

## The mark left by exiled Spanish neuroscientists in Mexico: Cajal's overseas legacy

F. J. Dosil

Institute of Historical Research. Universidad Michoacana de San Nicolás de Hidalgo

### ABSTRACT

Cajal's neuron doctrine was accepted promptly and enthusiastically in Mexico through the agency of his disciple Tomás Gutiérrez Perrín. Originally from Valladolid, Perrín moved to Mexico in 1908 and taught histology at the National University. Once the tumult caused by the Mexican Revolution had subsided, interest grew in Cajal's discoveries. Two of Cajal's distinguished colleagues, Francisco Tello and Pío del Río-Hortega, were invited to teach seminars in Mexico, and many Mexican doctors obtained fellowship positions in Spanish laboratories. Numerous researchers from the Cajal School (including Dionisio Nieto, Isaac Costero, and Gonzalo Rodríguez Lafora) left Spain for Mexico after the Spanish Civil War. With their arrival, neuron doctrine would become a permanent fixture in Mexico, especially in UNAM's Laboratory of Medical and Biological Studies. These doctors in exile were key figures in a dense network of scholars that promoted the considerable advances in Mexican neuroscience, which were partially based on Cajal's teachings.

### KEYWORDS

Santiago Ramón y Cajal, Mexico, Tomás Gutiérrez Perrín, exile, neurosciences, Laboratorio de Estudios Médicos y Biológicos.

### Introduction

Santiago Ramón y Cajal's neuron doctrine unravelled one of nature's best-guarded mysteries. This doctrine represented the culmination of a long and varied line of projects undertaken by such key figures as Remak, Deiters, Schleiden, Schwann, Virchow, Golgi, Sherrington, etc. The fact that this discovery took place in a country with only a sparse history of scientific contributions and very few resources dedicated to supporting research made Cajal famous even outside of the scientific sphere. Cajal was increasingly regarded as a role model, especially after he was awarded the Nobel Prize in 1906. Cajal, known as the "tireless microscope operator", provided incontestable proof that perseverance and intelligence could overcome social and historical barriers. His fame was by no means limited to Spain; in other countries, including Mexico, he was regarded as a pillar of scientific progress.

Cajal devised his neuron doctrine in 1888 based on his studies of cerebellar grey matter. Between 1897 and 1904,

he published instalments of his most important study, *Texture of the Nervous System of Man and the Vertebrates*. Cajal's discovery spelled out new horizons in the rational positivism that dominated his times, both in Spain under Alfonso XIII and in Mexico under Porfirio Díaz. His studies of nervous system tracts led him to recognise that they displayed cellular organisation, the law applicable to all life.

The purpose of our article is to illustrate how Cajal's theories spread through Mexico and gained acceptance, describe the role Spanish exiles played in promoting his teachings, and analyse the influence of that material on the development of the neurosciences in Mexico. We should also note that Cajal's contributions include two different but related types of knowledge: a theory, expressed as the neuron doctrine, and techniques, referring to his tissue staining and handling methods. Promoting both types of knowledge involved very different challenges. In the first case, once the theory had been accepted, it was relatively easy to assimilate and include in an academic corpus. In the second case, Cajal's techniques, which were vitally

Corresponding author: Francisco Javier Dosil Mancilla  
Instituto de Investigaciones Históricas, Universidad Michoacana de San  
Nicolás de Hidalgo

E-mail: fjdosil@yahoo.es

important for research, required dexterity and know-how that could not be acquired by reading textbooks.

#### Cajal's teachings pervade Mexico

The theories of Ramón y Cajal promptly reached Mexico thanks to his disciple Tomás Gutiérrez Perrín (1881-1965) (Figure 1). Perrín completed his secondary education in the General and Technical School in his hometown of Valladolid and earned his medical degree from the University of Valladolid in 1905. Perrín was a friend and classmate of Pío del Río-Hortega's. One of their professors was Leopoldo López García, who along with Cajal had studied under Maestre de San Juan. Perrín moved to Madrid, and during two years (July 1905 to December 1907) he worked as a distinguished assistant in Cajal's histological laboratory. The experience of taking part in a prestigious research group under Cajal was to leave its mark on his later career.<sup>1</sup> In 1907 he earned his doctorate from the Central University after presenting *El treponema de Schaudinn*, an original study on the bacterium causing syphilis.

Perrín moved to Mexico in 1908 to complete experimental studies on syphilis transmission. He had been invited to do so by the Mexican Superior Council of Public Health, which was launching its first campaign against the disease.<sup>2</sup> In the same year, he was made Chair of Histology and Descriptive and Topographical Anatomy of the Mouth and Adjacent Structures at the National School of Dentistry. In 1913, he became Chair of Histology at the National School of Medicine, where he created a laboratory for histological research. Perrín also taught bacteriology in 1921 at the School of Public Health (now the Mexican Institute of Public Health) and anatomical pathology in 1923 at the Military Medical School of Mexico.<sup>3</sup> During half a century, he trained Mexican doctors and histologists in Cajal's techniques and published numerous research projects drawing on his knowledge of anatomical pathology as well as his skill with micrographic and serodiagnostic techniques.

Perrín did not pass up the opportunity to sing Cajal's praises in his new country. In 1922, after the lengthy disruption caused by the Mexican Revolution, he organised a formal event to pay homage to Cajal upon his retirement. Cajal's name was given to the Chair of Histology at the National School of Medicine, and he was also granted a *doctor honoris causa* by Universidad Nacional, named honorary correspondent of the General Directorate for Biological Studies, and made an honorary member of leading Mexican scientific societies.<sup>4</sup>



**Figure 1.** Dr Tomás Gutiérrez Perrín was the first scholar to present Cajal's teachings in Mexico.

In his quest to strengthen the academic ties between his two countries, Perrín founded the Hispano-Mexican Institute for University Exchanges in 1925. Under the aegis of this institute, he invited Francisco Tello and Pío del Río-Hortega to travel to Mexico; these two emblematic representatives of the Cajal School had been Perrín's friends since his youth. In 1929, Tello designed a course titled "Cajal's techniques and their application to research in important neurobiological topics". Río-Hortega presented a seminar on Cajal's research one year later.<sup>5</sup> These two courses sparked enthusiasm about Cajal's work among younger doctors. Some of them, including José Joaquín Izquierdo, Manuel Martínez Báez, Clemente Villaseñor, and Isaac Ochoterena, travelled to Spain to witness the projects carried out by the Cajal School *in situ*. A decade later, Perrín used all of his academic and diplomatic influences to smooth the immigration process for exiled scientists seeking asylum in Mexico.<sup>6</sup>

#### Santiago Ramón y Cajal: a reference for doctors in exile

The Spanish Civil War and Franco's dictatorship had a devastating effect on the sciences in Spain. Nearly half of all Spanish university professors were removed from their positions and stripped of their research privileges.<sup>7</sup> Scientific groups were dissolved and their members scattered around the world. Such was the fate of the Cajal Institute. Some of

its members, such as José María Villaverde y Larraz, were killed in the war. Others were forced out of the academic world but remained in Spain, as in the cases of Francisco Tello, Fernando de Castro, Nicolás Ramón López Aydillo, and José Miguel Sacristán Gutiérrez. Still others sought refuge in foreign cities: Pío del Río-Hortega in Buenos Aires, Miguel Prados Such in Montreal, Francisco Llaveró Avilés in Munich, Juan Miguel Herrera Bollo in La Habana, and so on. Nevertheless, only in Mexico would several of Cajal's students be reunited and resume their collaborative efforts. Mexico was the country in which the Cajal School was finally able to rebuild itself after the conflict that ravaged Spain.

One explanation for this occurrence is that the figure of Cajal was highly symbolic for the doctors exiled to Mexico. He was viewed as a patriarch who, during those critical times, successfully united a family of expatriate scientists and strengthened their belief in the political and cultural ideals that had forced them into exile. In truth, Cajal's 'family' was larger than the group of Spanish scientists; his authority was recognised by Mexican doctors and even by influential members within the conservative Spanish colony, such as the businessmen Carlos Prieto and Santiago Galas. All things considered, the Spanish Nobel Prize winner was a cohesive element that joined

Spanish doctors together and also provided a means for their integration in Mexican society. It should come as no surprise that the first association of exiled doctors to form in Mexico was named *Ateneo Ramón y Cajal*. Their journal, *Anales de Medicina*, was published to serve as a link between members of the Spanish medical diaspora and as a means of contacting colleagues in other countries, including those doctors still living in Spain.<sup>8</sup>

#### Exiled Spanish Republican neuroscientists in Mexico

Some 300 Spanish doctors fled to Mexico because of the Spanish Civil War; in fact, they made up 10% of the doctors in Mexico at that time. Although only twelve or so were neuropsychiatrists (Spain had followed the German model which combined neurology with psychiatry), their impact on medicine in Mexico was significant.<sup>9</sup> Five had trained with either Cajal or his own students, as shown in Table 1.

Two noteworthy neurosurgeons went into exile: Wenceslao López Albo (1889-1944) and Sixto Obrador Alcalde (1910-1979). Both doctors hailed from Santander and had been trained in Cajal's laboratories in Madrid: the former worked with Nicolás Achúcarro and Luis

SPANISH DOCTORS	MENTORS	MEXICAN INSTITUTIONS
Isaac Costero Tudanca (1903-1979)	Pío del Río-Hortega	Laboratory of Medical and Biological Studies Hospital General National Institute of Cardiology UNAM Faculty of Medicine
Tomás Gutiérrez Perrín (1881-1965)	Leopoldo López García Santiago Ramón y Cajal	UNAM Faculty of Orthodontics UNAM Faculty of Medicine School of Public Health Military Medical School
Wenceslao López Albo (1889-1944)	Nicolás Achúcarro Luis Simarro	Faculty of Medicine (Monterrey) Hospital Muguerza (Monterrey) Institute of Neuropsychiatry Hospital Español
Dionisio Nieto Gómez (1908-1985)	Pío del Río-Hortega José Sanchís Banús	Laboratory of Medical and Biological Studies General Asylum UNAM Faculty of Medicine Institute of Neurology and Neurosurgery
Sixto Obrador Alcalde (1910-1979)	Santiago Ramón y Cajal Pío del Río-Hortega	Hospital Muguerza (Monterrey) Institute of Neuropsychiatry Hospital Español Laboratory of Medical and Biological Studies
Gonzalo Rodríguez Lafora (1886-1971)	Santiago Ramón y Cajal	La Casa de España Institute of Neuropsychiatry Laboratory of Medical and Biological Studies

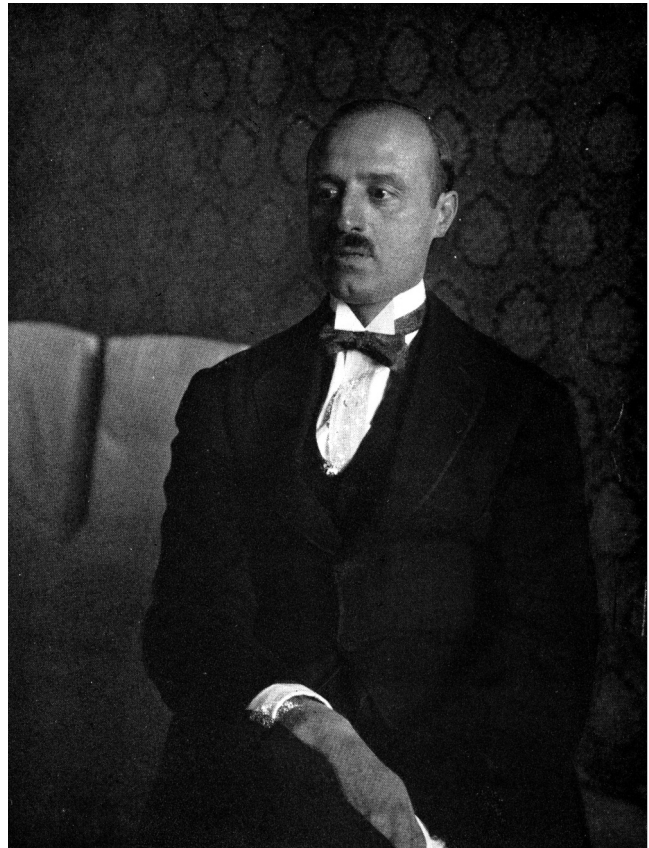
**Table 1.** Neuroscientists representing the Cajal School, their mentors in Spain, and the institutions where they worked in Mexico.



Simarro, and the latter worked directly with Cajal and with Pío del Río-Hortega. Furthermore, both had rounded out their training in neuropsychiatry with research experiences in Europe. López Albo studied in Berlin under F. Krause, Breslau under O. Foerster, and Paris under Levi and P. Marie. Obrador studied at Oxford under C. Sherrington (who had just been awarded his Nobel Prize) and H. Cairns. This tour of foreign research centres, an experience common to all the neuropsychologists and most of the other scientists in exile, had an impact on their later contributions to Mexican medicine. Upon returning to Spain, López Albo worked at Hospital de Basurto and directed the asylum in Zaldívar (Vizcaya province). He also directed Casa de Salud Valdecilla, an innovative hospital in what was then Santander province. In addition to publishing a number of clinical studies and a treatise on neuropsychological diagnosis, he was the founder and president of the Spanish Association of Neuropsychiatrists. He arrived in Veracruz in December 1939. Obrador, who was nearly 20 years younger, left Great Britain at the beginning of World War II. He arrived in Mexico in September 1940.<sup>10</sup>

López Albo settled in Monterrey, where he worked as a neurosurgeon at Hospital Muguerza and taught neurology and psychiatry at the Faculty of Medicine. In 1942, he moved to Mexico City and opened the Institute of Neuropsychiatry in partnership with Gonzalo Rodríguez Lafora. He was also the head of Neuropsychiatry and Neurosurgery at Hospital Español. His writings mainly focused on neurocysticercosis.<sup>11</sup> After López Albo, and somewhat shadowed by him, we find Obrador, who also practiced neurosurgery in Monterrey before travelling to the capital, at his mentor's orders, to work at its Institute of Neuropsychiatry and at Hospital Español. Additionally, Obrador worked at the Laboratory of Medical and Biological Studies; the laboratory's journal published several of his articles on epilepsy and the brain (vascular system and tumours). He returned to Spain in the late 1940s.

The Madrid-born neuropsychiatrist Gonzalo Rodríguez Lafora (1886-1971) had a much closer relationship with Cajal, considering that between 1906 and 1908 he had been his lead assistant; they later became colleagues (Figure 2). He earned his Doctorate in Medicine from Central University of Madrid and expanded his neuropsychiatric training under the most distinguished specialists of the time: T. Ziehen, H. Oppenheim, O. Minkowski, E. Kraepelin, A. Alzheimer, P. Marie, and J. Dejerine. In 1913, he returned to Madrid, where he



**Figure 2.** Neuropsychiatrist Gonzalo Rodríguez Lafora, one of Cajal's students. Founder and director of the Neuropsychiatric Institute in Mexico City.

directed the Laboratory of Nervous System Experimental Physiology and taught at the Cajal Institute. In 1933, he took on the directorship of the prestigious Department of Psychiatry at Hospital Provincial in Madrid.<sup>12</sup> One of the more privileged exiles, he arrived in Mexico at the invitation of La Casa de España, an institution created in November 1938 to offer asylum to prominent banished intellectuals.<sup>13</sup> He set up a private practice, directed the Institute of Neuropsychiatry, and published numerous articles on anorexia, encephalomyelitis, and homosexuality. In 1947, just before returning to Spain, he was named an honorary member of Mexico's National Academy of Medicine.

In contrast, neuropsychiatrist Dionisio Nieto Gomez (1908-1985) was closer to Pío del Río-Hortega and made joint use of his histological training and his studies as a psychiatrist (Figure 3). He was awarded a doctorate in medicine by the Central University, later studying



**Figure 3.** Neuropsychiatrist Dionisio Nieto followed in Cajal's footsteps in the Laboratory of Medical and Biological Studies.

neurology at the Max Planck Institute in Munich under W. Spielmeyer. He also studied clinical psychiatry in Berlin, Hamburg, and Paris. Once in Mexico, where he arrived in 1940, he undertook research at the Laboratory for Medical and Biological Studies and practised medicine at the General Asylum. He also taught at the Faculty of Medicine at the National Autonomous University in Mexico City (UNAM). His activities had a decisive impact on Mexican neurology. He studied the physiological basis of mental diseases, promoted treatment with psychopharmaceuticals, presented findings that were decisive for diagnosing neurocysticercosis, and explored anatomical pathology in schizophrenia.<sup>14</sup>

Another of Pío del Río-Hortega's students to make outstanding contributions to the neurosciences in Mexico was histopathologist Isaac Costero Tudanca (1903-1979). A native of Burgos, he earned his doctorate from Central University in Madrid. Costero Tudanca worked briefly at the Cancer Institute and the Department of Internal Medicine at Hospital General. He also spent two years polishing his histopathological training at the Pathologische Institut in Berlin and the Ehrlich Institut in Frankfurt. He arrived in Mexico at the invitation of Ignacio Chávez (with support



**Figure 4.** Histopathologist Isaac Costero in Mexico City, 1943.

from Perrín) to join the staff at the National Institute of Cardiology. While the Institute was still being built, he worked at Hospital General. He was named Chair of Anatomical Pathology at UNAM (Figure 4).<sup>15</sup>

Spanish exiles and the organisation of neuropsychiatric care in Mexico.

Spanish doctors contributed decisively to the creation of neuropsychiatric facilities in Mexico; neuropsychiatric care was only in its early stages when they arrived. The institutions that these doctors helped set up and maintain were staffed by exiled members of the Cajal School (Table 2).

In 1940, the Laboratory of Medical and Biological Studies was founded as a joint initiative between La Casa de España and UNAM, with support from the Rockefeller Foundation. This initiative arose as a way of providing a workplace for Cajal's students and other exiles. The name is a clear allusion to the Laboratory of Biological Research in Madrid, where the Cajal School was born; it was later renamed the Cajal Institute. All four of the laboratory's divisions, except for Cytology, were directed by Spanish doctors: Nieto and Lafora for Neuroanatomy and Neuropathology, Costero for Anatomical Pathology, and



SCIENTIFIC INSTITUTION	DOCTORS IN EXILE	
General Asylum (1910)	Dionisio Nieto Gómez	Augusto Fernández Guardiola
Laboratory of Medical and Biological Studies (1940), currently the Institute of Biomedical Research at UNAM	Dionisio Nieto Gómez	Gonzalo Rodríguez Lafora
	Isaac Costero Tudanca	Jaime Pi y Suñer
	Rosendo Carrasco Formiguera	Sixto Obrador Alcalde
	Manuel Rivas Chérif	Ramón Pérez Cirera
	Augusto Fernández Guardiola	Emilio Julio Muñoz Martínez
Institute of Neuropsychiatry (1942)	Gonzalo Rodríguez Lafora (director)	Wenceslao López Albo (subdirector)
	Sixto Obrador	Federico Pascual del Roncal
	Jesús María Sánchez-Pérez Sánchez	Manuel Rivas Chérif
	Victoriano Mateo Acosta Arce	Santiago Villanueva Sánchez
	Jaime Valdés Estrada	Germán Somolinos
National Institute of Cardiology (1944)	Isaac Costero Tudanca	
Institute of Neurology and Neurosurgery (1964)	Dionisio Nieto Gómez	Isaac Costero Tudanca
	Augusto Fernández Guardiola	

**Table 2.** Mexican scientific institutions that followed in the footsteps of the Cajal School and the Spanish doctors they employed

Jaime Pi y Suñer and Rosendo Carrasco Formiguera for Neurophysiology. It also employed other exiles, including Obrador, the ophthalmologist Manuel Rivas Chérif (a former co-worker of Cajal), and the pharmacologist Ramón Pérez Cirera. In 1943, the laboratory was absorbed by the UNAM, where it still exists as the Institute of Biomedical Research. As the years passed, most of the founding scientists moved on to other institutions. Dionisio Nieto, on the other hand, was to stay for the rest of his life, and he became the laboratory's leading figure. As a result, neuropsychiatry emerged as the centre's main line of research. The Laboratory followed Cajal's procedures and made important contributions to the diagnosis of neurocysticercosis and the study of histological changes in brain diseases. The Laboratory trained many outstanding Mexican neurologists, including Alfonso Escobar, Antonio Villasana, and Carlos Guzmán Flores, as well as two Spanish doctors, Augusto Fernández Guardiola (1921-2004) and Emilio Julio Muñoz Martínez (1938-). Like many other young exiles, these two doctors looked up to the great scholars who had fled Spain.<sup>16</sup>

Costero retired from the Laboratory in 1944 and became head of the Department of Histopathology of the newly created National Institute of Cardiology. Although he felt his duty was to study cardiovascular system pathologies, he also conducted interesting neurological research using Cajal's techniques. Some of his noteworthy studies exam-

ined central nervous system involvement in epidemic typhus, brain lesions caused by rheumatic fever, and fibroblastic activity in meningiomas. Costero's many students included Rosario Barroso Moguel and Ruy Pérez Tamayo.

In 1942, Lafora and López Albo created the Institute of Neuropsychiatry in Mexico City. This outpatient clinic for nervous diseases and mental illnesses employed a number of exiled Spanish doctors: Sixto Obrador (neurosurgery), Federico Pascual del Roncal (psychiatry), Jesús María Sánchez-Pérez Sánchez (neuroradiology), Manuel Rivas Chérif (ophthalmology), Victoriano Mateo Acosta Arce (otorhinolaryngology), Santiago Villanueva Sánchez (internal medicine), Jaime Valdés Estrada (general medicine) and Germán Somolinos (laboratory analyses). Their colleagues also included L. Deutch and Fritz Fränkel, a neurologist from Berlin who had joined the International Brigades.<sup>17</sup> The Institute's considerable prestige was due to its elite team of professionals and its coordinated procedure for carrying out research that involved direct cooperation between diverse specialists (Obrador would later implement this model in Spain).

The National Institute of Neurology and Neurosurgery, a division of the Mexican Secretariat of Health, was founded in 1964. It is one of the world's leading medical specialty centres. The Institute's scientific, academic, and clinical framework was strengthened by the contributions

of Spanish doctors and their students. Dionisio Nieto was the head of Psychiatry, Alfonso Escobar was head of Neuropathology, and Augusto Fernández Guardiola led the Cerebral Research Unit in which Isaac Costero and his student Rosario Barroso also worked.<sup>18</sup>

Spanish doctors in exile also made noteworthy contributions to an array of associations that included the Mexican Society of Neurology and Psychiatry (which became a prestigious association under Dr Nieto) and the centre for nervous system studies founded by Mexican neurologist Manuel Velasco Suárez. They also raised the level of such journals as *Boletín del Instituto de Estudios Médicos y Biológicos*, *Archivos de Neurología y Psiquiatría de México*, *Gaceta Médica de México*, *Revista Ciencia*, *Archivos del Instituto Nacional de Cardiología*, and more.

## Discussion

Cajal's teachings spread throughout Mexico in two distinct phases. The first phase was led by Tomás Gutiérrez Perrín, an early champion of neuron doctrine in the academic sphere who sparked interest in Cajal's research techniques among Mexican doctors. He also smoothed the way for the second phase, which was promoted by Cajal's students who entered Mexico as exiles. At that time, the Cajal School began to take root in that country. Spanish doctors in Mexico contributed on three different levels: research, primarily conducted in the Laboratory of Medical and Biological Studies; teaching, spearheaded by the chairs at the UNAM Faculty of Medicine; and clinical medicine, whose mainstay was the General Asylum (especially the Pilot Ward, directed by Nieto from 1941 to 1964, which promoted treatment with psychopharmaceutical agents). Doctors' activities included training hosts of students and publishing numerous articles. These articles demonstrate not only high-quality research, but also the authors' commitment to health priorities in their adopted country. Important examples were Obrador and Costero's studies of brain vasculature and Nieto's discovery of a method for diagnosing neurocysticercosis (a common parasitic infection in Mexico that manifests with a wide range of symptoms). Such divergent currents in research were common; rather than indicating that the Cajal School had fragmented, they actually constitute a sign of good health.

In truth, the contribution made by the exiled doctors as a group was greater than the sum of their individual studies, no matter how important those studies were.

This seeming paradox may be explained by the actor-network theory.<sup>19</sup> Spanish neurologists were the connection points for at least four large networks: 1) one created by Cajal and his many national and international collaborators before the Spanish Civil War; 2) one created by Perrín and his academic and social contacts; 3) the network of Mexican doctors; and 4) the network corresponding to the Spanish diaspora, including Spanish scientists, aid organisations, politicians, and other exiled professionals scattered around the world.<sup>20</sup>

As a result, the exiled neurologists, and Cajal himself, acted as nodes within a dense network of networks connecting multiple and varied actors. The most important players have already been mentioned, and listing every one of the actors would be outside the scope of this article. Instead, we would like to stress that this network transformed the scientific scene in Mexico and ushered in new possibilities. Let us consider an example. The Mexican doctors who, thanks to Perrín's efforts, showed an interest in Cajal's findings (including Martínez Báez, Ochoterena, Villaseñor, José Joaquín Izquierdo, and Ignacio González Guzmán) would later use their influence to help exiled neurologists settle in Mexico. Together with La Casa de España, they also participated in the creation of the Laboratory of Medical and Biological Studies, which received grants from the Rockefeller Foundation that were managed by other exiles. The Laboratory served as the dynamic core that gave rise to new connections within the network. It transformed clinical practice in the General Asylum, especially in Nieto's Pilot Ward. It also allowed the younger doctors, many of whom had been Nieto's and Costero's students at the UNAM Faculty of Medicine, to learn about Cajal's research and techniques. Some of these young doctors were to become key players in such institutions as the National Institute of Cardiology and the National Institute of Neurology and Neurosurgery, and they made instrumental contributions to numerous journals and neuroscientific societies. In summary, this network of networks played a decisive role in the Cajal School's rebirth in Mexico, and it also contributed to the brilliant advances in Mexican neuroscience in the following decades.

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