

Review Article

Professor Aristides Leão. Much More Than Spreading Depression

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Professor Leão described cortical spreading depression (CSD) in 1944 and changed the way migraine pathophysiology is scientifically conceived. This Brazilian professor and researcher developed his career in Rio de Janeiro. Because of him, the city once became the CSD world capital, attracting scientists from many laboratories around the globe. Aristides Leão was first and foremost a naturalist, a man genuinely interested in birds, fishes, plants, shells, and neuroscience. He could easily fascinate whoever would come for a chat, leaving no question without answers. He was born in 1914 and died in 1993. This report focuses on his life, family, habits, and hobbies, describing a little of Leão apart from CSD and the year of 1944.

Key words: Leão, migraine, spreading depression

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Few achievements have impacted the migraine field as much as the description of cortical spreading depression (CSD).¹ CSD is of crucial importance in the pathophysiology of migraine, as supported by neuroimaging,² genetic³ as well as pharmacological⁴ experiments. The ability to block CSD is a property shared by many migraine prophylactic drugs and therefore seems to predict their efficacy.⁴ New CSD propagation mechanisms related to the neuron-glia-blood vessels interaction⁵ further indicate that this complex neurophysiological phenomenon may play pivotal roles not only in migraine, but also in different neurological conditions, including epilepsy,⁶ cerebrovascular disorders,^{7,8} trauma,⁹ and transient global amnesia.¹⁰

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Headache care and research in Brazil would probably not have developed to the present stage without the major contribution of Professor Aristides Azevedo Pacheco Leão.¹¹ While in Boston for his PhD work under the leadership of Hallowell Davis and assistance of Arturo Rosenblueth, he first called attention for this hitherto unknown neurophysiological phenomenon. His publications became known worldwide and are still vastly cited.¹²⁻¹⁶ Leão not only identified CSD, but also first opened the possibility of its connections with migraine. Despite being totally unaware of Lashley's work published 3 years earlier¹⁷ (personal communication to P.M.-F.), Leão envisaged the potential role of CSD in the migrainous aura.¹³ Historical aspects related to CSD description are considered elsewhere.¹⁸⁻²⁰ In the present report, we review some aspects related to Leão's biography apart from his seminal work in neurophysiology.

Leão was born on August 3, 1914 in an expanding and rapidly developing Rio de Janeiro, son of Manoel Pacheco Leão and Francisca Azevedo Leão, or simply

Conflict of Interest: None

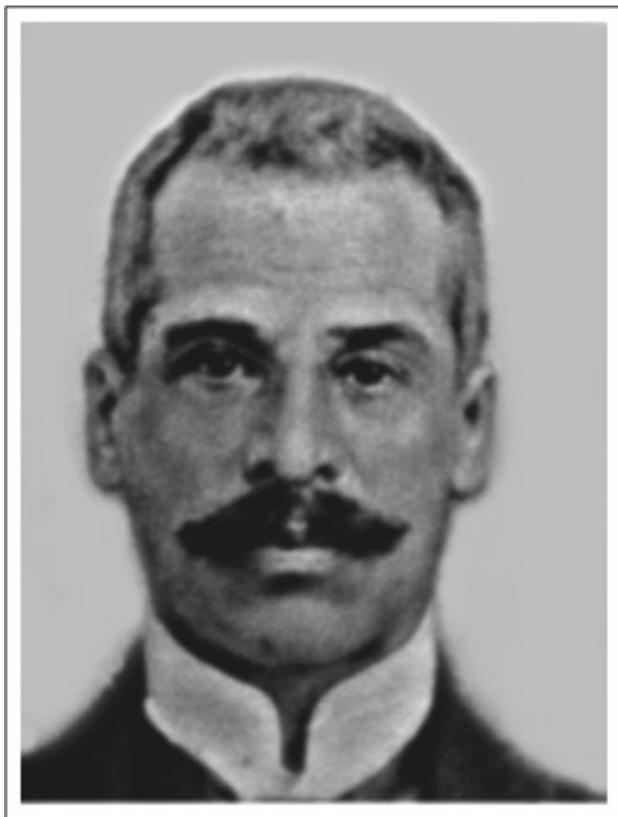


Fig 1.—Manoel Pacheco Leão, Aristides' father.

“Dona¹ Tita” (Figs. 1 and 2). Aristides was the youngest among 2 sisters and 5 brothers.

Brazil faced marked economic, social and political changes in the beginning of the 20th century. The former Empire became a republic in 1889, and the previous rural-based economy was progressively replaced by a more industry-devoted society. The Leãos profited the new opportunities in the Country and had a wealthy life. The grandfather from his mother side, José Eugênio de Azevedo, lived with his wife, “D. Maricota,” in a large house in Humaitá, a wealthy district in Rio by the end of the 19th century. He worked as a salesman offering products to other businessmen in villages and farmers at the countryside. Aristides' father, Manoel Leão, died in 1913 shortly before his birth because of encephalitis secondary to manipulation of an acne lesion in his nose. D. Tita enjoyed painting aquarelles, but she never

¹ A Portuguese honorific title attached to a person's given name. “Dona” (abbreviation: “D.”) may be roughly compared to the English “Lady.”

reached notoriety. Carlos Leão, one of his brothers, became a famous architect. Another brother, Theófilo, married Olga Portinari, sister of the famous Brazilian painter Cândido Portinari (1903-1962). Portinari won a Second Honorable Mention for the canvas “Café,” in New York, where he painted the panel “Guerra e Paz” (War and Peace) at the United Nations building. Leão's sister, Maria Augusta da Costa Ribeiro, nicknamed Magú, married the engineer José Cláudio da Costa Ribeiro and took part in the Flamengo park ornamental plants conception together with the world-famous landscape designer Roberto Burle Marx (1909-1994). This celebrated large public park, built on a landfill along Flamengo beach in Rio, was concluded in 1965. Aristides had a portrait of Costa Ribeiro by Portinari in his office, hanging on the wall behind his typewriter (Fig. 3). From Manoel Azevedo Leão, his oldest brother, Aristides earned his marked taste for the sea (Fig. 4). They pioneered the offshore fishing in Rio and supposedly caught the first Merlin in our coast. We found no reason to consider this fact just another fisherman's lie. His brother José died prematurely in 1932 by the age of 20, probably due to a rheumatic fever-induced heart disease.

Aristides Leão was culturally privileged from both sides of his family. They were fortunate to grow up in a comfortable and large house in Laranjeiras neighborhood (Fig. 5), under the constant care of a British nanny of whom there are unfortunately no



Fig 2.—Francisca Azevedo Leão, Aristide's mother, painting one of her aquarelles.

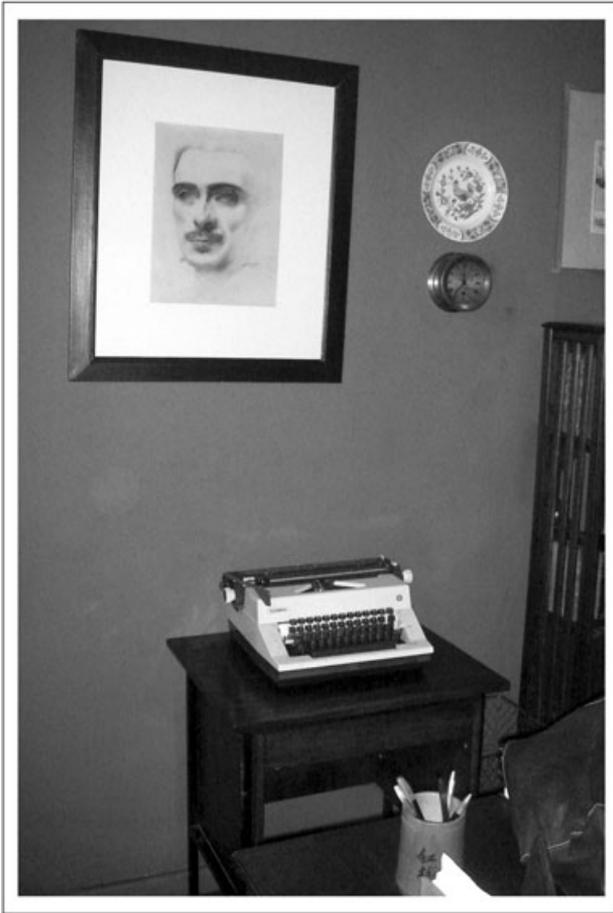


Fig 3.—Portrait of José Costa Ribeiro, Aristides Leão's brother-in-law, by Cândido Portinari.

records (Fig. 6). Paulo Azevedo, one of his uncles from his mother's side, and Manoel Pacheco Leão were co-owners of the well-known publishing company "Livraria Francisco Alves & Comp," established in Belo Horizonte, state of Minas Gerais. A second uncle, João Azevedo, became admiral. From his father's side, his uncle and biologist Antonio Pacheco Leão (1872-1931) decisively influenced the life of his nephew, and perhaps was the person who presented science to young Aristides. Member of the Brazilian Academy of Science (BAC) since its foundation in 1916 and director of the Rio de Janeiro Botanic Garden between 1915 and 1931, Antônio Leão received the visit of Albert Einstein in 1925 in Brazil. He published the "Arquivos do Jardim Botânico" journal and fought together with Oswaldo Cruz^{21,22} for the obligatory vaccination in the beginning of the 20th century.



Fig 4.—Leão with his brother Manoel's boat.

In 1932, Aristides Leão (at 18 years old) was admitted at the *Faculdade Paulista de Medicina* medical school in São Paulo. This faculty would soon become part of the São Paulo University, established



Fig 5.—The house in the district of Laranjeiras, Rio de Janeiro, where Leão grew up.



Fig 6.—Aristides Leão (the smallest to the left), a brother, a sister (to the right), and their English Nanny.

in 1934. He was forced to interrupt his studies for 2 years due to a pulmonary disease and moved to Belo Horizonte, Minas Gerais, for treatment. He was considered cured by the age of 26, but would never finish the medical school.

After recovering, Aristides traveled to the USA, and registered at Harvard University in the Medical Science Department (Physiology), where he obtained the Master of Arts and Doctor of Philosophy degrees in, respectively, 1942 and 1943. Sharing the costs with Aristide's brother-in-law José Cláudio Ribeiro, his brother Manoel Azevedo Leão paid for the ship ticket that took Aristides to the USA and financed his first year in Boston. In Harvard, he became Austin Teaching Fellow in the Department of Physiology (1942-1943) and Research Fellow in the Department of Anatomy (1944). His first scientific communication was in 1943, in collaboration with E.C. Del Pozo, about "the effects of hyperventilation and of blood-pressure changes on the self-sustained responses of the cerebral cortex."²³

Indifferent to career opportunities he was proposed in the USA, he moved back to South America in 1944. Aristides Leão was offered to work in a small room behind the physiology amphitheatre at the old Faculty of Medicine building in Rio, right between the stairs to the second floor and the barbershop area. He started his work having nothing more than a pen-knife, improvised benches, electric wires, and glassware he found here and there, plus a galvanometer taken from the Medical Physics Laboratory rubbish. Showing remarkable persistence, aptitude, and cleverness, Leão published his first work in Brazil.²⁴ In this paper, Leão described the 4- to 6-minute voltage variation that accompanies the spreading depression wave in the rabbit cortex and studied the effects of the interruption of circulation in the voltage changes.

Leão occupied many distinguished positions in his career. In the BAC, he became full member in 1951, vice president (1955-1957, 1965-1967), president (1966-1981), and president emeritus (1993). In the Carlos Chagas Filho Institute of Biophysics, Universidade Federal do Rio de Janeiro, among other positions, he was Professor of compared anatomy and physiology (1960-1981), director (1966-1970) and chief emeritus of the Neurobiology Department Laboratory (1984-1993). According to ex-students, his lab was always remarkably tidy. It is worthwhile mentioning his position as visiting scientist at the Laboratory of Neurophysiology, National Institute of Mental Health, N.I.H., Bethesda (1955-1956, 1961-1962), his position at the Department of Physiology, National Institute of Cardiology, México (1951-1952), the title of honorary member of the International Headache Society and of the Brazilian Headache Society (1985), and his election as member of the Lisbon Science Academy (November 20, 1969). He took part in several governmental and educational committees in Brazil. As the president of the BAC, Leão stimulated scientific cooperation between Brazil and other countries, establishing liaisons with the Fogarty International Center and the Japanese Society for the Promotion of Science. He also promoted studies in different areas such as "Systematic and chemical studies of the Amazon flora" or "Ecological studies of the semi-arid northeastern Brazil."²⁵ As president of the BAC, Leão took part in an international

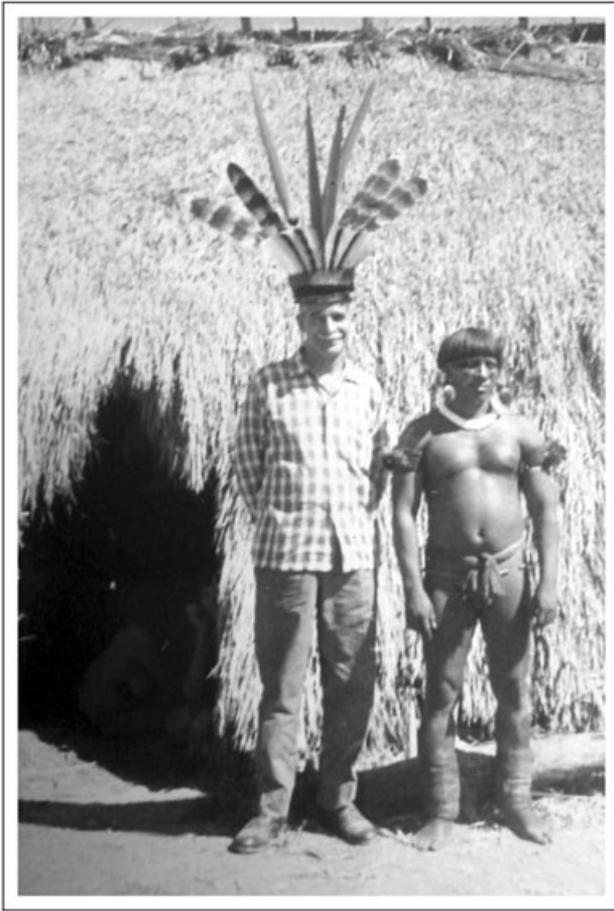


Fig 7.—Aristides Leão in a visit at the Xingu Indian Park, Brazil.

commission to study Indians for 8 years (Fig. 7). His laboratory was visited in Rio de Janeiro by researchers from all over the world interested in neurophysiology and the work performed by Leão and his close collaborators Hiss Martins Ferreira, Gustavo de Oliveira Castro, and Romualdo Carmo.

Professor Leão was essentially a naturalist. He was a great admirer of Darwin and developed a keen interest in zoology. He used to navigate in his brother Manoel's boat searching for sea life specimens. Despite general incredulity, Leão proved the existence of the "Agulhão de Vela" sailfish – *Istiophorus albicans* (Latreille, 1804) in the Guanabara Bay, Rio de Janeiro, a specimen previously considered absent in those waters. He gathered shells from various origins and carefully stored them in a bench.

Aristides also became a dedicated, high-level ornithologist and collected vast material about birds,²⁶ regarded as more impressive than that of the Brazilian National Museum. In an issue of the *Annals of the Brazilian Academy of Sciences* devoted to bioacoustics, Jacques M.E. Vielliard reported on the interest of Leão in this field: "It all began in Paris, on a nice day in the spring of 1973. My old master Henri Heim de Balzac invited me to join him at the next weekly session of the Académie des Sciences, where the President of the Brazilian Academy of Sciences was to be received and would present a project of cooperation in ecological field research in Northeastern Brazil. Dr. Aristides Azevedo Pacheco Leão was also anxious to bring to Brazil the recent technical advances in birdsong recording and analysis. When I was presented to him as a young PhD in Ecology and a field ornithologist with experience in bioacoustics, Dr. Aristides, as he was known by his friends in Brazil, invited me for lunch the following day. This is why I can, 30 years later, recognize Aristides Leão as the father of Bioacoustics in Brazil and pay at last the tribute I owe him."²⁷ He even published the book "*Ornitologia Brasileira*" together with Helmut Sick, ornithologist of the National Museum in Rio de Janeiro.

In Leão's library (Fig. 8) 4 subjects predominated: history and evolution of the natural sciences; nature in general, especially Brazilian natural history; spreading depression; and ornithology.²⁶ As an ornithologist, Leão was a meticulous observer. According to Paulo Emílio Vanzolini, director of the Zoology



Fig 8.—Leão's library at his house in Rio de Janeiro.

Museum, Universidade de São Paulo, he would leave very early in the morning and enter the woods elegantly dressed – gray trousers and white shirt, sleeves carefully folded up to his elbows, black leather oxford shoes – carrying his recording equipment, and return hours later full of enjoyment, dressed just as well. Few ornithologists knew Brazil, its macroclimates and vast natural diversity as much as Aristides Leão.²⁸ The special affinity for nature was reflected in his taste for arts. As an art enthusiast, he preferred aquarelles depicting birds and plants.²⁶

According to his wife, Aristides enjoyed nightlife. He was fond of classical composers but his favorite piece was the popular song *Carinhoso*, by Pixinguinha. Aristides married Elisabeth Raja Gabaglia – of simply “Bebeth,” as he called her – but had no children. Elisabeth’s grandmother lived in a very large house in Laranjeiras. Since the house had no yard, little Elisabeth, 9 years younger than Aristides, often played at his place. Leão died in 1993. He lived in a house at Portugal Avenue, Urca district, were Bebeth still resides.

Aristides was known as a determined, modest, perfectionist, and organized fellow. He loved to talk and could chat wisely on art, music, literature, or history. As a friend, admirer, and one of his last students, I (P.M.-F.) may state that Professor Leão was a true scientist, a clear example of a vaingloriousness-free knowledge. “A finished gentleman from top to toe.”

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