Gleb von Anrep (1890-1955). A student of Pavlov in the British Empire

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ABSTRACT

Gleb von Anrep (1890-1955) was a distinguished member of the British school of physiology. Born in Saint Petersburg, he studied under Ivan Pavlov in his early years, until emigrating to England in 1918. In London, where he collaborated with Ernest Starling, he published outstanding works on the cardiovascular function. In 1931, he moved to Egypt, where he remained until the end of his days. His most significant works within the Pavlovian school initially included studies dedicated to conditioned reflexes and the function of salivary glands and the pancreas. He also studied the cardiopulmonary and muscular circulation, metabolism, and the function of histamine, and conducted research into substances acting on the coronary circulation. Furthermore, he was Pavlov's main interlocutor among English-speaking scientists, with whom his master had close contact despite not speaking their language. His translation and editing of the English-language version of the classic Pavlovian work on conditioned reflexes, which resulted from this relationship, is worth mentioning.

KEYWORDS

Gleb von Anrep, Ivan Pavlov, Ernest Starling, University College London, Cairo University, conditional/ conditioned reflexes, cardiovascular physiology

Introduction

Gleb von Anrep (1890-1955) was a prominent British-Russian physiologist mainly dedicated to the study of blood circulation. From his Russian origins and early training under Ivan Pavlov (1849-1936) in Saint Petersburg (Petrograd at that time), he inherited an interest in conditioned reflexes and digestive function and developed a close relationship with his master, playing a central role in the translation and editing of the English-language version of Pavlov's work, *Conditioned reflexes*: *an investigation of the physiological activity of the cerebral cortex.* He has also, unfairly, been blamed for the incorrect use of the term conditioned reflexes rather than conditional reflexes, a mistake that currently persists in many Western languages.

The aim of this work is to describe the life of Gleb von Anrep, his eventful personal life and productive scientific career, as well as his long-standing relationship with Pavlov, whom he represented as his main ambassador in the English-speaking world. It also analyses his master's relationship with English scientists, who always showed great interest in Pavlov's work.

Material and methods

We performed a broad literature review on the life of Gleb von Anrep, as well as his scientific activity, both in the field of neurosciences and in cardiovascular, pulmonary, muscular, and digestive physiology. We also studied Ivan Pavlov's relationships with British and North American psychologists, as well as the Anrep's involvement in these.

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Received: 19 August 2021/ Accepted: 18 October 2021

Figure 1. A croquet party at William Bayliss' London house (circa 1912). Pavlov is seated on a chair in the middle row (second from the right). Seated on the ground in the front row, Bayliss is second from the left and Ernest Starling is the third from the right.[6]

Development

The Anrep family

Gleb von Anrep was a descendant of a prominent family from Westphalia with a military history dating back to the 10th century. Field Marshal von Anrep, leader of the Livonian Order of Knights, built an outpost of Christianity on the shores of the Baltic. General von Anrep travelled to Saint Petersburg at the invitation of Peter the Great, and founded a new Russian branch of the family in the 18th century.[1]

Professor Vassily von Anrep (1854-1925) was the first member of the family to work in science. He studied medicine in Saint Petersburg and two years of pharmacology in Leipzig, where he discovered the local anaesthetic action of cocaine and recommended its use four years before Karl Koller (1857-1944). He then became professor of pharmacology in Kharkiv and entered the Medical Academy of Saint Petersburg, where he later became director of the Institute of Experimental Medicine and the Medical Institute for Woman Doctors. He also promoted education reform, holding important offices in the medical administration and education, using these positions to promote compulsory education. The Bolshevik revolution forced him to emigrate to London in 1919, where he lived with his son Gleb, and later to Paris, where he died in 1925.[1]

Childhood and youth

Gleb von Anrep was born on 3 September 1890 in Saint Petersburg into a family of the Russian elite. He was

the youngest of four boys; the two eldest were from his mother's previous marriage. The third son, Boris (1883-1969), was a successful mosaicist in England, a member of the Bloomsbury Group, poet, and lover of Anna Akhmatova.[1-3]

Gleb was born in a time of social uncertainty, in a family dominated by an authoritarian father. He was a lonely child, interested in mysticism and the Bible, with considerable talent for languages and music, even becoming an excellent pianist. He was awarded a gold medal at the gymnasium, graduating in 1908. He joined the School of Science at the University of Saint Petersburg, but struggled to adapt, and he was sent for several months to Germany. After this initial failure, he started to study medicine at the University of Saint Petersburg, graduating in 1914. During his medical studies, he worked as a physiology demonstrator at the Military Medical Academy (MMA), where in 1911 he began working as researcher at Ivan Pavlov's laboratory, becoming a devoted student and friend. Under Pavlov, he worked on pancreatic secretion, behavioural psychology, and conditioned reflexes.[1-4]

First stays in London

Due to his particular interest in cardiovascular physiology, at the suggestion of Ivan Pavlov he joined the laboratory of Ernest Starling (1866-1927) at University College London (UCL) in June 1912, where he also worked the two following summers.[1]

While Starling developed his "law of the heart" as part of his cardiovascular research, a messenger from Pavlov arrived. It was Gleb von Anrep, a medical student from Saint Petersburg, for whom Pavlov had the greatest consideration. He was sent with two tasks related to William Bayliss' (1860-1924) and Starling's previous work on secretin, which they discovered in 1902 (Figure 1). The first task consisted of demonstrating to them that vagal stimulation elicited pancreatic secretion in dogs, which they believed to be exclusively the result of secretin action. The second task was for him to learn to isolate this hormone. One of Pavlov's reservations about secretin was due to his inability to isolate it. Already in his Nobel Prize acceptance speech in 1904, he spoke about the nervous mechanisms of digestion, but did not mention the humoural mechanisms or secretin, the first hormone to be discovered. The term hormone was coined by Starling. Anrep was much more than a messenger. He saw Starling's works on the heart-lung preparation and became so interested in the technique that, after a month or two, he was making his own preparations at the UCL and, encouraged by Starling, wrote two articles for *The Journal of Physiology*. The articles mentioned that they had been written by a Russian researcher who had only been in England for a few weeks.[5] In 1913, Anrep was elected a member of the British Physiological Society.[6]

Anrep was very intelligent. Over his life, he learnt English, French, German, Italian, and Arabic, all of which he spoke fluently, in addition to a certain knowledge of Latin and Greek.[1]

Years of uncertainty

Anrep's third visit to London in 1914 was brief. After the outbreak of the First World War, he returned to Russia with his brother Boris and completed his medical studies, graduating from the University of Petrograd, the new name of the city of Saint Petersburg from that same year. He was deployed as a military physician to a field hospital; after being injured twice, he was awarded the Cross of Saint George and was discharged in 1916.[1,4,6]

In March of the same year, he returned to the MMA and resumed his scientific activity at Pavlov's department of physiology.[2] In 1916-1917, he passed the examinations to obtain the degree of doctor in medicine, and in 1918 he was admitted as intern to the department of physiology at the Institute of Experimental Medicine, where he assumed the role of deputy director alongside Leon Orbeli (1882-1958) while continuing his work at the MMA.[4]

Second period in London

During the Russian Civil War, Anrep fought with the White Army of Lieutenant General Denikin against Trotsky's Bolsheviks; after the defeat, at the end of 1918, he returned to UCL with his first wife Olga Volkova (1893-1929), the daughter of a businessman, whom he married in 1917. He rejoined Starling's group for seven productive years during which he was also awarded several prizes for physiology. During that time, he successively worked as assistant (1920-1921), senior assistant (1921-1925), and lecturer (1925-1926) in physiology. He particularly focused on the physiology of digestion and blood flow. Anrep published several articles in physiology journals and was awarded significant scientific prizes. In 1923, he earned his doctorate in science, specifically in physiology,

Figure 2. Gleb von Anrep working at the laboratory of Ernest Starling (1920s).[53]

and in 1925, he obtained the degree of Master of Art Cantabrigian. The same year, when he also gained British citizenship, he was granted the Sharpey-Schafer Prize Lecture in physiology and the William Julius Mickle Fellowship. He also delivered the Sydney Ringer Lecture. Anrep was a skilled surgeon and made heart-lung preparations with great dexterity (Figure 2). Likewise, he was an outstanding lecturer and speaker. In 1923, his only son, John (1923-1983), was born; his godfather was Ivan Pavlov, and he was educated in England, where he dedicated his career to the military. Father and son had a distant and cold relationship throughout their lives.[1,2,4]

In 1923, collaborating with Daniel T. Harris, Anrep published *Practical Physiology*, a book intended mainly for students.[7]

Anrep made several discoveries in the physiology of the higher nervous activity, such as the phenomenon of statistical irradiation or the limit of inhibition and the presence of a maximal inhibitory after-effect in the cerebral cortex.[4,8,9] Almost all of his work on higher nervous activity and conditioned reflexes was performed at Pavlov's laboratories in Petrograd.[4] He published five articles on conditioned reflexes, three in Russian and two in English. The first study published in English, in 1920, addressed the discrimination of pitch stimuli. Dogs have very sharp hearing and some are able to discriminate between quarter-tones.[8] In the other study, published in 1923, conditioned reflexes were triggered by a tactile stimulus applied to a point on the skin of the thigh. Stimulation of other points in the body triggered new responses whose intensity depended on the distance from the point of the original stimulus. Stimulation of symmetrical points on both sides triggered identical responses, although the reflex was generated only on one side.[9] The articles in English had previously been published in Russian,[1] and the findings were also included in Pavlov's book on conditioned reflexes.[10]

Initially, his main research focus in London was the function of salivary glands and pancreatic secretion, as a

result of his previous work with Pavlov; however, he soon began to prioritise cardiovascular physiology, especially of the coronary arteries.[1,11] Pavlov had also studied the physiology of the heart in his early years.[12]

Between 1925 and 1933, Anrep's most significant works on this subject addressed the regulation of cardiac circulation, its behaviour in the different stages of the cardiac cycle, and its response to different substances. With great dexterity, he made Starling's heart-lung preparations in dogs, even perfecting the technique.[1,3] He soon developed a heart-lung-brain preparation model, and a crossed model using two animals. In Egypt, he made preparations using the heart and lungs of recently deceased humans.[1] He attributed the first heart-lung preparation to Pavlov in the 1880s.[12]

In 1912, still a student, he described the Anrep effect or homeometric self-regulation. This phenomenon refers to the gradual recovery of dilation of the left ventricle after acute constriction of the ascending aorta. He erroneously attributed this effect to the release of adrenaline by adrenal glands.[2,13,14] The Anrep-Segall reflex was also described, referring to the fact that increased cardiac output in an innervated heart-lung preparation is accompanied by increased blood flow in the coronary sinus.[15,16]

He studied the pulmonary circulation, its nervous regulation, and the physiology of hyperventilation and gasping.[17-19]

Between 1926 and 1931, he was lecturer of physiology at Cambridge University with Sir Joseph Barcroft (1872-1947). In 1928, he was designated a fellow of UCL and the Royal Society of London (Figure 3).[2]

Anrep was the third Russian author to publish in *The Journal of Physiology* in London, and one of the most prolific, with no fewer than 35 articles published in the journal.[6,11]

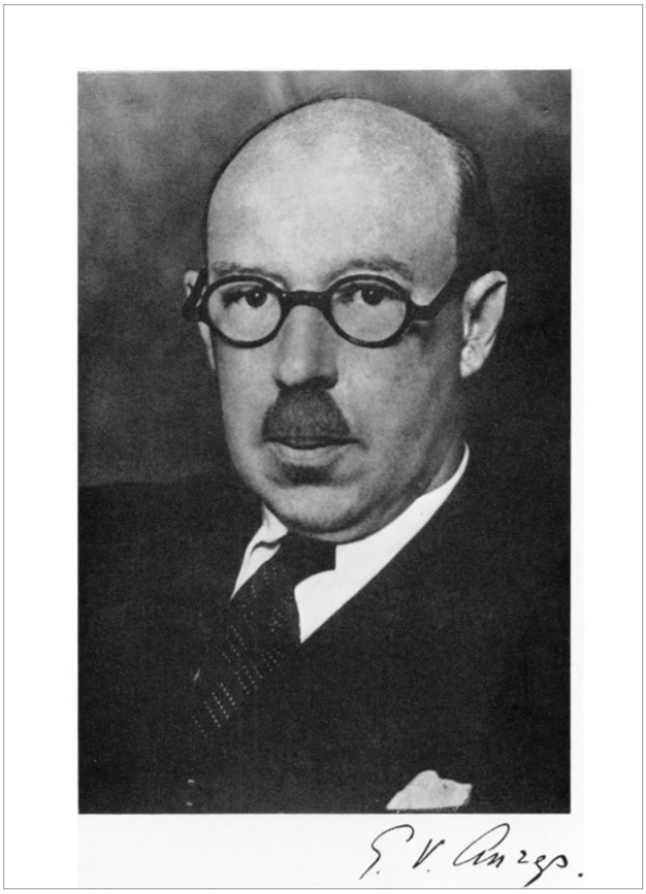

Figura 3. Gleb von Anrep (1928).[1]

A British-Russian in Egypt

The careers of British scholars frequently included periods at universities in the colonies and the Commonwealth. Details on his departure from Cambridge University, where he was a candidate for the chair of physiology, are confusing. Henry Barcroft (1904-1998), son of Sir Joseph, who collaborated with Anrep at the time, commented that during Anrep's stay in Cambridge, it was rumoured that he had murdered his wife and therefore emigrated to Cairo.[2,20] John Gaddum (1900-1965) reports that Olga, Anrep's wife, committed suicide in November 1929 using morphine. Anrep remarried with a distant cousin, the German Dina von Anrep (1903-1994), in August 1930, but they divorced in 1938.[2]

In 1931, he left England for Cairo, where he directed the department of physiology at the King Fuad I University and the Kasr El Aini Hospital, having visited Egypt as external examiner in 1930. He soon learned to speak fluent Arabic. Anrep understood Egyptians well and integrated into their social life. He travelled the Egyptian deserts in his Ford for 25 years. He was also a keen philatelist.[1]

In March and April 1935, Anrep visited New York to give a Harvey Lecture on the cardiovascular physiology and was scheduled to give another two lectures at Ohio State

University on 3 April, one on conditioned reflexes and another on blood flow.[21] In Cleveland, he met Claude Beck (1894-1971), a pioneer of cardiac surgery, to learn from his experience in the surgical treatment of coronary artery disease.[1]

He subsequently travelled to California to give the Lane Lectures from 23 to 26 April at Stanford University.[21,22] He delivered five lectures on his work on the regulation of cardiac and vascular circulation, which were published in a book in 1936. The preface was dedicated to Ivan Pavlov, who had died while Anrep was correcting the final proofs of the text.[2] In the book, he addresses the proprioceptive mechanisms regulating cardiovascular function, the association between breathing and heart rate, coronary circulation, and muscular circulation.[23,24]

In one of the lectures, he expressed his gratitude to Pavlov and Starling, who had played a vital role in his career as physiologist. The Pavlov studying digestion belonged to the old school, whereas the Pavlov studying conditioned reflexes belonged to the future school. However, Starling was part of the transition from the old school of observation to the new physiology of scientific analysis.[1]

Anrep studied blood flow in the skeletal muscles, which he compared with the cardiac muscle, demonstrating that its contraction causes an interruption of the blood flow followed by reactive hyperaemia and release of vasodilator substances.[25]

In 1935, he began studying the metabolism and vasodilator effect of histamine, its action on skeletal muscle, and its release with curare, independently of the paralysing effect of this substance.[2,25-27] He also observed a significant decrease in histamine levels in the circulating blood of pregnant women.[28]

From 1945, he studied the effects of the plant *Ammi visnaga* and its active alkaloid, khellin, a smooth muscle relaxant and coronary vasodilator that does not cause hypotension. Its chemical structure was the basis for the subsequent development of such drugs as amiodarone, nifedipine, and sodium cromoglycate.[2,29,30]

His third wife was the Italian Ida Wieninger (1907-1950), who died after being bitten by a dog. Anrep then married his sister-in-law Annie Wieninger (born in 1905), who survived him. In 1952, he found himself the victim of the nationalist uprising led by General Naguib and Colonel Nasser, which forced him to abandon his position at the university and his research at the laboratory.[1,2]

Gleb von Anrep was happy in Egypt, directing a well-equipped physiology research laboratory. He dedicated significant time to the training of his assistants. His most significant collaborators included Harold Segall (1897-1990) and Alfred Blalock (1899-1965) in England, and John Gaddum, Mohamed Talaat, and especially Giorgi Barsoum, who worked with him between 1936 and 1953, in Egypt.[1]

In 1955, the Ciba Foundation invited him to London to preside over a symposium on histamine, but he initially declined the invitation as he was not familiar with the latest research on the subject. At the insistence of the hosts, he eventually accepted, but was unable to attend as he had a heart attack in the first days of that year, followed by a second infarction that led to his death on 10 January.[1]

Pavlov, Anrep, and their work in the Anglophone world

Ivan Pavlov maintained close contact with Gleb von Anrep, by post and in meetings on his trips abroad, in which Anrep served as interpreter.

In the 20th century, Pavlov first travelled to Madrid to attend the Fourteenth International Congress of Medicine in 1903, and to Stockholm in 1904, to receive the Nobel Prize. In 1906, he visited London as a guest of the Physiological Society to give the Huxley Lecture at Charing Cross Hospital. In 1907, he was elected a foreign member of the Royal Society and in 1909, he became an honorary member of the Physiological Society.[6] In 1912, during celebrations for the 250th anniversary of the Royal Society, he visited Cambridge to receive an honorary doctorate. The following year, he participated in the International Physiological Congress in the Netherlands. At many of these events, he spoke in grammatically correct but thickly accented German.[3,6]

Pavlov's decision in 1904 to shift his research focus from gastroenterology to the study of conditioned reflexes has been interpreted as being due to the discovery of secretin two years earlier, which forced him to study hormones, a topic that did not interest him.[12] Despite this, he kept a cordial relationship with Ernest Starling, who discovered secretin, and the pair exchanged researchers between their laboratories. Pavlov's students, Gleb von Anrep, in different periods between 1912 and 1926, and Boris

Figure 4. From left to right: Ivan Pavlov, Gleb von Anrep, and Boris Babkin (1928).[6]

Babkin, between 1922 and 1924, were sent to work at Starling's laboratory (Figure 4).[5,6]

The Bolshevik revolution made Pavlov vulnerable due to Russia's difficult situation between 1919 and 1923, when the country was hard hit by epidemics and famine. In the West, there were rumours of his arrest and subsequent death. Autumn 1920 was especially hard for Pavlov and his family and collaborators. In October 1920, a French magazine announced that Pavlov was dying of starvation in Petrograd. All circumstances suggested that he would not survive the winter. Upon hearing of Pavlov's struggles, Walter Cannon (1871-1945) took action to help him. He contacted Charles Sherrington (1857-1952), and particularly Robert Tigerstedt (1853-1923) of the University of Helsinki. According to Anrep, Pavlov feared that any money they sent him would be seized. Tigerstedt was authorised to send food and clothes for him and his relatives by train from Helsinki, as well as food for his dogs.[3,31] Starling, Bayliss, and Anrep helped him from England. They proposed that he move to England or another country where he could continue with his research or give lectures, which was not very feasible due to his difficulties with foreign languages. Finally, in early 1921, the Bolsheviks decided to treat him favourably because his theories on conditioned reflexes were well aligned with the official doctrine of dialectical materialism.[5]

Visits to England and North America in the 1920s

In June 1923, Ivan Pavlov travelled to the United States with his son Vladimir, who spoke English, visiting New York, New Haven, Woods Hole (Massachusetts),

Chicago, and the Battle Creek Sanitarium (Michigan), and delivered several lectures. Despite having 800 dollars stolen in New York city, Pavlov was able to continue his journey thanks to the help received. His lecture in Battle Creek, translated by his student Vasily Boldyrev (1872-1946), who directed a Pavlovian laboratory there, was published several months later in *Science*.[32] He later travelled to Britain to participate in the 11th International Physiological Congress in Edinburgh, where he delivered the same lecture as in the United States. By the end of July, before returning to the USSR, he visited London and Cambridge to meet with Anrep and Babkin.[3,31]

By the end of April 1928, Pavlov visited London as official representative of the USSR for the third centenary of the discovery of the circulation of blood by William Harvey, and delivered a Croonian Lecture of the Royal Society entitled "Certain problems in the physiology of the cerebral hemispheres," which was translated by Anrep and published in English.[33] At that time, his book on conditioned reflexes had just been published and was receiving positive reviews in the scientific press. Pavlov was a celebrity with numerous admirers in England, but very few could understand his studies. He was the iconic elderly man, wonderfully passionate, who survived the Russian Civil War and challenged the Bolsheviks, and revealed the mysteries of the human psyche.[3]

As he had done during a previous trip to England 15 years earlier, he addressed a crowded audience at Cambridge University in Russian. Sir Joseph Barcroft, who witnessed the event, recalls how Pavlov started to deliver his speech, as planned, in segments of three minutes in fast Russian, with each followed by the corresponding translation from Anrep. After alternating his speech with his student several times, he became so absorbed in his speech that he forgot about the audience, who could not understand a word he was saying. He realised only five minutes later; he then wrung his hands and burst into loud laughter, in front of a devoted audience.[3]

In August 1929, Pavlov attended the 13th International Physiological Congress in Boston, the first held outside Europe. Everyone was impressed by the 80-year-old's vivacity. The following month, he attended the 9th International Congress of Psychology, held in New Haven.[34]

In Boston, he delivered a special lecture to a select audience, which was not mentioned in the programme. In the speech, dedicated to conditioned reflexes, he attempted to integrate physiology with psychology and psychiatry. His lecture was translated into English by Anrep.[34] Harvey Cushing (1869-1939) describes Pavlov's lecture:

> Before a small and select group […] we had Pavlov serving up his latest ideas of inhibition in relation to neuroses […]. Vivid, alert, and gesticulating, the old man poured out his phrases […]. Pavolv would suddenly stop and point menacingly to Anrep, [who sat calmly alongside smoking innumerable cigarettes], who would possibly ask a question or two to make sure of his ground […]. Anrep would then composedly begin and give a most brilliant, concise, clear presentation in English. Pavlov would then pick up the thread and continue. This went on for an hour and […] you could have heard a pin drop.[35]

Physiologists and psychologists in the audience respected his scientific knowledge and achievements, but very few understood his esoteric terminology and even fewer commented on the scientific content; rather, they mentioned his great liveliness and energy. After the lecture, Cushing lamented not having recorded it and requested that Anrep write down its content, to which the latter answered that it would be impossible for him: he had translated the speech under the hypnotic influence of the old man and found himself unable to synthesise it.[31,34,36]

Despite the language barrier, Pavlov was the most important personality at the 13th International Physiological Congress. He used his peculiar German and French to communicate with Cannon. Everyone was impressed by the personality of the 80-year-old man, who, "lively as a cricket and although lame, moves with the energy of a boy of 15."[35] John Fulton described another scientific lecture that Pavlov delivered several days later: "he spoke briefly on inhibition in the normal activity of cerebral hemispheres and Anrep translated."[35] Anrep also transmitted to his master the questions from the audience and translated his quick answers. After giving "fiery gesticulations" during his speech, Pavlov "seemed a little distressed over the complacency of the translator, who rendered what he had said with no gesticulations whatever."[35] After the congress, Pavlov travelled to Montreal to visit Boris Babkin, who worked at McGill University.[31,35]

Pavlov participated in the First International Congress of Neurology, held in Bern in the summer of 1931, and was a special guest at the following congress of neurology held in London in the summer of 1935, where, at the age of 86, he delivered a special lecture in German on the types of higher nervous activity, their relationship with neurosis and psychosis, and the physiological mechanism of neurotic and psychotic symptoms.[35,37]

The Oxford book

On the cold morning of Christmas Day of 1916, Ivan Pavlov was walking with Maria Petrova (1874-1948) near the Institute of Experimental Medicine, when he slipped and fell on the ice. Gleb von Anrep, who was also on his way to the Institute, observed how an elderly man was hanging onto an iron fence, nearly falling. When he approached the man, he found to his dismay that it was his master, deathly pale and weak. He flagged down a car and took him to the laboratory, where he was diagnosed with impacted fracture of the femoral neck that led to residual lameness.[3,12]

Pavlov attempted to write his first monograph on conditioned reflexes in 1917, while he was confined to bed due to the hip fracture. In a letter to Walter Cannon in December 1922, Pavlov confessed that he was not satisfied with the initial draft he had been preparing for more than four years, as new data were emerging that forced him to modify the draft and open new lines of research. It was impossible for him to restrict his experimental data. He wrote several manuscripts between 1921 and 1922.[3,12]

Pavlov wanted his study to be published first in English due to the special interest of North American researchers of behaviour. Walter Cannon and the psychologist Robert Yerkes (1876-1956), like many of their countrymen, were intrigued by his investigations, which were largely unknown to them, and insisted that he publish them. Outside the Soviet Union, the only data available was from a small number of articles, references from lectures, and brief reviews in English, French, and German.[38]

In 1923, Pavlov published a compilation of lectures and reports under the title *The twenty years of objective study of animal higher nervous activity*. In the second edition, published in 1924, he added the word "behaviour" in parentheses to the title, as a nod to behaviourists.[39] He admitted that he had difficulties systematically writing a monograph, in addition to the difficulties that affected his country. For example, it was very difficult for him to obtain copies of his own publications. Pavlov's trip to the West in 1923 whetted the appetite of his foreign admirers, who rekindled their efforts to coax a monograph from him. Walter Cannon, Jacques Loeb (1859-1924), Edward Sharpey-Schafer (1850-1935), Ernest Starling, and former collaborators Gleb von Anrep, Boris Babkin, Vasily Boldyrev, William Horsley Gantt (1892-1980) insisted that he write the book.[3]

During his stay in London, after Anrep asked him about the unwritten book, they had a fierce argument. Only violent methods made an impression on him. His student asked him whether he planned to live another 50 years and questioned the sincerity of Pavlov's efforts to write the book. Pavlov was perplexed and admitted that he should publish a complete review of his work, but he mentioned that he was obtaining very interesting new findings that he wanted to include in the text. As he grew older, he realised he was losing faculties as well as enjoying certain advantages, such as greater freedom of thought, and quickly reaching conclusions, which he attributed to the loss of capacity for self-criticism. Pavlov's collaborators suffered his temperament and unpredictable reactions to disagreement on several occasions. Anrep, initially his student and later his assistant, frequently found him to be intolerant and always extraordinarily demanding of himself and others, but never vindictive.[12]

Anrep visited New York in the summer of 1923 to deliver a course on conditioned reflexes. After giving a speech at Cornell University, he convinced Howard Liddell (1895-1967) of the potential of the Pavlovian technique for overcoming the problem of studying mental processes. In 1923, under the direction of Anrep, Liddell established a laboratory arranged according to the Pavlovian method and set about applying the conditioned reflex to the study of mental dullness in normal and thyroidectomised sheep.[40]

In 1924, Anrep informed his colleagues of Pavlov's great interest in delivering the content of a series of lectures on conditioned reflexes to the British and North American audience. In a letter to Pavlov in April 1924, Starling requested a copy of those lectures and commented that he had asked Anrep to write a book on the subject. As Anrep would only do this with Pavlov's approval, Starling was asking his consent. Cushing and Cannon had also requested the book from Anrep. Cushing wrote to Pavlov to tell him that he had never heard of a medical

work that raised so much interest. He only lamented that they were unable to access Pavlov's research in English from the previous years, and feared that they would have to learn Russian, just as they had had to learn Spanish to follow the works by Santiago Ramón y Cajal (1852-1934) in Madrid. Cannon argued that Anrep's lectures were so stimulating, and revealed so many findings that were still unpublished in English, that he wished to know more about Pavlov's work. He hoped that Anrep or one of his former collaborators who were familiar with Pavlov's work would report his findings.[3]

Pavlov eventually agreed to write a book, motivated by the great acceptance of the most outstanding Western scientists for Anrep's lectures on conditioned reflexes in England and the United States. Events conspired to pressure Pavlov, who wished to avoid Anrep being the one to satisfy the Western demand for a book on conditioned reflexes. He should himself be the author of an understandable book that might overcome the fragmented research and the lack of a coherent theory.[3,41]

To organise his ideas, in May 1924 he delivered a series of 23 lectures at the MMA in Leningrad, "On the work of the large hemispheres of the brain of the dog," whose text, once transcribed, he found unsatisfactory.[3] In these lectures, he gave an exhaustive, systematised presentation of his research on the activity of the hemispheres of dog's brain, the result of 25 years of work. These lectures were recorded by a stenographer for subsequent publication. The drafting and review of these texts took up 18 months of his leisure time. His lectures were limited to purely experimental material and his personal point of view.[1,10,42]

Pavlov struggled to accept the possibility that Anrep might synthesise and publish two decades of his own research. But he could not gracefully refuse permission without providing a manuscript written by himself. Therefore, in a project funded by the Royal Society of London, Anrep took on the role of translator and editor of his master's monograph, with Pavlov sending him the text in instalments between August 1925 and May 1926. At Anrep's suggestion, he eliminated the reference to the dog brain from the book's title to broaden its appeal, leaving it as *Lectures on the work of large hemispheres of the brain*.[43] For the same reason, he added a final chapter on the possible applications of his research in humans.[3,42,44]

In the preface, Pavlov mentioned how fortunate he was that the book should be translated by Gleb von Anrep; in turn, Anrep considered himself lucky to have been assigned the task, as it was the ideal way to show his vision of his old professor. The book was the first comprehensive analysis presented outside of the Soviet Union in one of the most widely spoken languages in the world. In the interest of clarity, Pavlov permitted Anrep to introduce certain modifications and additions to the text to make it easier to understand for British and North American readers, who were not familiar with the literature in this field. Anrep, who was not a native English speaker, was granted 100 pounds by the Royal Society of London,[5] which enabled him to hire professional translators to prepare a draft of lessons I-XII, which he later reviewed and corrected; he personally translated the rest of the text until lesson XXIII.[3,10]

Translating also entails interpretation. It required familiarity with such concepts as reflex, inhibition, discipline, behaviour, constitution, and psyche, which involved a great deal of metaphorical stretch that he had to adapt to British and North American audiences. Anrep undertook this task in a calculated way to present Pavlov as a scientist, particularly bearing in mind the North American behaviourists. He was aware he was creating new English words for many of the technical terms used by Pavlov. Despite his ability as a translator, readers had to master the esoteric language of conditioned reflexes, which constituted an obstacle to understanding the methods, arguments, and aims of the author.[3,10]

When in May 1926 Anrep was near completing the translation, he discovered with horror that, with Pavlov's approval, Horsley Gantt had finished his translation of the collection of articles that his master had published in 1923,[39] which was being prepared for publication with the support of Walter Cannon. Anrep implored Pavlov to arrange for Gantt's translation to be published 6 months after his own, as it put Anrep in a very difficult situation before the Royal Society, which had funded his project. Starling agreed, Pavlov accepted, and Gantt's translation was published in 1928.[3]

The scientific journalist James Crowther (1899-1983) secured the publication of the book for Oxford University Press and advertised it in various journals around the time of its publication. Although it is unclear how he convinced both parties that the book be published at Oxford, it was Crowther's idea, which he suggested to Anrep. Crowther stereotyped Anrep as the temperamental Russian: sensitive, brutal, gentlemanly,

treacherous, brilliant, lacking in character; a small and moody man.[44]

The book *Conditioned reflexes: an investigation of the physiological activity of the cerebral cortex*[10] offers a powerful vision and discussion of experiments, but does not synthesise both aspects. It is replete with admissions of error, misunderstandings, and gaps that do the author no credit. This combination of "colossal" factual material, powerful grand vision, and uncertainty about the fusion of the two reflected Pavlov's discomfort as he confronted the difficulties of systematisation.[3]

The monograph is more a history of his research than a synthesis. It is divided into four sections. Part 1 lays out his basic scientific vision and methodology in lectures I and II. Part 2 explains the basic picture of higher nervous processes, excitation, inhibition, analysis, and synthesis, as he understood them in 1921. Lectures XI-XVIII, in part 3, are dedicated to the contradictions, complexities, and new lines of research that emerged during the 1920s: mutual induction, hypnosis, sleep, nervous types, and nervous disease. Lectures XX and XXI discuss basic neuroanatomical conclusions. Part 4, including lectures XXII and XXIII, takes stock and looks to the future, correcting mistakes in the pre-1921 chapters and interpreting his findings. Following Anrep's advice, he expresses in the final lecture his hope that his research would illuminate the complex mechanisms of human nature.[3,10,38]

Before the publication of Anrep's translation, little was known in Britain of the details of Pavlov's work. The book was published in late 1927 and received favourable reviews: despite its difficult reading and the high price of 28 shillings, which was not affordable for everyone, it still sold 200 copies in the first month. Many non-specialists were aware of conditioned reflexes through articles such as those written by Crowther. These texts underscored how Pavlovian research did away with the mystical element of thought, explaining intelligent actions in animals in terms of cause and effect; these actions were previously attributed to mysterious mental phenomena. Pavlov, who was not a behaviourist, did not deny the subjective aspects of thought.[41,44]

Horsley Gantt translated two of Pavlov's books from Russian with the help of Georg Volborth (1885-1960). The first book, published in 1928, was based on the third edition of his collection of articles and lectures, to which he added five articles covering the period 1903-1928, a biographical text on Pavlov, and an introduction by Cannon, which associated Pavlov with the behaviourist tradition.[39,45] The second, published in 1941, collected Pavlov's articles and lectures published between 1928 and 1936.[46] Volborth, another collaborator of Pavlov's, translated some of his books into German.

Conditional versus conditioned

On 1 October 1906, Ivan Pavlov delivered a lecture in Thomas Henry Huxley's honour at Charing Cross Medical School in London, which was published in *The Lancet*.[47] The published version was the translation of his lecture in German by an anonymous translator who made the long-standing error of using the terms conditioned and unconditioned reflexes, instead of conditional and unconditional. This article caught the attention of Robert Yerkes, a psychology professor at Harvard, who requested Pavlov's permission to publish a summary in English of his research method and his main articles on the subject. With the collaboration of the zoology student Sergius Morgulis (1885-1971), who spoke Russian, Yerkes published the article in 1909.[48] In a footnote to the article, Morgulis indicated that the correct translations of *uslovnyi* and *bezuslovnyi refleks* were conditional and unconditional reflexes, but as professor *Pawlow* himself had approved the use of the terms conditioned and unconditioned reflexes in the article in *The Lancet*, he decided to use the second translation, which was used in the following decade by such scientists as John Watson (1878-1958) and in the general press. He was not aware of Pavlov's poor command of English.[3]

In 1923, *Science* published a summary of the lecture delivered by Pavlov in July of the same year at Battle Creek Sanitarium (Michigan), translated by Vasily Boldyrev, who also used the term conditioned reflexes.[32]

Anrep's concern with establishing a standardised English-language Pavlovian lexicon perhaps explains his adherence to a long-standing practice that he surely knew was incorrect when he adopted the term conditioned reflexes in the book.[3] In two articles published in English in 1920 and 1923, he had already referred to conditioned reflexes.[8,9]

Gantt repeated the mistranslation of the Pavlovian term conditional as conditioned. In a footnote, he explains that as conditioned reflex had already become fixed in English usage, rather than conditional reflex, he adhered to the former term.[3]

Conditional is the correct translation of *uslovnyi*. The first translations of Pavlovian texts into German and French used the original term. The term "conditioned" implies the determined quality of the reflex, whereas "conditional" places the emphasis on the dependence of the reflex on varying circumstances and conditions, which is what Pavlov was describing.[49]

An Internet search shows that in German, the term *bedingte Reflexe* (conditional reflex) predominates over *konditionierte Reflexe* (conditioned reflex), which was already used in 1926 in a chapter by Pavlov in a book, and in a translation of a book collecting his articles, published the same year.[39,50,51] However, a first edition in French published in 1927, also collecting articles translated from Russian, uses the term *réflexes conditionnels,*[39,52] although the subsequent French literature preferentially used the term *réflexes conditionnés*. The first Spanish-language version of the book that Anrep translated was published in 1929, and was a direct translation from the Russian with a brief preface by Pavlov. Published by Javier Morata, this version uses the term *reflejos condicionados*, the predominant term used in the subsequent Spanish literature.[42,43]

After Pavlov's death due to pneumonia in February 1936, Anrep wrote an extensive obituary describing the most important details of his biography, personality, and scientific achievements. The text has subsequently been used by numerous other authors to refer to the great Russian physiologist.[12]

Conclusions

Gleb von Anrep played a dual role in the development of British and international physiology. On the one hand, we should mention his research on the cardiac and pulmonary circulation and activity and his studies on striated muscle, histamine, and active agents on coronary arteries. On the other hand, we should not forget his Russian origins and the tradition of researching conditioned reflexes, the salivary glands, and the digestive system, as well as the close contact he kept with his master Ivan Pavlov, of whom he was the main collaborator in the English-speaking world. He was translator and editor of the English version of Pavlov's classic work on conditioned reflexes, and was unfairly accused of originating the mistranslation of that term, which should have been conditional reflexes. This mistranslation has been perpetuated in most of the main Western languages. This text analyses the origin of this mistake, which dates back to the 1900s, and also describes Pavlov's relationship with the English-speaking world with his lectures and attendance at congresses, and well as the role of Anrep in this relationship.

Conflicts of interest

The author has no conflicts of interest to declare. This is an original article. This study has not been presented at the SEN's Annual Meeting or at any other meeting or congress, nor has it been submitted to other journals. The author has received no public or private funding for this study.

References

1. Gaddum JH. Gleb Anrep, 1891-1955. Biogr Mem Fellows R Soc. 1956;2:19-34.
2. Yentis SM. Minds and hearts: themes in the life of Gleb von Anrep. J R Soc Med. 1998;91:209-12.
3. Todes DP. Ivan Pavlov: a Russian life in science. Oxford (UK): Oxford University Press; 2015.
4. Anrep Gleb Vasilievich Fon [cited 6 Jun 2021]. Available from: https://rus-emigration-history.slovaronline.com/15-анреп_глеб_васильевич_фон.
5. Henderson J. A life of Ernest Starling. London: Academic Press; 2005. Chapter 4: Starling's law and related matters; p. 77-98.
6. Tansey T, Ziganshin AV. British physiological journals 1878-1925, and links with Russian physiologists. Kazanitskiy meditsinskiy zhurnal. 2011;92:764-76.
7. Anrep GV, Harris DT. Practical physiology. London: J. & A. Churchill; 1923.
8. Anrep GV. Pitch discrimination in the dog. J Physiol. 1920;53:367-85.
9. Anrep GV. The irradiation of conditioned reflexes. Proc R Soc Lond B. 1923;94:404-26.
10. Pavlov IP. Conditioned reflexes: an investigation of the physiological activity of the cerebral cortex. Anrep GV, ed. and trans. Oxford (UK): Oxford University Press; 1928.
11. Chemistry Tree: The Academic Genealogy of Chemistry Researchers [Internet]. [s.l]: The Academic Family Tree; ©2005-2022. Gleb V. Anrep – Publications; [cited 8 Jun 2021]. Available from: https://academictree.org/chemistry/publications.php?pid=72689
12. Anrep GV. Ivan Petrovich Pavlov, 1849-1936. Obituary Notices of Fellows of the Royal Society. 1936;2:1-18.
13. Anrep GV. On the part played by the suprarenals in the normal vascular reactions of the body. J Physiol. 1912;45:307-17.

14. Bansode OM, Miao JH, Sarao MS. Physiology, Anrep Effect. In: StatPearls [Internet]. Treasure Island (US): StatPearls Publishing; 2022 [updated 21 Apr 2021; cited 16 Jun 2021]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537003/
15. Anrep GV, Segall HN. The central and reflex regulation of the heart rate. J Physiol. 1926;61:215-31.
16. Mirsky AI. Studies on the effect of rate and rhythm of the heart on the coronary circulation [doctoral thesis]. Montreal (CA): McGill University; 1929.
17. Anrep GV, Bulatao E. Observation on the pulmonary circulation. J Physiol. 1925;60:175-92.
18. Anrep GV, Hammouda M. Observations on panting. J Physiol. 1932;77:16-34.
19. Anrep GV, Saman A. Double vagotomy in relation to respiration. J Physiol. 1932;77:1-15.
20. Boyd R, Boyd CAR. Sir Joseph Barcroft, Cambridge placental and fetal research (1933-1966) and intergenerational science. Int J Dev Biol. 2010;54:257-68.
21. The Ohio State University: University Libraries [Internet]. Columbus (US): The Ohio State University; [s.d.]. Cairo professor to deliver 2 talks; [s.d.] [cited 28 Jun 2021]. Available from: https://osupublicationarchives.osu.edu/?a=d&d=LTN19350402-01.2.5&e=-------en-20--1--txt-txIN-------
22. Medical News. JAMA. 1934;103:1783-7.
23. Anrep GV. Lane Medical Lectures: studies in cardiovascular regulation, vol. 3. Stanford (CA): Stanford University Press; 1936.
24. Problems of cardiovascular regulation. Br Med J. 1937;1:275-6.
25. Anrep GV, Barsoum GS. Appearance of histamine in the venous blood during muscular contraction. J Physiol. 1935;85:409-20.
26. Alam M, Anrep GV, Barsoum GS, Talaat M, Wieninger E. Liberation of histamine from the skeletal by curare. J Physiol. 1939;95:148-58.
27. Anrep GV, Barsoum GS, Talaat M. Release of histamine by the liver. J Physiol. 1953;120:419-26.
28. Anrep GV, Barsoum GS, Ibrahim A. The histaminolytic action of blood during pregnancy. J Physiol. 1947;106:379-93.
29. Anrep GV, Kenawy MR, Barsoum GS, Misrahy G. Therapeutic uses of khellin; method of standarisation. Lancet. 1947;1:557-8.
30. Hollman A. Amiodarone, nifedipine, sodium cromoglycate. Br Heart J. 1991;65:57.
31. Wolfe EL, Barger AC, Benison S. Walter B. Cannon, science and society. Cambridge (US): Harvard University Press; 2000.
32. Pawlow IP. New researches on conditioned reflexes. Science. 1923;58:359-61.
33. Pavlov IP. Croonian lectures: certain problems in the physiology of the cerebral hemispheres. Proc R Soc B Biol. 1928;103:97-110.
34. Rall JA. The XIIIth International Physiological Congress in Boston in 1929: American physiology comes of age. Adv Physiol Educ. 2016;40:5-16.
35. Shahlaie K, Watson JC, Benson DR. The intriguing encounters of Pavlov and Cushing. J Neurosurg. 2004;100:568-71.
36. Fulton JF. Ivan Petrovitch Pavlov. New Engl J Med. 1936;214:487-9.
37. World Neurology [Internet]. London: World Federation of Neurology; ©2022. Reynolds EH. The Second International Congress of Neurology; 11 Dec 2018 [cited 2 Jul 2021]. Available from: https://worldneurologyonline.com/article/the-second-international-congress-of-neurology/
38. Boakes RA. The impact of Pavlov on the psychology of learning in English-speaking countries. Span J Psychol. 2003;6:93-8.
39. Pavlov IP. Dvadtsatiletniy opyt ob"yektivnogo izucheniya vysshey nervnoy deyatel'nosti (povedeniya) zhivotnykh [Twenty years of experience in the objective study of higher nervous activity [behaviour] in animals]. Leningrad: Medgiz; 1951.
40. Kirk RGW, Ramsden E. Working across species down on the form: Howard S. Liddell and the development of comparative psychopathology, c.1923-1962. Hist Philos Life Sci. 2018;40:24.
41. Hill-Andrews O. Lamarckism by other means: interpreting Pavlov's conditioned reflexes in twentieth-century Britain. J Hist Biol. 2019;52:3-43.
42. Pavlov IP. Los reflejos condicionados. Lecciones sobre la función de los grandes hemisferios. Madrid: Morata; 1997.
43. Pavlov IP. Lektsii o rabote bol'shikh polusharii golovnogo mozga [Lectures on the work of large hemispheres of the brain]. Moscow: Akademiia Nauk; 1927.
44. Hill-Andrews O. Interpreting science: JG Crowther and the making of interwar British culture [doctoral thesis]. Brighton (UK): University of Sussex; 2015.
45. Pavlov IP. Lectures on conditioned reflexes: twenty-five years of objective study of the higher nervous activity (behaviour) of animals. Gantt WH, trans. New York: Liveright Publishing Corporation; 1928.
46. Pavlov IP. Lectures on conditioned reflexes, vol. 2. Conditioned reflexes and psychiatry. Gantt WH, trans. and ed. New York: International Publishers; 1941.
47. Pavlov IP. The Huxley Lecture on scientific investigation of the psychical faculties or processes in the higher mammals. Lancet. 1906;168:911-5.

48. Yerkes RM, Morgulis S. The method of Pawlow in animal psychology. Psychol Bull. 1909;6:257-73.
49. Simon B, ed. Psychology in the Soviet Union. London: Taylor-Francis; 2003.
50. Pawlow JP. Bedingte Reflexe bei Hunden nach Zerstörung verschiedener Teile der Grosshirnhemisphären. In: Die höchste Nerventätigkeit (das Verhalten) von Tieren. Munich: J.F. Bergmann; 1926.
51. Pawlow IP. Die höchste Nerventätigkeit (das Verhalten) von Tieren: eine zwanzigjährige Prüfung der objektiven Forschung Bedingte Reflexe Sammlung von Artikeln, Berichten, Vorlesungen und Reden. Volborth GV, trans. Munich: J. F. Bergmann; 1926.
52. Pavlov IP. Les réflexes conditionnels. Étude objective de l'activité nerveuse supérieure des animaux. Grigouroff G, trans. Paris: Félix Alcan; 1927.
53. Van der Kloot W. A.V. Hill's photograph album. Physiology News. 2010;81:17-21.