

The neuroserologist Felix Plaut (1877-1940) and general paralysis of the insane in Kraepelin's Munich

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ABSTRACT

Felix Plaut was one of the most distinguished German neuroscientists of the first half of the 20th century. As a specialist in serology, he made important advances in the field of neuroimmunology: based on positive Wassermann reaction findings in the cerebrospinal fluid, he discovered that general paralysis of the insane was a form of neurosyphilis; he also demonstrated the autochthonous production of antibodies in the central nervous system. His scientific research focused on the understanding of general paralysis of the insane, exploring pathophysiological, immunological, epidemiological, clinical, and therapeutic aspects. Regarding the latter point, he pioneered the use of *Borrelia* to induce relapsing fever as a treatment for general paralysis of the insane. In the clinical sphere, he discovered the form of syphilitic psychosis that bears his name, Plaut hallucinosis. Plaut was a member of the psychiatrist Emil Kraepelin's inner circle in many of the latter's initiatives in Munich, working as a scientific assistant at the university Psychiatric Clinic, directing the laboratory of serology at the German Institute for Psychiatric Research, and even accompanying Kraepelin on a research trip to the United States, Mexico, and Cuba. Plaut produced important scientific publications, particularly in the field of neurosyphilis. He was persecuted by the Nazis due to his Jewish heritage, and took exile in England, where he killed himself in 1940.

KEYWORDS

Felix Plaut, Emil Kraepelin, syphilis, general paralysis of the insane, University of Munich Psychiatric Clinic, German Institute for Psychiatric Research.

Introduction

*Quod non est in actis, non est in mundo*¹

What is not kept in the records, does not exist.

Syphilis was one of the great scourges of humanity during the 19th century and first half of the 20th century. As it frequently involves the central nervous system, one clinical form, general paralysis of the insane (GPI), became the most frequent reason for admission to psychiatric institutions. GPI progressed rapidly, leading to death within a few years, and was resistant to treatments that had been shown to be efficacious against other forms of syphilis in the 1910s. Pyretotherapy

was the only moderately effective treatment against the disorder. It was not until the 1940s that, with the discovery of penicillin, the disease was practically eradicated, and only its memory remained.

Felix Plaut (1877-1940) was one of the most distinguished researchers of neurosyphilis, and particularly its most severe form, GPI. For three decades, he dedicated most of his fruitful scientific career to the subject, from his collaboration with August von Wassermann (1866-1925) in the discovery of a serological technique for the diagnosis of GPI to his interest in pathophysiological, epidemiological, clinical, and therapeutic aspects of the disease.

Another noteworthy aspect of Felix Plaut's career is his involvement in the inner circle of researchers surrounding the psychiatrist Emil Kraepelin (1856-1926) in Munich in the early decades of the 20th century. Plaut was one of the most active members of the university Psychiatric Clinic (Nervenlinik) and of the Deutsche Forschungsanstalt für Psychiatrie (DFA; German Institute for Psychiatric Research). He was even director of the Institute for a time following the death of Kraepelin. With the Nazis' rise to power, he was marginalised and forced into exile in England.

Material and methods

An extensive review was conducted of the international literature on the life and scientific work of Felix Plaut, as well as that of Emil Kraepelin and his milieu in Munich, from the political fluctuations resulting from the First World War to the Nazis' rise to power. Plaut's distinguished role in the study of neurosyphilis is explored, and particularly his focus on all aspects of GPI and his collaboration with Kraepelin. The latter part of the article gives an overview of the Spanish neuropsychiatrists who had relevant relationships with Kraepelin, Plaut, and the psychiatric institutions of Munich.

Development

A bourgeois Jew from Kassel

Felix Plaut was born on 7 July 1877 in Kassel. He was the second of three children born to Hermann Plaut (1844-1889), who belonged to a family of wealthy Jewish bankers who owned the Bankhaus H.C. Plaut, and Johanna Ullmann (1858-1927). Felix was raised in Kassel, where he graduated from the Wilhelmsgymnasium in early 1896. The same year, he began his medical studies in Geneva, which he completed rapidly despite performing military service in a regiment of Hessian hussars, as well as successive transfers between universities, moving first to Berlin and subsequently to Munich. He received his medical licence in spring 1902, and was awarded his doctorate by the University of Munich, with a thesis entitled "On cryptogenic septicaemia," supervised by Otto von Bollinger (1843-1909).²⁻⁴

After graduating, he was an assistant at the Am Urban hospital in Berlin, an academic clinic belonging to the Charité university hospital in the Kreuzberg district; opened in 1890, Am Urban was the city's third hospital. He was also a collaborator of the Robert Koch Institute, directed by Paul Ehrlich (1854-1915). In Berlin, working

alongside August von Wassermann, he began performing serology research using the cerebrospinal fluid (CSF) of patients with syphilis.⁵

Plaut also completed training at the Liverpool School of Tropical Medicine, working under Ronald Ross, who had discovered the malaria parasite. In 1904, he joined the University of Munich Psychiatric Clinic as a volunteer physician, and became Emil Kraepelin's scientific assistant in 1907. He began researching subjects proposed by Kraepelin, such as the effect of long, hot baths on mentally ill patients, or psychological studies of victims of accidents.^{3,6,7}

Kraepelin allowed assistants at his clinic to take "scientific vacations"; Plaut did so in 1906, working for seven months in Berlin with August von Wassermann, with whom he observed that the diagnostic reaction recently discovered by the latter yielded positive results in the CSF of patients with GPI. Kraepelin was fascinated by Plaut's discovery that neurosyphilis could be easily detected by performing a lumbar puncture, and a serology laboratory was created at the Munich Nervenlinik in 1907, where studies were performed on a large scale to research the relationship between syphilis and GPI. With the new method, they were able to establish reliable foundations for explaining cases of neurosyphilis.^{3,8} The serological diagnosis laboratory in Munich was modelled on Wassermann's in Berlin, and was soon as renowned as the latter, both in Germany and abroad. Many colleagues visited the Munich clinic to learn the new serological research methods.⁹

Thanks to his personal fortune, Plaut was able to offer his services without remuneration. In 1909, he completed his training in psychiatry, and in 1915 he was made a senior lecturer in psychiatry at the University of Munich. The same year, he married a third-degree relative, Adelheid (Ada) Liepmann (1892-1980), 15 years his junior, whom he divorced in 1929.^{3,4}

With the outbreak of the First World War, Plaut was arrested in England, where he had been invited to give a lecture. He was soon released due to his acquaintance with Violet Asquith (1887-1969), daughter of the Liberal prime minister Herbert Henry Asquith (1852-1928).⁸

In 1918, Plaut was appointed director of the DFA's department of serology, founded a year earlier. The department remained at the Psychiatric Clinic until 1928, when it was transferred to the institute's new premises (Figure 1).^{3,7,10}



Figure 1. Felix Plaut.¹⁰

Emil Kraepelin, Felix Plaut, and Munich's psychiatric institutions

Emil Kraepelin was born in 1856 in Neustrelitz, in the Mecklenburg region. He was a professor of psychiatry in Dorpat (today Tartu), Estonia, and later in Heidelberg, until he was called to the University of Munich in 1903 to occupy the chair of psychiatry.⁸

According to Plaut, psychiatry in a strictly scientific sense only came into existence with Kraepelin, who brought light and clarity to the chaos of ideas he found. Kraepelin was the father of modern clinical psychiatry, and was considered the highest authority in his day. He also laid the foundations for experimental psychology

and fought against the consumption of alcohol and other recreational drugs.¹¹ His magnum opus was his *Treatise of psychiatry*, which he wrote systematically and meticulously throughout his lifetime, and which was published in eight editions (he was revising the ninth at the time of his death). He was the great systematiser of psychiatric practice, analysing the natural history of diseases from the first symptom, as well as their prognosis and treatment. Throughout his long professional career, he gathered a vast body of clinical and laboratory data.^{8,12}

After 12 years in Heidelberg, in October 1903 Emil Kraepelin set out a plan for a new psychiatric clinic at Ludwig-Maximilians-Universität in Munich, with the help of Alois Alzheimer (1864-1915). He created the official figure of research assistant for Alzheimer, aiming to formalise an unpaid professional relationship, enabling the latter to freely use his time and the centre's scientific resources. Soon thereafter, Felix Plaut, the Swiss researcher Ernst Rüdin (1874-1952), who had collaborated with Kraepelin in Heidelberg, and Max Isserlin (1879-1941) also joined the centre as research assistants. The help of these assistants was essential in promoting scientific life at the Psychiatric Clinic. The new hospital, located at number 7, Nussbaumstrasse (Figure 2),^{9,10} was inaugurated in November 1904. In 1912, Alzheimer departed from the project, having been appointed to the chair of psychiatry in Breslau; he remained there for a short time, dying in 1915.⁷⁻⁹

In 1912, the German Association for Psychiatry requested that Kraepelin create an institute for psychiatric research⁸; the project gave rise, in 1917, to the DFA, known today as the Max Planck Institute of Psychiatry (Max-Planck-Institut für Psychiatrie). It was initially established inside the university Psychiatric Clinic, with Kraepelin acting as director of both institutions. Furthermore, the Institute entered into an agreement with the Municipal Hospital of Schwabing for the installation of a psychiatric inpatient department.¹³

Kraepelin attracted a prestigious group of researchers to the institute, who were responsible for clinical and laboratory tasks.¹⁴ Research activity at the centre began in April 1918 in the facilities of the Nervenlinik. The departments were led by Franz Nissl (1860-1919; "Histopathology I"), Walther Spielmeier (1879-1935; "Histopathology II"), Korbinian Brodmann (1868-1918; "Histotopography"), Felix Plaut ("Serology"), Ernst Rüdin ("Psychiatric genetics"), and Emil Kraepelin with



Figure 2. Top: university Psychiatric Clinic (Nervenklinik) at number 7, Nussbaumstrasse, Munich.⁹ Bottom: German Institute for Psychiatric Research (Deutsche Forschungsanstalt für Psychiatrie [DFA]) at number 2, Kraepelinstrasse, Munich.¹⁰

Johannes Lange (1891-1938; “Experimental psychiatry”). Spielmeyer, Plaut, Rüdin, and Lange had belonged to the university’s psychiatry department for several years; they had to officially resign from their positions there, but retained their links with the centre as they continued occupying the same facilities. Spielmeyer had replaced Alzheimer in 1912, when the latter left for Breslau. Brodmann and Nissl died shortly after starting work in Munich, and their departments merged with Spielmeyer’s.¹³

At that time, Plaut’s serology department was analysing the effects of arsphenamine (Salvarsan) on the Wassermann reaction and CSF changes in encephalitis lethargica. He also began studying disabled children to identify cases of congenital syphilis, and studied the prognosis of patients with GPI but without CSF alterations.¹³

The DFA was severely affected by the economic crisis that followed the First World War, and was saved from bankruptcy in 1922 and the hyperinflation of 1923 with the support of the Jewish American financier James Loeb (1867-1933). In 1924, the DFA became part of the Kaiser Wilhelm Society (Kaiser-Wilhelm-Gesellschaft [KWG]), thus joining the group of Kaiser Wilhelm Institutes, affording it financial stability. Kraepelin, Spielmeyer, Plaut, and Rüdin were appointed as scientific members of the KWG. In 1922, Kraepelin retired from the university, remaining as head of the DFA until he died in 1926; after his death, disagreements arose between the DFA and the Psychiatric Clinic.¹³

On the recommendation of Spielmeyer and Plaut, a spirochaete laboratory was created in 1923, to be led by Franz Jahnelt (1885-1971), in the light of the discovery of psychiatric disorders caused by different types of spirochaetes, on the one hand, and the therapeutic effect of malaria and relapsing fever on the course of GPI, on the other.¹³

The research on GPI was conducted across several departments of the DFA, encompassing clinical, serological, anatomical, and social hygiene aspects, and required close collaboration, with the leadership of Kraepelin. This work led to a massive evaluation of patient records from the university Psychiatric Clinic and polyclinic, as well as the Municipal Hospital of Schwabing, the local asylum for alcoholics, and the local mental asylum.¹⁵

In spring 1925, Kraepelin and Plaut travelled to the United States, Mexico, and Cuba to conduct comparative psychiatry research, studying the effect of GPI in different ethnicities in those countries. The other aim of the trip was to secure funding to build new premises for the DFA; this was provided by the Rockefeller Foundation, which also began funding the research of Plaut and Spielmeyer. Construction began in 1927, and the building, located at number 2, Kraepelinstrasse (Figure 2),^{9,10} was inaugurated in June 1928. All the departments were now based in the same building, with the transfer of Plaut’s and Spielmeyer’s departments, the last two remaining at the university Psychiatric Clinic; the move resulted in a significant weakening of the latter institution’s scientific capacity.^{7,13}

Emil Kraepelin died from cardiac disease in October 1926. He was a reserved, disciplined man, a great traveller, who did not seek renown or recognition in his lifetime. His great project was the creation of an important research centre, enabling links to be established between all branches of science and psychiatric understanding and practice. In January 1927, in his eulogy for Kraepelin, Felix Plaut recounted how in spring 1925, after spending a long time contemplating the statue of Moses in front of the Library of Congress in Washington, D.C., the veteran psychiatrist gravely told him that: “I shall meet the same fate as Moses. I shall see the Promised Land from afar and then lay myself down and die.” And that was what destiny held in store for him. Like the prophet, when he was at the borders of the Promised Land, where he had led his followers on a prolonged voyage through the difficulties of the post-war period, he closed his eyes and died, just a few weeks before the construction of the new Institute was secured.^{11,12} After Kraepelin’s death, Spielmeyer and Plaut shared the directorship of the DFA, until Rüdin assumed the role in 1931.⁷

The DFA was guided by a strictly positivist and empirical-clinical biological approach; on this foundation, the institution achieved significant scientific advances, in a short period of time. The evolution of the DFA reflected the social and political upheavals that rocked Germany after the First World War (Figure 3).^{5,10,13,16}

The Nazi regime

Ernst Rüdin was appointed director of the DFA in 1931. In 1933, he became president of the Society of German Neurologists and Psychiatrists, becoming the most



Figure 3. From left to right, top: Emil Kraepelin,⁵ Alois Alzheimer,⁵ and August von Wassermann¹⁶; bottom: Walther Spielmeier,¹⁰ Ernst Rüdin,¹⁰ and Franz Jähnel.¹⁰

powerful psychiatrist in the country.¹⁴ He was a member of the German Society for Racial Hygiene, an organisation inspired by his father-in-law Alfred Ploetz (1860-1940) and Julius Lehmann (1864-1935), which disseminated ideas about eugenics and the superiority of the Aryan race. During this period, Rüdin openly and intentionally worked with the National Socialists,

although he did not join the party until 1937. In 1934, he co-authored the “Law for the prevention of genetically diseased offspring,” whose implementation led to the forced sterilisation of hundreds of thousands of mentally ill individuals across Germany.¹³

He also sought to dominate the institute’s development with his racial hygiene initiatives. Thus, he personally

suspended Plaut in October 1935, and wondered whether the serology department should even be disbanded, as many of its staff were not Aryan and it would be difficult to find suitable replacements for them. Rüdín took no issue with his salary being paid by James Loeb, or with the fact that the DFA's survival had previously depended on those funds, but he would not allow Jews to work in the institution.¹⁷

Plaut was deeply saddened by the death of Spielmeyer, whom he had considered his best friend, in February 1935. Spielmeyer, whose wife was of Jewish descent, had openly defended his Jewish colleagues and maintained a firmly anti-Nazi stance. After his death, shortly after the death of the financier James Loeb, there was no opposition to Rüdín's power in the DFA. He applied for continued funding from the Rockefeller Foundation, even after the death of Spielmeyer and the sacking of Plaut, when he knew perfectly well that the funds provided by the foundation were contingent on the work of these two researchers.¹⁷

In August 1934, Plaut had requested that the Rockefeller Foundation help him to find a position abroad, but remained in Munich for another five years, suffering increasingly harsh persecution. The next year, he informed the foundation that he had been notified of the termination of his connection with the Institute and the University, which apparently was not a personal action taken against him, but rather a general regulation concerning Jewish persons who continued to hold positions in government and in official bodies. After this heavy blow, Plaut did not know what the future held in store, and soon found himself in a situation of prolonged unemployment. Despite his excellent academic reputation, and even though he had left the Jewish religious community in 1932, he was considered a "full Jew" under the Nuremberg Laws, and was at the mercy of the Nazis.¹⁷ Also in 1932, Plaut joined the liberal, nationalist German People's Party, which had been led for many years by Gustav Stresemann (1878-1929).³

The efforts of Walther Spielmeyer and the physicist Max Planck (1858-1947), director of the KWG, to oppose the imminent antisemitic dismissal of Plaut and other colleagues were futile. In late October 1935, a month after the adoption of the Nuremberg Laws, Ernst Rüdín informed Plaut, on behalf of the education minister of the Third Reich, that he would be relieved of his duties at the Institute from 1 January 1936. Around the same time, he

was also stripped of his licence to teach at the University of Munich.³ Plaut's successor as director of the department was Franz Jahnel, with whom he had had a very tense relationship for years due to the hostile antisemitism of the latter, whose origins were in the Sudetenland region of Czechoslovakia. Following the directives of the ruling Nazi Party, Rüdín's Institute justified the atrocities of racial hygiene initiatives, which included sterilisation and potentially euthanasia of patients with neuropsychiatric disorders.^{6,17}

Exile in England

Plaut's dismissal caused him great suffering, as at the age of 58 years he had little chance of finding suitable employment in another country. The Rockefeller Foundation seems to have permitted him to continue performing some research work in Munich, but the pressure to emigrate was inevitable. In January 1937, a representative of the Foundation who visited Plaut noted that he was visibly aged and urgently needed assistance to leave Germany.³

During his repeated visits to England, Plaut had made contacts in the country and tried to continue his scientific work there as a refugee. However, given the overwhelming circumstances, with thousands of intellectuals in exile, as well as his late departure from Germany, the available resources and positions were becoming increasingly scarce, even for a brilliant international figure like Plaut. Several attempts to find a position failed, until in 1939 he obtained a position at Horton Hospital in Epsom, Surrey, funded with a modest six-month grant awarded by the Society for the Protection of Science and Learning, an organisation that supported exiled foreign scientists; subsequently, the position was funded by the Rockefeller Foundation. The hospital had a large clinic for patients with GPI,¹⁸ and he was thus able to continue with his research on pyretotherapy.^{3,6,17}

However, as a German citizen, he lost this role in June 1940, when the Nazis invaded France and the British government banned foreign nationals from working in hospitals where military personnel were admitted, as was the case in Epsom. Plaut informed his contact at the Rockefeller Foundation that he had immediately ceased his research and left the hospital, taking all his belongings, within 30 minutes because he had been labelled an "enemy alien." Further complicating the situation, the Foundation was forced to close its Paris office

and to leave Europe due to the Nazi occupation. Plaut had nobody left to turn to, and did not even have any opportunity to emigrate to the United States, where the Foundation had tried fruitlessly to secure a position for him in Iowa with the neuropsychiatrist Andrew Woods (1872-1956). The depression that Plaut was already suffering became worse and, when he was threatened with internment in a camp for enemy aliens, he could not bear this new humiliation; on 27 June 1940, he ended his own life with an overdose of sleeping pills.^{3,6,17}

Felix Plaut and general paralysis of the insane

GPI was discovered in 1821 by Antoine Bayle (1799-1858), and since 1859 it had been the most characteristic model of mental illness, with these patients representing a large percentage of those admitted to psychiatric institutions. Although it had been linked to syphilis, it was not until 1905 that Fritz Schaudinn (1871-1906) and Erich Hoffmann (1868-1959) detected the micro-organism *Spirochaeta pallida*, now known as *Treponema pallidum*, in the chancre and inguinal lymph nodes of patients with syphilis, identifying it as the cause of the disease.¹⁹

In May 1906, August von Wassermann, Albert Neisser (1855-1916), and Carl Bruck (1879-1944) discovered a method based on the antigen-antibody reaction and complement fixation, using samples of tissue infected with syphilis as the antigen; this technique could be used to diagnose the infection. The method was named the Wassermann reaction.²⁰ In November of the same year, Wassermann and Plaut reported their experience using the method to study CSF obtained via lumbar puncture from 41 patients with GPI, many from the Nervenklinik in Munich. They concluded that the central nervous system of these individuals was actively producing antibodies against syphilis, indicating current or past infection by the pathogen (Figure 4).²¹ Plaut gathered the study data in a monograph in which he expanded the patient series, published in 1909 in Germany²² and in 1911 in New York, translated into English by Smith Ely Jelliffe (1866-1945) and Louis Casamajor (1881-1962), contributing to the international dissemination of the work.^{23,24} In 1913, Hideyo Noguchi (1876-1928) and J.W. Moore reported the presence of *Treponema* in the brains of 12 paralysed patients. Thus, it took less than a decade for a relationship to be established between the clinical presentation, the histopathology, and the aetiology of GPI.¹⁹

The Wassermann reaction was particularly useful in the early differential diagnosis of parasymphilitic diseases (GPI and tabes dorsalis) accompanied by mental disorders and other forms of psychiatric disease, on the one hand, and between cerebral syphilis and parasymphilitic, on the other. Thus, negative results in the CSF study ruled out GPI, which was in fact the only syphilitic condition for which a negative result was informative, as it could rule out the disease, whereas a positive result only indicated presence of syphilis.²⁵ Of the 1420 cases of GPI studied by Plaut between 1907 and 1920, only 8 (0.6%) presented negative Wassermann reaction results in the CSF.²⁶ Approximately one-third of patients admitted to psychiatric institutions in the 19th and early 20th centuries presented GPI.²⁷

Dementia paralytica was not the only mental disease related to syphilis. While it presented some characteristic symptoms, there were a great number of mental syndromes attributed to syphilis, although the precise relationship could not be established. Hallucinatory syndromes are a key example. On this subject, Plaut presented the communication "Syphilitic hallucinosis" at the 1913 Annual Meeting of the Bavarian Association of Psychiatrists, held in Munich.²⁸ He classified these syndromes as acute and chronic, fundamentally characterised by paranoid beliefs; hallucinations were most frequently auditory, with variable affectivity, in distressed patients who presented delusions of persecution and influence. Symptoms lasted six to eight weeks, and sometimes recurred. Plaut addressed the subject in greater detail in a subsequent monograph.²⁹ In Spain, José María Villaverde (1888-1936) raised awareness of the syndrome, known as Plaut hallucinosis, and contributed his own cases. He described the German as the greatest authority on the application of the new serology methods to mental syndromes of syphilitic origin.³⁰

At his laboratory in Munich, Plaut and his collaborators conducted animal experiments and clinical studies on the pathogenesis and treatment of GPI, including pyretotherapy with relapsing fever. The immunology of the disease was the central focus of his research for three decades.²⁷

In a lecture he delivered in Amsterdam in November 1919, Plaut gave a general review of what was known at the time about neurological involvement in syphilis. Advances in the understanding of the disease had led to the discovery of specific treatments that acted against



Aus dem Institut für Infektionskrankheiten in Berlin.
**Ueber das Vorhandensein syphilitischer
 Antistoffe in der Cerebrospinalflüssigkeit
 von Paralytikern.**

Von Prof. A. Wassermann in Berlin und Dr. F. Plaut
 in München.

A. Wassermann hat in Gemeinschaft mit C. Bruck auf Grund der Arbeiten von Bordet, Gengou, Moreschi, Neisser und Sachs eine Methode angegeben, mittels deren es gelingt, in Körpersäften einerseits geringste Mengen vorhandener gelöster Bakterienstoffe, andererseits deren Reaktionsprodukte, d. h. die Antikörper, nachzuweisen. Wassermann und C. Bruck haben diese Methode benutzt um bei Tuberculösen

Klinik in München, weiterhin den Anstalten Dalldorf und Herzberge, wofür wir den Leitern und Aerzten dieser Anstalten, insbesondere Herrn Geh.-Rat Moeli (Herzberge) und Herrn Prof. Liepmann (Dalldorf) unsern verbindlichsten Dank aussprechen.

Das zur Ausführung der Reaktion nötige syphilitische Material stammte zum Teil aus der unter Leitung von Geh.-Rat A. Neisser stehenden Dermatologischen Klinik in Breslau, dem wir ebenfalls an dieser Stelle unsern wärmsten Dank abstaten. Die zum größten Teil für unsere Versuche verwendeten Extrakte aus syphilitischen und normalen fötalen Organen wurden von uns aus Material hergestellt, das uns Herr Geh.-Rat Bumm in freundlichster Weise aus der geburtshilflichen Klinik der Charité überließ, wofür wir demselben ebenfalls herzlich danken.

Figure 4. The article "On the presence of syphilitic antibodies in the cerebrospinal fluid of paralytics."²¹

Treponema in cerebral syphilis, but did not improve GPI or tabes dorsalis. Plaut proposed several hypotheses to explain the origin of GPI: the possible existence of a mild form of syphilis infection among patients who would later develop GPI; differences in the body's defences; or the involvement of different types of spirochaetes. The family members of patients with GPI or tabes dorsalis rarely showed similar symptoms to the patients. In one experiment, rabbits inoculated with blood from patients with GPI displayed a very long incubation period and peculiar symptoms. Another possibility was that *Treponema* did not present differentiated characteristics at the time of infection, but rather developed them through interaction with the host. Thus, it would be a neurotropic micro-organism that infected the nervous system in a secondary phase. If during the follow-up of a patient with syphilis, a CSF serology study returned negative results and the patient subsequently presented GPI or tabes dorsalis, this would rule out the hypothesis that these were

derived from secondary processes, or at least would oppose the idea of continuous processes in effect from the secondary phase until the appearance of these diseases. This, in turn, would rule out the idea that spirochaetes penetrated the cortex during the secondary phase, remaining there for years without triggering the paralytic process.³¹

In an attempt at immunisation, Plaut demonstrated that subcutaneous or intracutaneous injection of small cultures of spirochaetes was well tolerated. He conducted experiments at the Wassermann Institute in Berlin, in which he administered six injections, at intervals of five or six days, of 0.5 cm³ (intracutaneous) of 2 cm³ (subcutaneous) of cultivated germ. The treatment was administered to a group of 22 patients with GPI, in whom the infection had been detected approximately a year earlier, observing no clinical changes. Plaut considered it impossible to solve the problem of GPI without better understanding the pathophysiology of syphilis.³²

In his lecture in Amsterdam, Plaut also demonstrated extensive knowledge and experience in the diagnosis and treatment of GPI and tabes dorsalis.³¹ Various therapeutic alternatives were tried without success until, in 1917, Wagner von Jauregg (1857-1940) in Vienna began experimenting with pyretotherapy, inoculating the live malaria parasite; in early 1919, Plaut did the same in Munich, injecting the relapsing fever germ.³³

The treatment of GPI by triggering episodes of relapsing fever was the preferred therapeutic alternative of Felix Plaut and Gabriel Steiner (1883-1965) in the first eight months of 1919. It had been four decades since Aleksandr Rosenblum (1826-1903) had published the results of his studies in Odesa on the positive effects of relapsing fever in 22 patients with mental illnesses.³⁴ The two German authors proposed the hypothesis that, as the fever was caused by infection with *Borrelia recurrentis*, a spirochaete closely related to *Treponema pallidum*, antibodies against the former bacterium may also affect the latter. In this first study, the African strain of *Borrelia* was injected into six patients with GPI and two with schizophrenia. Among the patients with GPI, one entered remission, two improved, and the other three remained stable. No change was observed in the clinical course of the patients with schizophrenia. These results were promising but awakened little interest, as numerous publications had previously described the inoculation of malaria to treat GPI.^{35,36}

In 1925, Plaut and Steiner analysed their personal experience from 1919 to late 1922, with follow-up data until late 1923. They had treated 76 patients with GPI, with good results in 34.2%. These patients were from Munich and from Heidelberg, where Steiner had transferred in 1920. The authors were very prudent in including follow-up data, as it was not possible to talk about success until at least 10 years had passed and, though they cited other German authors who had used the same procedure, they decided not to comment on any experience other than their own. They also treated patients by inoculating them with the malaria parasite, reporting similar results to those observed with relapsing fever. However, it was necessary in this case for malarial infection to be maintained active in patients with GPI who had never received quinine, which meant that the treatment could only be administered at large hospitals, whereas *Borrelia* could be kept in laboratory mice. Furthermore, malaria caused disability in patients, whereas relapsing fever was innocuous. *Borrelia* was inoculated via an intravenous

injection of mouse blood, causing a characteristic initial episode of fever. The intervals between subsequent episodes were longer than in malaria, and relapses spontaneously ceased within six to eight weeks.³⁷ These reports, some of which included data from five years of follow-up, demonstrated considerable benefits for GPI, according to Kraepelin.³⁸

In 1928, Plaut and his collaborator Christiane Grabow at the serology department demonstrated the autochthonous production of antibodies in nervous tissue, laying the foundations of modern neuroimmunology.³⁹ Thus, they were able to show that the presumed immune weakness of the nervous system was a misconception. In addition, collaborating with the chemistry department, Plaut attempted to isolate substances with antigenic effects in spirochaetes, using laboratory-synthesised lipids.¹³

Visit to North America. The epidemiological concerns of Kraepelin and Plaut

During spring 1925, Emil Kraepelin and Felix Plaut undertook a research trip to North America to conduct comparative psychiatry research in the field of GPI.¹ They hoped to gather further data on the disease in Native American, Hispanic, and African-American patients during their tour of the United States, Mexico, and Cuba. After months of preparation, on March 12 they set sail for New York, where they were left reeling by the city's hustle and bustle. They travelled along the East Coast, visiting Philadelphia, Baltimore, and Washington, D.C., where they examined numerous African-American patients at St Elizabeth's Hospital and studied the contemporary medical literature at the Library of the Surgeon General's Office. From there, they continued inland via Buffalo, Detroit, and Chicago, to visit the Asylum for Insane Indians in Canton (South Dakota), where they spent three days examining patients. Next, they travelled to Pasadena (California), for a private consultation, then to Mexico City, where they arrived in May, to examine more patients at the La Castañeda Insane Asylum.^{15,40} The pair subsequently returned to New York via New Orleans and Havana, and embarked on their return voyage to Europe on 24 June.¹⁵ They examined patients from four mental institutions: two hospitals for African-Americans (St Elizabeth's Hospital and the Mazorra psychiatric hospital, near Havana) and two for Native Americans (the Canton Asylum for Insane Indians and the La Castañeda Insane Asylum).¹

Before examining the patients in Washington, they took several days to review the existing medical literature on Native American and African-American patients at the Library of the Surgeon General's Office. Based on these studies, they concluded that the health of both populations had suffered as a result of the oppressive conditions they had lived under. They were very impressed by the Native Americans in Canton, who were proud of their heritage, whereas black patients more closely resembled white individuals, whom they tried to emulate.¹

The results of the clinical examinations partially confirmed their general impressions. Plaut and Kraepelin concluded that there was no discernible difference between black and white patients in terms of susceptibility to GPI, although the disease was proportionally more frequent in the former group. Establishing conclusions about the Native American patients was less straightforward. They observed no cases of GPI at the Canton asylum; with the support of the Department of the Interior and the Bureau of Indian Affairs, they collected information from asylums across the country with Native American patients, but were informed of very few cases of syphilis and GPI. They considered these data to be unreliable, but noted that Native Americans were less susceptible to the disease.¹

Plaut wrote a monograph on this trip, which they had undertaken in order to study unresolved questions on the causal factors in GPI and the apparent variability in the effects of syphilis infection in different races. They had expected to observe separate statistics for black, Native American, and white patients, and believed that they would discover why GPI occurred in some patient groups and not others. Plaut dedicated many pages of his book to analysing the results of their research. The statistics showed that syphilis was more frequent in black than in white patients, and that the clinical manifestations were different. Plaut believed that tuberculosis and syphilis had not been widespread among black slaves, who rarely presented madness. The abolition of slavery in 1864 changed their lives and their relationship with the exterior world, and they suffered from poverty and syphilis. Through the serological examinations he had conducted in the 10-15 years prior to his visit to North America, he saw that syphilis was more common among black men and women than in the white population. Native Americans seemed to present a very low incidence of syphilis and GPI. However, syphilis was frequent among Native Americans in Mexico, as was GPI.^{41,42}

However, research into GPI was not the main objective of Kraepelin's and Plaut's trip; rather, they sought to secure funding for their institute from American philanthropists. Kraepelin was in contact with potentially interested parties, especially James Loeb, months before their departure, and was searching for donors from their first day in New York. He travelled to Detroit in the hopes of arousing the interest of Henry Ford (1863-1947) in the DFA's psychology department, explaining to him the benefits of occupational psychology. Kraepelin's arguments with his hosts about politics and his belligerent anti-alcohol posture caused some friction, despite which they received support from the Rockefeller Foundation, due to complex motives, such as Kraepelin's scientific excellence and the research potential of the leading scientists at the institute.¹⁵ The financial aid they were granted enabled the construction of specific premises for the DFA, and subsidised the research of Plaut and the neuropathologist Walther Spielmeier.¹⁴

In 1925, a new theory emerged whose main proponent was the Latvian psychiatrist Leon Daraszkievicz (1866-1931), an old collaborator of Kraepelin's in Dorpat.⁸ According to Daraszkievicz's theory, the spread of GPI coincided with the spread of smallpox vaccination, which promoted or caused the disease by modifying the body's defences against syphilis infection. He argued that GPI was absent in countries that did not vaccinate against smallpox. Plaut and Jahnel demonstrated the inconsistency of this theory using data provided by Kraepelin and Plaut after their trip to North America. For instance, in Cuba, where smallpox vaccination had been mandatory for 23 years, GPI was rare in the black population and more common among white patients. In Mexico, where vaccination was not mandatory, smallpox was prevalent and GPI was frequent in all ethnic groups. Furthermore, smallpox vaccination did not influence the appearance of exanthematic infectious diseases, parotiditis, or scarlet fever.^{15,43}

In Munich, for the first time in a large city, a study was conducted to analyse the prevalence of syphilis among psychiatry inpatients at the university Psychiatric Clinic over an 8-year period; the study was directed by Plaut and Ehrismann and published in 1926. Of a total of 7733 patients, 25.4% of men and 15% of women presented syphilis infection. Serological study results were positive in 22.4% of men and 13% of women, and congenital syphilis was reported in 6.4% of men and 5.6% of women. Central nervous system involvement was the main

reason for admission among patients with syphilis: 877 had GPI, 32 had tabes dorsalis, and 73 had cerebral syphilis. Patients with GPI accounted for 11.4% of psychiatric admissions. Excluding the cases of neurosyphilis, 9.2% of the total sample of 7733 patients presented syphilis infection. However, few cases of syphilis were reported in the registry of the Internal Medicine Clinic.⁴⁴

From 1915, the Wasserman test was performed on all patients admitted to the university Psychiatric Clinic to determine the prevalence of syphilis at the centre. Furthermore, Kraepelin began a massive review of the records of patients with neurosyphilis at his hospital and in the local asylums. He conducted extensive reviews of the records of all patients with syphilis admitted to his clinic since its opening in 1904, and in 1921 he designed a protocol for an international study of GPI.^{1,45}

Other research

In the early years of the Nervenlinik, Kraepelin entrusted Plaut with several research studies of patients, showing a change in methodology compared to the studies conducted in the 19th century. For instance, in 1905 Plaut and Alfred Bosch (b. 1876) published a trial intended to provide physiological proof of how long, hot baths could alleviate states of excitation in psychiatric patients. The authors developed a thorough experimental design, using various standardised measurement parameters to guarantee the comparability and reproducibility of the data obtained. They concluded that the results were inconclusive and that various additional studies were needed.^{7,46,47}

Although the relationship between scurvy and lack of fruit in the diet had been known since the 16th century, it was not until 1933 that Albert Szent Györgyi (1893-1986) synthesised ascorbic acid (vitamin C), a highly reductive substance. The first attempts to isolate it were related to its presence in the brain. Felix Plaut, collaborating with Margarete Bülow (1902-1981) of the DFA's Chemistry Department, was one of the first to study the presence of the substance in different parts of the nervous system and to determine its concentration in the blood and CSF of humans and experimental animals. They demonstrated that levels of the vitamin in the nervous system decreased with age. They also studied vitamin C levels in relation to diet and metabolic states derived from febrile syndromes, such as malaria and ingestion of thyroid hormone.⁴⁸⁻⁵¹

The syndrome known as Plaut-Vincent angina was not related to Felix Plaut, but rather to a distant relative of his, Hugo-Carl Plaut (1858-1928), a medical bacteriologist from Hamburg.²

Spanish researchers with links to psychiatric institutions in Munich

Several Spanish neuropsychiatrists had more or less direct links with Munich's psychiatric institutions in the time of Kraepelin and Plaut. Firstly, Nicolás Achúcarro (1880-1918) arrived in the Bavarian capital in 1906, remaining there for two and a half years, working with Alois Alzheimer at the university Psychiatric Clinic. In 1908, he left for the United States, after his mentor recommended him for the directorship of the anatomical pathology laboratory at the Government Hospital for the Insane in Washington, D.C., colloquially known as St. Elizabeth's, where he remained until May 1910.⁵² That year, Achúcarro published a review of a study by Plaut, in which he demonstrated good understanding of the German's research into CSF alterations in syphilitic mental disorders.⁵³

Gonzalo Rodríguez Lafora (1886-1971) received a grant from the Junta para Ampliación de Estudios (JAE; Board for Study Extensions) to work with Alzheimer at the Munich Psychiatric Clinic for the winter term of 1908-1909, studying the neuropathology of senile dementias and schizophrenia. In 1910, he replaced his master Achúcarro at the Government Hospital for the Insane in Washington, where he worked for three years.⁵⁴ In the first half of the 1920s, Lafora published reviews of the intrathecal treatment of GPI and the treatment of the disease with induction of relapsing fever, with numerous references to Plaut and other German authors.⁵⁵⁻⁵⁷

José Miguel Sacristán (1887-1957) applied for and obtained a grant from the JAE to study neurohistopathology under Alzheimer in Munich, following in the footsteps of his master Achúcarro. He arrived there in summer 1912 to find that Alzheimer had transferred to Breslau; he travelled there to visit him, and discovered that he was severely ill. He returned to Munich and joined Kraepelin's Psychiatric Clinic, on the advice of Achúcarro. There, he worked in the chemistry laboratory of Rudolf Allers (1883-1963), and attended successive psychiatry courses taught by Kraepelin, who became his true foreign master and whose teachings he sought to disseminate in Spain. He stayed in Germany



Figure 5. From left to right: Nicolás Achúcarro⁵², Gonzalo Rodríguez Lafora⁶², José Miguel Sacristán,⁵⁸ and José María Villaverde.⁶²

for approximately a year and a half, returning to Spain in spring 1914.⁵⁸ Back in Madrid, he collaborated with Achúcarro and Santiago Ramón y Cajal (1852-1934), and founded the JAE's Laboratory of Physiological Chemistry at the Residencia de Estudiantes, as well as the journal *Archivos de Neurobiología*, alongside Lafora and José Ortega y Gasset (1883-1955), in 1919. Sacristán was the greatest Spanish student of the work of Kraepelin and the true importer of his ideas in Spain.⁵⁴

José María Villaverde trained in Germany in the first half of the 1910s, but did not work in Munich; however, he dedicated his first article (published in 1920) to Plaut hallucinosis, which the German had described in a meeting of Bavarian psychiatrists in Munich in 1913.^{30,59}

In February 1922, Miguel Prados Such (1894-1969) began his training at the DFA in Munich, with a grant from the JAE. He worked in Spielmeyer's laboratory and attended lectures by Kraepelin, Isserlin, and Plaut, expanding his knowledge of the histopathology of mental diseases and Felix Plaut's CSF studies. Prados was particularly interested in the histopathology of senile dementia and the pathogenesis of infantile amaurotic idiocy (Tay-Sachs disease), as well as the physiology of the striatum. A year later, in March 1923, he wrote a letter to the JAE renouncing the two remaining months of his grant, as he had accepted the position of director of the new San José psychiatric sanatorium in Málaga. At the time of his

departure from Munich, he had two articles pending publication from his work at the laboratory, on senile dementia and infantile amaurotic idiocy^{60,61} (Figure 5).^{52,58,62}

On 30 December 1924, one day after the creation of the Spanish National Association of Neuropsychiatrists, Kraepelin gave a lecture in Barcelona. In the conclusions of the meeting, the attendees requested that Kraepelin's nosology be adopted throughout Spain. From then on, Spanish psychiatry became German. This was the first time that the psychiatrist had presented a scientific communication in Spain, although he knew the country from previous trips to the Canary Islands in 1894 and 1908, and around the mainland and Balearic Islands in 1896. During the trip, he paid a visit to Santiago Ramón y Cajal in Madrid.^{8,54} It is not known whether Plaut ever visited Spain.

The legacy of Felix Plaut

For three decades, Plaut's main area of research was the immunology of GPI. He published around 180 articles in specialised journals and was coeditor of the journal *Zeitschrift für die gesamte Neurologie und Psychiatrie* from 1920 to 1935, and author of at least four books: *The Wassermann sero-diagnosis of syphilis in its application to psychiatry* (1909),^{22,23} *On the hallucinosis of the syphilitics* (1913),²⁹ *Guide to the examination of the cerebrospinal fluid* (1913) (as co-author),⁶³ and *Study of paralysis in*

African-American and Native American patients. A contribution to comparative psychiatry (1926).⁴¹ His obituary was published in the British journal *Nature* in August 1940.⁶⁴

Conclusions

Felix Plaut achieved international renown alongside his mentor Emil Kraepelin, who counted Plaut among his closest collaborators in Munich's psychiatric institutions.

It is difficult to understand the history of GPI without considering Plaut's contributions, as he was the greatest expert in the serological diagnosis of the disease and made important discoveries about its pathophysiology, clinical presentation, epidemiology, and treatment with pyretotherapy, as well as the mental disorders that accompany syphilis. His destiny evolved in parallel to the history of GPI, which was the most important mental illness at the time, but which today is practically unknown.

Plaut is also considered one of the fathers of modern neuroimmunology, as he was the first to demonstrate the production of antibodies in the brain.

A Jew of bourgeois origins, he suffered personally when the Nazis entered power in the 1930s, and was marginalised and forced into exile.

Conflicts of interest

This is an original article and the author has received no public or private funding for this study.

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