin: Urban & Schwarzenberg; 1911.
- Bacigaluppi S, Bragazzi NL, Martini M. Fedor Krause (1857-1937): the father of neurosurgery. Neurosurg Rev. 2020;43:1443-9.
- 33. Dieterich M, Brandt T. The parietal lobe and the vestibular system. Handb Clin Neurol. 2018;151:119-40.
- 34. Riechars RG II, Walker MF, Ruff RL. Post-traumatic headaches. Hand Clin Neurol. 2015;128:567-78.
- 35. Minen MT, Boubour A, Walia H, Barr W. Post-concussive syndrome: a focus on post-traumatic headache and related cognitive, psychiatric, and sleep issue. Curr Neurol Neurosci Rep. 2016;16:100.
- Sedillot CE. Plaie de tête avec fracture: trépanation. Bull Soc Chir. 1870;11:140-3, 149-51.
- Lucas-Championnière J. Trépanation du crâne faite pour une fracture de la voûte sans plaie communicante; guérison complète. Bull Mem Soc Chir Paris. 1875;1:226-31.
- Lucas-Championnière J. La trépanation guidée par les localisations cérébrales. Paris: Masson; 1878.
- 39. Filley CM. The frontal lobes. Hand Clin Neurol. 2010;95:557-68.
- Pick A. Über die Biezehungen der senilen Hirnatrophie zur Aphasie. Prager Med Wochenschr. 1892;17:165-7.
- Immonen A, Jutila L, Muraja-Murro A, Mervaala E, Äikiä M, Lamusuo S, et al. Long-term epilepsy surgery outcomes in patients with MRI-negative temporal lobe epilepsy. Epilepsia. 2010;11:2260-9.
- 42. West S, Nolan SJ, Newton R. Surgery for epilepsy: a systematic review of current evidence. Epileptic Disord. 2016;18:113-21.
- Baratham G, Dennyson WG. Delayed traumatic intracerebral haemorrhage. J Neurol Neurosurg Psychiatry. 1972;35:698-706.
- 44. Ziechmann R, Pathak SM, Welch J, Villanueva P. Delayed traumatic intracerebral hematoma: a pathophysiological classification and literature review. Cureus. 2023;15:e42987.
- 45. Zarranz-Imirizaldu JJ. Wenceslao Lopez Albo y su relación con la Academia de Ciencias Médicas de Bilbao. Gac Med Bilbao. 2021;118:128-32.
- Zarranz JJ. Wenceslao López Albo: precursor de la neurología en Bilbao. Neurosci Hist. 2019;7:83-96.
- López Albo W. Tumor del lóbulo frontal derecho operado. Presentación del enfermo y de la pieza operatoria. Gac Med Norte. 1917;XXIII:13-28.
- López Albo W. Diagnóstico precoz de un tumor de cerebelo. Gac Med Norte. 1918;XXIV:104-14.