

Spanish influence in the life and work of Walter B. Cannon (1871-1945)

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ABSTRACT

Walter B. Cannon was the most illustrious American physiologist of the first half of the 20th century. From his laboratory at Harvard University, this multi-talented researcher completed pioneering radiological studies of the digestive tract and explored the autonomic nervous system, emotions, and chemical transmission of nervous stimuli. Treading the path traced by Claude Bernard, he developed the concept of homeostasis, referring to the mechanisms that regulate stability of the internal environment. A liberal thinker fully committed to the issues of his time, he participated in numerous social and humanitarian initiatives. He maintained a long-standing relationship with Spanish physiologists, especially the members of the Catalan school. One of them was Rossend Carrasco i Formiguera, one of his best-known students. He also enjoyed a close friendship with the physiologist and politician Juan Negrín. Cannon was the most influential figure in the United States to defend the Second Spanish Republic as the legitimate government of Spain during that country's civil war (1936-1939). He also offered considerable assistance to Spanish physiologists and other scientists who went into exile after the war.

KEYWORDS

Walter B. Cannon, physiology, homeostasis, Spanish Civil War, Rossend Carrasco i Formiguera, Juan Negrín

Introduction

Walter Bradford Cannon was a key figure in 20th century American physiology. He was also the first great physiologist in the United States not to have been trained in Europe. Gifted with enormous scientific curiosity, he was a pioneer in multiple fields of medical research, including radiology, endocrinology, and neurophysiology. As a moral person of liberal ideals who was deeply engaged with the issues of his time, Cannon was known for his involvement in initiatives ranging from debates on animal testing to his commitment to his country during the two world wars, the fight against Nazi fascism, and his support for the Second Spanish Republic's legitimate mandate. He managed to create a school including many students of different nationalities, including Spaniards. Beginning in the 1920s, he formed a special relationship with the Catalan school of physiology and also with Juan Negrín, the physiologist and politician from the Canary Islands.

The purpose of this article is to provide an overview of the life and scientific work of Walter B. Cannon while

analysing his connection with Spain, both as a physiologist and as a politically-minded humanitarian. To this end, we reviewed the literature on this subject.

On the trail of a researcher

Walter Bradford Cannon was born in 1871 in Prairie du Chien, a small rural town in the state of Wisconsin (Figure 1). The son of a railroad worker and a school-teacher, he came from a Presbyterian family of French-Canadian and Irish origin. Cannon was an outstanding student and applied for scholarships to attend either Johns Hopkins University in Baltimore or Harvard. Upon receiving a favourable response from Harvard, he moved to Boston and was able to cover the cost of his studies with his scholarship and wages.^{1,2}

Cannon began his studies at Harvard College in 1892 and graduated summa cum laude in 1896. He was then accepted to medical school (1896-1900) and soon displayed an interest in neurology and psychiatry. During his final year of medical school, he also taught comparative vertebrate anatomy. While enrolled at Harvard College, he conducted a study under the guid-

ance of his professor Charles B. Davenport to observe the orientation of microorganisms toward light. In 1896, still in his first year of medical school, he began conducting research with X-rays, which had been discovered by Wilhelm Röntgen only the year before. Henry P. Bowditch, Cannon's mentor, suggested that he study the mechanical factors of digestion using this new technique. After several attempts, Cannon concluded that the best animal test subjects were cats, which he forced to ingest bismuth and barium salts. This procedure showed that movements in the digestive tract were peristaltic and not spasmodic as it was believed at the time.^{2,3}

Dr Cannon's professor and predecessor, Henry P. Bowditch, had studied at the University of Leipzig with Carl Ludwig, whom he considered his mentor, and also in Paris under Claude Bernard, Charcot, and Ranvier. In 1906, Cannon succeeded Bowditch as chair of the physiology department at Harvard Medical School. Bowditch had held that position for 35 years, and Cannon would chair the department for 36 years, until 1942.²

Walter B. Cannon married Cornelia James in 1901, and they had five children. Both had been high school



Figure 1. Walter B. Cannon (circa 1940)

students in Saint Paul, Minnesota, when they met. Cornelia studied at Radcliffe College in Boston and is known as a novelist and a proponent of eugenics. The couple belonged to the Unitarian Church in Boston.¹

In the course of his radiology research, Cannon observed that the cats exposed to situations inducing fear and anxiety suffered gastrointestinal paralysis as well as increases in arterial tension, glycaemia, and adrenaline levels. He published these findings in a book titled *The mechanical factors of digestion* (1911).^{2,3}

Cannon also used surgical techniques to study heart rate response, the sympathetic nervous system (SNS), and adrenal glands in cats exposed to such stimuli as pain, asphyxia, emotional arousal, or hunger, all of which trigger adrenaline secretion by those glands.^{2,4} Based on this research, he developed the concept of the fight-or-flight response (emergency theory) derived from Darwinian ideas. This theory states that natural selection contributes to the development of certain bodily functions in an organism's struggle for survival, and that the animals exhibiting the fastest reaction to bodily damages will prevail. Results from this research were published in *Bodily changes in pain, hunger, fear and rage* (1915).⁴

With his colleague Philip Bard, Cannon formulated a theory stating that emotions are experienced before their somatic expression appears, and that they are associated with the activation of hypothalamic structures (Cannon-Bard theory). It contradicted the James-Lange theory, formulated in 1884 by Cannon's professor William James, who believed that emotions manifested after the somatic response. Relations between master and student became strained in 1908 due to frictions between proponents of animal testing, led by Cannon, and antivivisectionists, including William James.^{3,5}

In 1917, when the United States entered World War I, Dr Cannon joined the Harvard University medical team as a volunteer, together with Harvey Cushing and a number of other doctors. While assigned to a hospital in Béthune, in northern France, Cannon completed important studies on traumatic and haemorrhagic shock and would later publish his findings as a book, *Traumatic shock* (1923). In 1925, he devised safe methods for drying human plasma. Almost twenty years later, during World War II, he became chairman of the U.S. National Research Council Committee on Shock and Transfusion.^{1,2}

Cannon resumed his studies of the autonomic nervous system (ANS) after World War I. An extraordinarily skilful surgeon, he developed the denervated heart model as an indicator of sympathetic activity. He also showed that the ANS is responsible for maintaining uniformity in body fluids, in line with the concept of *milieu intérieur* developed by Claude Bernard. In 1926, he coined the term 'homeostasis' to describe the sum of these autoregulatory mechanisms, a concept that he explained in detail in his most famous book, *The wisdom of the body* (1932).^{2,4} The concept of homeostasis englobes all the regulatory mechanisms that automatically lend stability to the internal conditions of an open system (water, ions, pH, glucose, proteins, temperature, hunger, thirst, etc.). This biological notion was borrowed by researchers in other fields and thus the idea of social homeostasis emerged in the context of the Great Depression. Years later, it would be reincarnated as the Gaia hypothesis that proposes that the Earth is a self-regulating living organism.^{1,2}

Intense emotions in animals elicit increased secretion of adrenaline by the adrenal glands in order to satisfy energy needs. An interruption of homeostasis triggers a stress response due to hyperfunction of the SNS. Cannon also studied the sympathetic and adrenal mechanisms that mobilise glucose in response to insulin-induced hypoglycaemia, as well as the important role of adrenal glands in regulating body temperature.²

Assisted by his most outstanding student, Arturo Rosenblueth of Mexico, (1900-1970), Cannon explored the chemical transmission of nervous stimuli. In 1933, they isolated adrenaline-like substances from sympathetic nervous terminals and highlighted their role in mediating impulses between nerves and muscles. They also demonstrated that muscle fatigue is caused by the exhaustion of acetylcholine at the neuromuscular terminal. As a result of their research, they published *Autonomic neuro-effector systems* in 1937.²

Mathematician Norbert Wiener was responsible for another approach to the concept of homeostasis. His father, a professor of Slavic languages and literature at Harvard, was a friend of Walter B. Cannon's; Norbert, a frequent visitor to Cannon's laboratory during his childhood, was also a great admirer. In 1933, Wiener met Arturo Rosenblueth, and the two scholars collaborated in the development of cybernetics. Their concept of biofeedback is a logical extension of the concept of homeostasis.⁶

Cannon also had the opportunity to teach abroad, presenting physiology lessons at La Sorbonne in Paris in 1929 and at Union Medical College in Peking in 1935.¹

Walter B. Cannon and Spanish and Catalan physiology

The Walter B. Cannon Archive in the Countway Library of Harvard Medical School in Boston is home to a vast collection of letters which Dr Cannon exchanged with numerous Catalan and Spanish physiologists, as well as documental evidence of his humanitarian activities in support of the Second Spanish Republic.⁴

Although the archive contains no evidence that Cannon corresponded with Catalan physiologists before 1922, we know that Cannon and Ramón Turró (1854-1926) shared an interest in the physiological aspects of hunger. Cannon did exchange letters with members of the Institut de Fisiologia in Barcelona, including its director August Pi i Sunyer (1879-1965). One of the youngest and most brilliant members of the Institut, Manuel Dalmau (1890-1918), spent several months between 1916 and 1917 working in the physiology laboratory at Harvard. Dalmau died shortly after his return to Barcelona while studying the influenza pandemic of 1918. Cannon was deeply saddened to hear of Dalmau's death when Turró passed on the news in 1922.⁴

The most brilliant of Walter B. Cannon's Spanish students was Rosend Carrasco i Formiguera (1892-1990), who worked at Harvard between June 1921 and August 1922 thanks to a grant from the Commonwealth of Catalonia. Carrasco i Formiguera introduced Claude Bernard's method of puncturing the floor of the fourth ventricle (*piqûre diabétique*, 1855) in Cannon's laboratory. This method was combined with the denervated heart model to study the action of adrenaline. Other techniques, such as asphyxia and denervation of hepatic nerves in cats, were also used in this laboratory. When Carrasco returned to Barcelona, he and Cannon corresponded to analyse the methodology and results of their own experiments and exchange comments on the latest scientific news. Carrasco informed Cannon about José Puche's techniques combining the denervated heart method with ablation of the stellate ganglion (Figure 2). Carrasco presented an article on the denervated heart of dogs in the Eleventh International Physiological Congress, held in Edinburgh, in 1923.^{1,4}

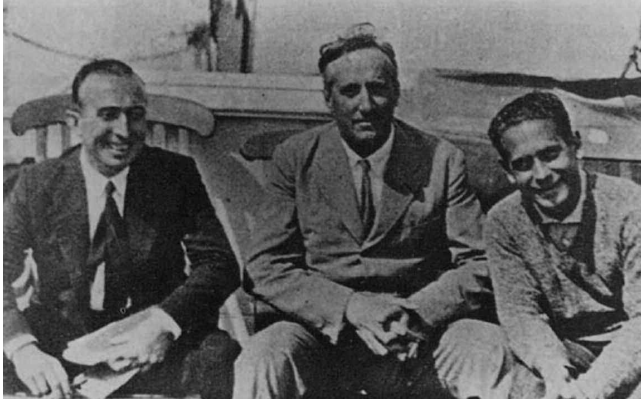


Figure 2. From left to right, José Puche, August Pi i Sunyer, and Rossend Carrasco i Formiguera (1929)

Rossend Carrasco was a witness to the discovery of insulin during his stay in the United States, and he began studying the pathogenesis and treatment of diabetes in 1922. In October 1922, he became the first European researcher to isolate this hormone and administer it to a patient.^{1,7} By 1926, Jaume Pi-Sunyer Bayo (1903-2000), the son of August Pi i Sunyer, was working with John Fulton at Yale University and with Walter B. Cannon at Harvard University.⁸

Physiologists from Madrid and Barcelona took Cannon's part in the debates of the day. Cannon clashed with Stewart and Rogloff of Cleveland, and with French scientist Eugène Gley, all of whom questioned his results regarding the response to adrenaline in the presence of emotional stimuli. From 1923 on, Cannon corresponded regularly with Gregorio Marañón (1887-1960), who was performing experiments in similar areas. These debates revolved around the role played by the emerging field of endocrinology.⁴

A large group of Catalan doctors including August Pi i Sunyer, Jesús María Bellido i Golferichs, and Rossend Carrasco i Formiguera, attended the Thirteenth International Congress of Physiology (Boston, 1929), which was organised by Walter B. Cannon.⁴

Until that moment, his interest in Spain had been purely scientific. This would change after his extended stay in Paris in the spring of 1930, when he was able to visit Barcelona, Madrid and Seville with his family. He admired the Magic Fountain of Montjuic and travelled to Montserrat with Rossend Carrasco. In Madrid, Juan

Negrín (1892-1956) took Cannon to visit El Escorial and the construction site of the campus known as Ciudad Universitaria (Figure 3). That visit was to forge a bond of lasting friendship and mutual admiration, and it was Michel Weinberg of the Institut Pasteur whose timely letter to Francisco Tello ensured that Cannon and Negrín would meet. In a speech delivered in April 1937 before the North American Committee to Aid Spanish Democracy, Cannon mentioned three events that had moved him greatly during his visit to Spain in 1930 (Figure 4). Firstly, there were Rossend Carrasco's explanations of the abuses of power and injustices committed by the dictator Primo de Rivera. Secondly, the crowd's uncomfortable silence during Alfonso XIII's procession through the streets of Seville in Holy Week had made a deep impression. And thirdly, during his stay in Madrid, Cannon was able to hear Negrín and his circle speak openly about revolution. Negrín had informed Cannon that the crypt at El Escorial would be able to receive only one more king due to space constraints.^{1,4}

Cannon showed mounting interest in the political events in Spain and was enthusiastic about the proclamation of the Second Republic, which he considered the most interesting political event in Europe at that time. He wrote letters congratulating Marañón, Negrín, Pi i Sunyer and Carrasco on 17 April 1931. Although his ties



Figure 3. Juan Negrín (circa 1940)



Figure 4. Poster issued by the Medical Bureau and the North American Committee to Aid Spanish Democracy (March 1939)

to Spain were less pronounced during the earlier years of the Republic, he was elected to the medical academies of Barcelona in 1932 and of Madrid in 1935.⁴

In 1933, Cannon suggested to Juan Negrín that Spain should provide refuge to the German Jewish professors who had escaped after Hitler's rise to power. In Cannon's opinion, this would revitalise the scientific level in our country. The two friends would meet and renew their friendship in 1935, during the Fifteenth International Congress of Physiologists in Leningrad.^{1,4,9}

The Spanish Civil War

When Cannon learned of the events of July 1936, he wrote a letter to Rossend Carrasco emphasising his support for the Second Republic. Thanks to information provided by Carrasco, Negrín, and the Pi i Sunyer family, Cannon was able to closely monitor the plight

of Spanish physiologists during the war. He was surprised when August Pi i Sunyer, who had left Barcelona for Paris in the autumn of 1936, asked him for a job in Boston. Cannon asked him hard questions about where his sympathies lay, but in the end he did write to the Rockefeller Foundation to arrange a position for the Catalan physiologist.⁴

Dr Cannon organised and presided over the Medical Bureau for Aid to Spanish Democracy, also known as the Spanish Medical Bureau, which was founded in October 1936. He accepted the presidency on March 1937 and collected money to send medical equipment, ambulances, medicine, and healthcare workers to Republican Spain.^{1,10} In February 1937, Rossend Carrasco sent word that he was still working in Barcelona and trying to obtain insulin with only limited means. Bellido had also remained in Barcelona, but August Pi i Sunyer was by that time presenting lectures all over Latin America, and Marañón, like many other wealthy Spaniards, was living in Paris.⁴

In March 1937, Cannon protested the U.S. Department of State's decision to prohibit citizens from travelling to Spain. The prohibition was later revoked, making it possible to send medical aid. Humanitarian action by the Medical Bureau was redoubled in May 1937 after Negrín became president of the Spanish Republican government. Cannon asked that he appoint a manager who would process the requests for medical and surgical assistance. The doctor designated to that end was Rafael Fraile, the ranking medic in the Spanish Carabineros.⁴ Cannon travelled the length and breadth of the United States to participate in talks and meetings; meanwhile, the conservative press accused him of directing a Bolshevik organisation based in Moscow.^{1,11}

On 17 April, 1937, he delivered a speech in the New York Hippodrome before thousands of supporters of the Spanish Republic. He presented his reasons for supporting the cause based on liberal and antifascist ideals. Just a few days later, on 26 April, he was shocked by the news that the town of Guernica had been bombed by the Condor Legion.^{1,2}

American support for Spanish Republicans materialised in the form of six hospitals and the assistance of 99 healthcare professionals including 23 doctors, 46 nurses, 20 ambulance drivers, and 10 technicians. Surgical equipment, drugs, and 18 ambulances were also shipped to Spain.^{9,11} In 1938, Cannon dispatched the insulin zinc



Figure 5. Ivan P. Pavlov and Walter B. Cannon (1923). © Countway Medical Library.

suspension requested by Rossend Carrasco and the quinine requested by Gustavo Pittaluga together with the nicotinic acid used to treat pellagra.¹

In December 1937, Dr Cannon also sent a congratulatory message in celebration of the 25th anniversary of the Societat Catalana de Biologia, presided over by Negrín, who had also been a member ever since it was founded.^{4,12} In August 1938, Negrín journeyed incognito to Zurich to attend the Sixteenth International Congress of Physiologists and meet Walter B. Cannon, but the latter was unable to attend due to last-minute illness.¹³

In November 1938, the relief ship *Erica Reed* docked in Barcelona; its cargo of food, medical equipment, and medicine made Cannon hugely popular among the locals. Several doctors, including Juan Negrín, Rossend Carrasco, Jesús María Bellido, and Rafael Méndez, signed a letter expressing their gratitude to all members

of the Spanish Medical Committee and to Walter B. Cannon in particular.^{1,10} On 19 December, 1938, during the last faculty senate meeting of the Universidad de Barcelona before the fall of Catalonia, the university awarded the degree of *doctor honoris causa* to Dr Cannon, and also to Pau Casals and French physicist Paul Langevin. Cannon remained unaware of this honour until October 1941, when he happened to read Rossend Carrasco's article in *Revista dels Catalans d'Amèrica*, an émigré journal. The press release on the conferral of that degree had been published in *La Vanguardia* on 21 January 1939.¹⁰

Midway through April 1939, when the war in Spain had already drawn to a close, an ailing Walter B. Cannon resigned the presidency of the Spanish Medical Bureau.^{1,2}

Spanish Republicans in exile

Walter B. Cannon endeavoured to help the Catalan physiologists who had at first benefited from the hospitality of Dr Camille Soula in Toulouse. Some emigrated to the Americas, including Rossend Carrasco and Jaume Pi-Sunyer, who were given a warm welcome in Mexico by Cannon's student José Joaquín Izquierdo. August Pi i Sunyer journeyed on to Venezuela.^{10,12} Between 1939 and 1940, Cannon exchanged volumes of correspondence with Spanish physiologists and tried to help them find positions in different institutions in North and South America.⁴ These scientists were not accustomed to clinical practice and could only work in academic institutions and research centres. As a result, they were scattered far and wide.¹⁰

In August 1939, Cannon invited pharmacologist Rafael Méndez (1906-1991), who had collaborated closely with Negrín, to join him at Harvard. They had met previously in Madrid in 1930. Méndez worked there for four years with Otto Kraye, a German professor who had escaped from the Nazis.¹³

Cannon promoted the Spanish translation of his book *The wisdom of the body* (published by Editorial Séneca, Mexico City, 1941) as a means of helping exiled scientists. The translation was largely completed by Dr Jesús María Bellido (1880-1952), and Rossend Carrasco and Jaume Pi-Sunyer also contributed. The prologue was written by José Joaquín Izquierdo and the epilogue by August Pi i Sunyer. Editorial Séneca was a publishing house established by the evacuation service for Spanish

refugees (*Servicio de Evacuación de Refugiados Españoles, SERE*) as a cultural platform for Republicans in exile. Bellido, the deputy director of the Barcelona School of Physiology, translated the book between the autumn of 1939 and the winter of 1940 in France, where he spent his time in exile. Catalan physiologists, who had a strong tradition of translating scientific literature into Spanish, considered this task to be a show of scientific resistance.¹⁰ Cannon was deeply frustrated by his inability to draw Bellido out of France, where he was at great risk since he had headed the Republican government's Church Affairs Commission during the Civil War. Cannon wanted Bellido to move to the Americas.¹

Juan Negrín visited his friend Walter B. Cannon in May 1939 in New York,¹ and once more in June 1945 in Chicago, a few months before Cannon's death.¹⁵

In homage to the stalwart defender of the Second Republic, Hôpital Varsovie in Toulouse, which treated exiled Spaniards living in the region, was renamed the Walter B. Cannon Memorial Hospital in 1946.^{11,14}

Walter B. Cannon and Ivan Pavlov

The physiologists Cannon and Pavlov forged a lasting friendship based on their mutual interest in digestive processes and how they are linked to the nervous system (Figure 5). Ivan Pavlov (1849-1936) responded to Cannon's invitation and travelled to Boston with his son in 1923. He visited that city once again in 1929 to attend the Thirteenth International Physiological Congress. Pavlov was the star attraction at that event, rated even higher than Cannon's spectacular exhibition of animals that had survived complete sympathetic system ablation. Cannon would visit Pavlov in turn in August 1935, on the occasion of the Fifteenth International Congress of Physiologists in Leningrad. This time, Cannon would become the man of the hour in the plenary session by arguing in favour of freedom in scientific research and against aggressive nationalism.^{1,9}

His last years

Dr Cannon took part in organisations that provided medical support to China, then at war with Japan (1937). Although he was critical of Stalinism during World War II, he presided over the American-Soviet Medical Society between 1943 and 1945.^{9,11}

Cannon retired from his chair at Harvard in 1942, but he continued to teach as a visiting professor at New York

University. He also travelled to Mexico to complete research projects with his student Arturo Rosenblueth, who had returned to his own country.¹

In 1942, he published the article "‘Voodoo’ Death" in the journal *American Anthropologist*. Based on his observations and interviews, he formulated a scientific explanation of death triggered by voodoo rites. The intense stress provoked by these rites is able to cause ANS hyperactivation and the release of adrenaline and other substances, as well as severe constriction of peripheral arterioles. This, together with vascular collapse and cardiac arrhythmias, can result in the death of a subject.¹⁶

Cannon suffered from the scourge of all pioneers in the study of radiology: cancer due to repeated exposure to X-rays. The lesions on his hands caused by radiation were visible as early as 1897. He was diagnosed with mycosis fungoides in 1931, epidermoid carcinoma on one wrist in 1940, and a basal cell cancer on his nose in 1944. While visiting Rosenblueth in Mexico in 1945, he fell ill and made a hurried trip back home to Franklin, Maine, where he died on 1 October as a result of mycosis fungoides complicated by bronchopneumonia. The doctors who treated him over the course of his illness published an article titled 'Mycosis fungoides followed for fourteen years; the case of Dr. W. B. Cannon' in 1955. This article described the entire process.^{1,2}

Dr Cannon was a humble and easy-going man who usually went to work by bicycle or in his old car. His writing style was agile and entertaining and he published many books and articles intended to be read by general public, thereby preventing other parties from skewing his messages. As an example of a manipulated message, he cited the sensational Associated Press headline describing his finding that rage elicits release of glucose into the bloodstream: "Man is sweeter when angry".² Despite having received three nominations, Cannon never won the Nobel Prize in Medicine.⁹

Conclusions

Walter B. Cannon was the most noteworthy figure in American physiology during the first half of the 20th century. After initially focusing on X-rays and their uses in the study of the digestive system, he channelled his efforts into the autonomic nervous system and the func-

tions of adrenaline and emotions. This led him to formulate the concept of homeostasis. He also researched the activity of internal secretion glands, the transmission of nervous stimuli, and the mechanisms at work in traumatic shock. While some might label him a gastroenterologist, neurophysiologist, psychologist, or pharmacologist, the most appropriate term would simply be 'physiologist'.

Cannon was an open-minded man who was particularly generous with his students. He defended medical research from the antivivisectionist movement and showed great selflessness in joining and leading several social and humanitarian initiatives.

His ties to Spain were intense and long-lasting, especially his association with Juan Negrín and with the Catalan School of Physiology, which included one of his most outstanding students, Rossend Carrasco i Formiguera. Walter B. Cannon was undoubtedly the most outstanding internationally-known scientist to defend the legitimacy of the Spanish Republic during the Spanish Civil War of 1936 to 1939.

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