Neurasthenia as a model of a disease thought to have disappeared. On an unpublished letter by Jean-Martin Charcot

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ABSTRACT

Introduction. George Miller Beard first described neurasthenia in 1869 as a clinical picture characterised by fatigue, caused by the modern lifestyle of the 19th century. However, patients often also presented sleep disorders, cognitive complaints, digestive disorders, and symptoms of sexual dysfunction. The concept was disseminated internationally from 1880 by Jean-Martin Charcot, and became one of the most frequent diagnoses at the Salpêtrière at the time. However, from the 1930s the entity practically disappeared in the history of Western medicine.

Material and methods. This article reviews the concept of neurasthenia and its historical development. We present a previously unpublished private letter from 1888 by Prof Charcot, which includes real data on his clinical management of neurasthenia.

Results. Charcot followed a similar diagnostic and therapeutic approach to that of Beard. Today, patients with chronic fatigue syndrome, fibromyalgia, and more recently post–COVID-19 syndrome present similar symptoms to those initially described in neurasthenia.

Discussion. The emergence of post–COVID-19 syndrome or "long COVID" has resulted in an epidemic of patients with similar symptoms to those described by Beard in 1869. Nineteenth-century clinicians may already have described this patient profile, suggesting a shared pathophysiological basis.

KEYWORDS

George Miller Beard, Jean-Martin Charcot, long COVID, neurasthenia, chronic fatigue syndrome, post–COVID-19 syndrome

Introduction

In the late 19th and early 20th centuries, a new disease spread, almost epidemically, across North America and Europe. In 1869, George Miller Beard published an article defining the concept of neurasthenia in the *Boston Medical and Surgical Journal* (the predecessor to the *New England Journal of Medicine*).[1] The study presented his experience with 30 patients with symptoms characterised by "weakness" of the nervous system secondary to prolonged or excessive intellectual activity. The central element of the clinical picture was fatigue or physical or mental tiredness. However, the entity also encompassed all manner of subjective complaints. Patients often presented headache, insomnia, diffuse pain, gut rhythm disorders, sexual issues, and cognitive complaints. Regarding the origin of the disease, Beard considered the main cause to be the demands of the modern world and the technological advances of the day. In his opin-

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ion, the modern American lifestyle was characterised by rapid communication, excessive mental work, and an obsession with the efficient use of time. In the early years the concept was present in North America, and the entity came to be known as the "American disease"; in the 1880s, it crossed the Atlantic through the work of Jean-Martin Charcot. For most authors at the time, Charcot was responsible for introducing the term in European and international academic settings. One of his disciples, Ferdinand Levillain, published a monograph on the disease in 1891, underscoring his master's contribution: "If Beard was the father of neurasthenia, we may assert that in France, Charcot is its godfather."[2]

The concept of neurasthenia was widely disseminated on both sides of the Atlantic in the early decades of the 20th century, and began to decline in scientific journals from the 1930s. However, it persisted in Eastern countries, particularly China. It is listed in the tenth edition of the International Classification of Diseases as a discrete nosological entity. However, the Diagnostic and Statistical Manual of Mental Disorders only included the syndrome in its second edition (1968), removing it from subsequent editions.[3] From the perspective of the history of medicine, we must consider the possibility that the concept has evolved into other nosological entities, with a novel neurobiological approach. Two phenomena seem particularly relevant in this paradigm shift: firstly, the development of the concept of neurosis and the new psychosomatic approach adopted in psychiatry from the 1940s[4]; and secondly, the appearance of such new entities as chronic fatigue syndrome (CFS) from 1965, with the seminal publication by Holt.[5] In any case, the concept remains active in certain areas. The recent emergence of post–COVID-19 syndrome (PCS) has led to renewed focus on the profile of patients with neurasthenia.

We present a previously unpublished handwritten letter by Jean-Martin Charcot, dated 29 January 1888, a few weeks after his final trip to Spain to give expert testimony in the famous case of the Marquis of Larios.[6-8]

The primary objective of this study is to contribute information on Charcot's real clinical practice. The analysis of this kind of private document provides an opportunity for medical historiography to evaluate whether the guidelines issued in textbooks or lectures were followed in clinical practice. To the author's knowledge, there are no references in the literature to any prior publication of the letter. As a secondary objective, we will explore the evolution of the concept of neurasthenia, from its appearance in the 19th century to its near-complete disappearance from Western medicine in the early 20th century. The study also presents some data on the status of the concept today, and its relationship with such other entities as CFS, fibromyalgia, and the recently described PCS.

Material and methods

A systematic review was conducted to analyse the concept of neurasthenia in the academic context, with particular focus on its origins and its dissemination by Jean-Martin Charcot in the late 19th century. For that reason, the literature search included the term in English, French (*neurasthénie*), and Spanish (*neurastenia*); the search was conducted on the PubMed portal (pubmed.ncbi.nlm.nih.gov/) and in digital libraries including scans of original documents. The libraries searched were the University of California's HathiTrust portal (www.hathitrust.org), the Gallica portal of the Bibliothèque Nationale de France (gallica.bnf.fr/accueil/es/content/accueil-es), and the National Library of Spain's Biblioteca Digital Hispánica (bdh.bne.es/bnesearch/Inicio.do). Relevant information was also gathered from Teseo, a repository of Spanish doctoral theses (www.educacion.gob.es/teseo/irGestionarConsulta.do); articles in the grey literature were identified using the Google search engine (www.google.com).

The handwritten letter by Jean-Martin Charcot was transcribed using the Transkribus software (readcoop.eu/transkribus/). Transkribus is an artificial intelligence–based text recognition platform that analyses images of historical documents. The platform was created as part of a project within the European Union's Horizon 2020 programme. The project was initially led by the University of Innsbruck (Austria) and currently includes several European academic groups, including the Pattern Recognition and Human Language Technology (PRHLT) group at Universidad Politécnica de Valencia (Spain) and the Computational Intelligence Technology Lab (CITlab) at the University of Rostock (Germany). The letter was analysed using the Transkribus French Model 1 database, developed by the software community for 17th-20th century French handwriting. The letter was obtained at the bookshop Luces de Bohemia in Zaragoza, which specialises in old books and documents.

Figure 1. George Miller Beard, MD (1837-1883), ca. 1870. Source: The National Library of Medicine, public domain

Following the transcription procedure, the text was reevaluated by one of this journal's reviewers, and the majority of their suggestions were accepted for the definitive translation of the letter.

Results

The description of neurasthenia in the United States

George Miller Beard (1839-1883; Figure 1) was an American physician practising in New York in the late 19th century. Beard became interested in the incipient specialty of neurology and the use of electricity to treat psychiatric and neurological diseases. The city of New York was in the midst of a rapid expansion due to the mass arrival of immigrants, drawn to the city by its dynamic economy. Lifestyles were transformed by the technological innovations of the day, including the telegraph, the steam engine, and increasing industrialisation. This was the context in which, in a study published in 1869, Beard described the appearance of a group of patients with diverse symptoms that he attributed to modern living.[1] For Beard, the clinical condition, which he named "neurasthenia," was caused by exhaustion of the nervous system. The fundamental symptom of the disease was tiredness and fatigue after minimal efforts. However, both Beard and subsequent authors continued to add various other symptoms to this initial clinical picture. Frequently reported symptoms included insomnia, memory loss, headache, irritability, diffuse pain, gut rhythm disorders, and sexual impotence. Some objective signs were also described, including tachycardia, elevated blood pressure, and exaggerated tendon reflexes. Some patients also presented cutaneous hyperaesthesia on the head and back.[3,9,10]

The onset and course of the disease were variable, with both chronic and acute forms being described. Some patients even presented a relapsing-remitting course with transient symptom resolution. Insidious onset and chronic development of symptoms seemed to be associated with poorer prognosis and greater difficulties administering treatment. Although the general impression was that the disorder was not excessively severe, Beard himself underscored the accumulation of suffering and disability over the course of the disease. This heterogeneity of onset and symptoms led some authors to draw distinctions between different subtypes. For instance, digestive and sexual forms of neurasthenia were diagnosed in patients with predominance of each set of symptoms. Some authors considered these forms to be associated with "exhaustion" of nervous flow in the autonomic nervous system.

Ever since its original description, the disease was associated with the stress caused by modern lifestyles. Thus, Beard[11] established that neurasthenia was a disease of modern living, of the 19th century, and of the United States, as it was thought to be less frequent in Europe. Associated factors included excessive intellectual effort, the appearance of the telegraph, the widespread use of pocket watches to better use time, and the demanding social life of the fin de siècle. As we might expect, in its early days the disease was restricted to upper-class men in intellectual professions. The pathophysiological mechanism was thought to involve excessive energy con-

sumption in the nervous system, due to inappropriate demands. Beard clearly explained this by way of comparison to an electromechanical system: "An electric machine of definite horse-power, situated at some central point, is to supply the electricity needed to run a certain number of lamps—say one thousand, more or less. If an extra number of lamps should be interposed in the circuit, then the power of the engine must be increased; else the light of the lamps would be decreased, or give out."[12] Thus, if the patient did not reduce their "energy consumption," they would quickly develop symptoms of nervous exhaustion. However, over the following decades, some authors began to develop biological hypotheses, such as the association with tobacco, alcohol, excessive sexual arousal, and even hereditary factors.[9]

Since the seminal publication by Beard, the treatment of neurasthenia was based on electrotherapy and rest. The objective was for patients to withdraw, for a time, from their professional duties and the stresses of modern life. This intervention was called "climatotherapy" and included extended seaside holidays or relaxation cruises. Silas Weir Mitchell (1829-1914; Figure 2), one of the fathers of American neurology, developed one of the most popular methods for attending patients with neurasthenia. Weir Mitchell was the first to describe causalgia (complex regional pain syndrome), erythromelalgia, and rest in the treatment of neurasthenia, which came to be known internationally as "Weir-Mitchell therapy." His method was based on a holistic intervention including a combination of rest, confinement to bed, massage, and electrotherapy. The intervention usually lasted two to three months, combining mental and physical rest. It was not unusual for patients also to be prescribed dietary changes, with increased milk consumption and calorie intake.[13] Electric stimulation was recommended in nearly all cases. As the disease was assumed to involve a deficiency of electric energy, it seemed reasonable to remedy this with electrotherapy. Beard advocated this treatment from the time of his original description, writing that: "The nervous tonic which I largely employ in neurasthenia is general electrization. In this method of treatment the feet of the patient are placed on a sheet of copper to which the negation pole is attached, while the positive, either a large sponge or the hand of the operator, is applied over the head (the hair being previously moistened) […] down the entire length of the spine."[1] The strategy sought to recharge the nervous system through the cautious, repeated use of electricity. However, this intervention was not free of risk, and proper training of therapists and the use of adequate equipment were advised. Other authors, especially with regard to patients showing no response to treatment, recommended such treatments as serum therapy, consumption of rabbit nervous system extracts, and the use of alcohol or even opioids and cannabis. Ironically, physical exercise was also reported to be effective in some cases. This intervention sought to reduce fatigue by improving tolerance to exercise. In any case, exercise therapy was usually recommended after several weeks' bed rest, with progressive onset.[9]

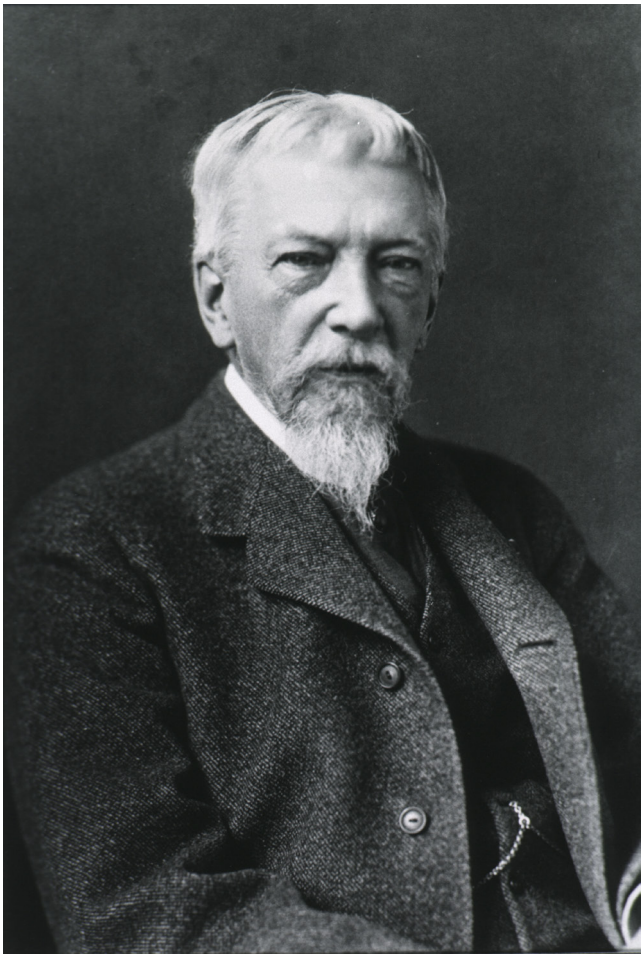

Figure 2. Silas Weir Mitchell, MD (1829-1914), ca. 1881. Source: The National Library of Medicine, public domain.

The dissemination of neurasthenia in Europe

Knowledge of neurasthenia spread rapidly in North America, both in academia and among the general

public. Its acceptance among local colleagues was more heterogeneous, with an initially lukewarm reception in the majority of cases. When Beard was accepted into the American Neurological Association, William A. Hammond (1828-1900), one of the founders of the association, quipped that accepting Beard's view would amount to "throwing his diploma away and joining the theologians."[14]

However, from the 1880s neurasthenia spread at increasing pace across Europe. It is not clear exactly when Charcot first learned of the disease. The first reference to neurasthenia at the Salpêtrière appears in a bibliographic commentary in volume 1 of *Archives de Neurologie* (1880-1881).[15] This edition summarised Beard's work on neurasthenia of January 1880, published in the American journal *Alienist and Neurologist*.[16] The commentary was written by D'Olivier, an intern of Bourneville's at the Salpêtrière, and summarised the clinical picture in detail. Over the following years, neurasthenia became one of the most prevalent diagnoses in Charcot's setting. The monograph published on the subject by his disciple Ferdinand Levillain underscores the importance of the condition in 1891. Levillain writes that: "The large number of neurasthenic patients attending outpatient consultations at the Salpêtrière, who account for nearly a quarter of the total, has led [Prof Charcot] to acknowledge the amplitude and frequency of this ailment."[2] At Charcot's famous Tuesday lessons at the Salpêtrière, for which transcriptions have been published for lessons from the period 1887-1889, numerous references were made to neurasthenia. In the first volume, which includes sessions from 1887-1888, the term "neurasthénie" appears as many as 18 times[17]; in the second volume, compiling lessons from 1888-1889, it appears 59 times.[18] Charcot introduced the concept of neurasthenia in the European academic context, considering it relevant due to the high frequency of the disorder. In the second lesson of Tuesday, 22 November 1887, a specific case of neurasthenia was presented (p. 25). Charcot's introduction was fairly descriptive: "There is a category of patients whom I would like to interview in front of you, although in fact I do not much like to do it because they are insufferable. They make up the great majority of patients that I see in the city [in his private practice]. They are the neurasthenics. They write memoirs on their condition and come to us with a notebook. They will approach you notebook in hand, telling you that they have prepared some notes, which they will promptly read out; in a majority of cases it seems they will never finish."

Jean-Martin Charcot's letter dated 29 January 1888

The letter presented here is dated barely two months after the introduction of Charcot's second lesson, mentioned in the previous paragraph. The Transkribus software was able to identify approximately 95% of words in the original manuscript (Figure 3). The letter was subsequently reevaluated by one of this journal's reviewers, who presented a more faithful transcription, enabling identification of all words in the letter. The header "217, Boulevard St-Germain" refers to Charcot's home address, and therefore to his private practice. The letter text reads as follows:

> Cher Monsieur
>
> Je me rappelle parfaitement le cas, et tous les details que vous me donnez sur votre etat actuel ne changent en rien mon diagnostic.
>
> Il s'agit purement et simplement d'un etat nerveux neurastenique produit sans doute par l'excès de la contention intellectuelle et que ne presente en tous cas aucune gravité. Une des conditions de la guerison si l'etat persistait serait l'eloignement des affaires pour une periode de temps de 2 ou 3 mois. Alors la guerison definitive deviendrait plus fácile; elle le será beaucoup moins avec la continuation incessante des affaires qui ont ete la veritable cause du mal.
>
> En attendent que vous preniez cette resolution que je crois presque indispensable, vous pouvez suivre le traitement indiqué ci contre. Si vous suspendez tout travail il faudra bien employer son temps, quilter la maison XX mais dans ce cas la vous demanderez avis.
>
> Je vous prie de croire a mes sentiments distingués.
>
> Charcot, 1888, Janvier 29
>
> J'avais eu l'intention dans mon dernier voyage a Malaga de rentrer en France para Saragosse et Barcelone mais j'en ai ete empeché par les neiges.

The translated text is as follows:

> Dear sir,
>
> I remember the case perfectly, and all the details you report on your current state do not change my diagnosis.

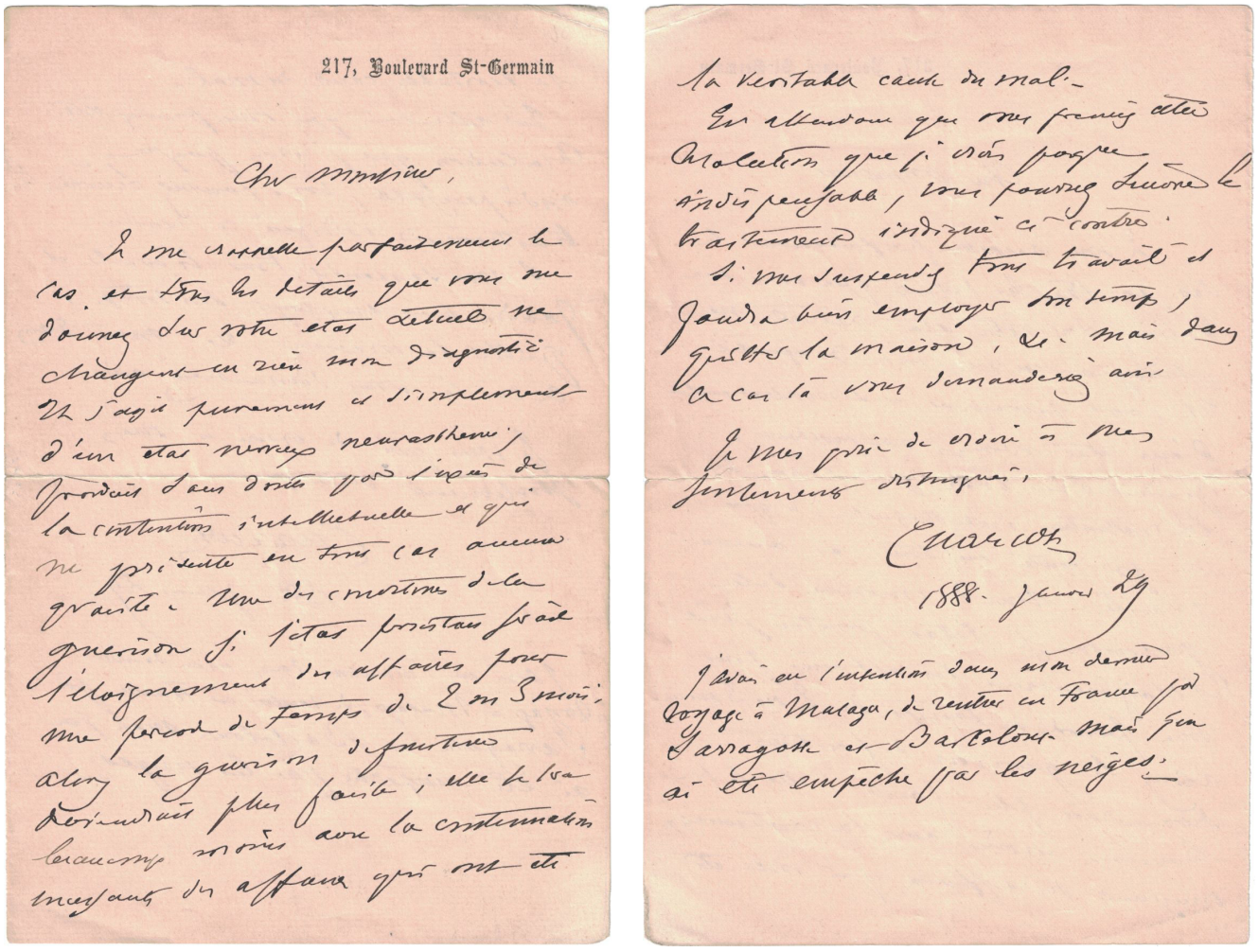

Figure 3. The letter by Prof Charcot. The first page features the header "217, Boulevard St-Germain," Jean-Martin Charcot's home address.

It is purely and simply a state of nervous neurasthenia, undoubtedly caused by excessive intellectual effort, and in any case is not at all severe.

If it persists, you must distance yourself from your business for a period of two or three months; then the definitive cure will be simpler; it will be much less so should you continue working, which is the true cause of the ailment.

Until my instructions are completed, which I believe crucial, you may follow the enclosed prescription.

If you suspend working, you must of course make use of your time, decorate the house with fabrics, xx, although in this case you must seek advice.

Please accept my best wishes.

Charcot

29 January 1888

On my last trip to Málaga I had intended to return to France via Zaragoza and Barcelona, but I was unable to due to the snow.

The letter sheds light on Charcot's real clinical practice in his treatment of patients with neurasthenia. Firstly, he seems to subscribe to Beard's original idea of the psychosocial origin of the disease. He notes that the condition is "undoubtedly caused by excessive intellectual effort" and suggests that the patient "distance

Table 1. Clinical profiles described in neurasthenia and post–COVID-19 syndrome or "long COVID."

Symptoms	Neurasthenia	PCS
Fatigue	++	++
Anxiety/depression	+	+
Sleep disorders	+	+
Cognitive symptoms	+	+
Dyspnoea/cough	+/-	+
Sexual dysfunction	+	+/-
Digestive disorders	+	+

PCS: post–COVID-19 syndrome; ++: cardinal symptoms; +: frequently associated symptoms; +/–: occasionally associated symptoms.

himself from his business" as the main intervention, noting that that this activity was the "true cause of the ailment". It is noteworthy that he does not advocate other therapeutic guidelines, such as rest therapy, massage, diet, and particularly electrotherapy. Perhaps these approaches were reserved for more complex or refractory cases. He clearly comments that the case "is not at all severe," and therefore it seems reasonable that he does not recommend an invasive intervention. The complete treatment may also appear in another letter or enclosed document. He establishes that the patient should rest for "a period of two or three months"; this is consistent with the guidelines at the time. Finally, he emphasises his certainty about the diagnosis. Prof Charcot obviously enjoyed enormous prestige at the time, but he also displays great familiarity with and understanding of the condition, which is consistent with the bibliographic sources consulted.

Evolution and current situation of the concept of neurasthenia

From the 1930s, and especially after the Second World War, the term neurasthenia fell into disuse in Western academia. In 1930, a review on diagnostic errors in neurasthenia concluded that: "Whatever you cannot diagnose on a physical basis you can safely call neurasthenia. […] it serves as a cover for a multitude of falsities begotten of ignorance and laziness."[19] A study analysing patients admitted with neurasthenia to the National Hospital for the Relief and Cure of the Paralysed and Epileptic, in Queen Square (London), includes some highly relevant details. The first patients with neurasthenia were admitted in 1885, and by 1934 almost no cases were recorded. The analysis of patients' definitive diagnoses shows an increase in the category of psychoneuroses from 1930, which makes up for the corresponding decrease in admissions due to neurasthenia. The authors suspected that this change was due to a taxonomic reclassification of the patients admitted.[20]

In Eastern countries, perhaps for cultural reasons, the concept of neurasthenia has persisted under various names. It is known in China as *shenjing shuairuo*,[3] a disorder listed in the Chinese Classification of Medical Disorders, characterised by physical and mental fatigue, insomnia, irritability, and difficulty concentrating.[21] In a study comparing both disorders, detailed analysis revealed high agreement with the concept of neurasthenia ($P < .001$).[22]

To many authors, one fact seems obvious: patients with similar symptoms to those described by George Miller Beard continue to attend consultations in the 21st century. This disorder seems not to have disappeared; rather, it has mutated into other entities with a distinct diagnostic taxonomy. Different studies have analysed the diagnostic labels that may be applied to these patients. The greatest similarity seems to be with CFS, with an overlap of 40%-97% according to a study comparing the two disorders.[23] In both entities, the cardinal symptom is fatigue, aetiology is unclear, and diagnosis is not supported by any clear objective evidence. Another option is fibromyalgia. According to one study, up to 70% of patients with CFS also meet diagnostic criteria for fibromyalgia, which suggests that the two disorders may be related, resembling the original clinical picture described in classical neurasthenia.[24]

Beginning in early 2020, healthcare practice changed as a result of the COVID-19 pandemic. In addition to the terrible repercussions of the pandemic across the globe, a new disorder emerged, known as PCS or "long COVID."[25] A systematic review of the literature on PCS established that the most frequent symptom is fatigue (44%), followed by dyspnoea (40%), anxiety (34%),

sleep disorders (33%), depression (32%), cough (22%), and cognitive symptoms (15%). Clearly, PCS presents a striking similarity with classical neurasthenia (Table 1). Both disorders are of unclear cause, frequently present with emotional disorders, and are usually multisystemic, with fatigue as the central axis. However, PCS has a clear trigger, SARS-CoV-2 infection, although the pathophysiological mechanism at play is unclear. In neurasthenia, in contrast, no infectious or inflammatory triggers were identified in the classical studies. However, some authors have postulated that the sudden onset and resolution of neurasthenia may suggest an infectious or postinfectious mechanism.[20]

Discussion

Neurasthenia was a very popular disorder in the late 19th and early 20th centuries, receiving great attention in the incipient specialty of neurology. Jean-Martin Charcot was one of the great supporters of neurasthenia in academia, and played a significant role in its international dissemination. The letter presented in this study sheds light on his real activities in private practice in 1888. As we have seen, he did not depart significantly from the views initially presented in Beard's 1869 paper.[1,10-12] Private documents are of great historical value, as they show the actual clinical practice of the time without the restrictions that may be placed on scholarly publications.

The debate around the evolution of neurasthenia continues today. From the 1930s, the reported cases became gradually rarer, practically disappearing after the Second World War.[3,4,9] However, the symptoms described in neurasthenia are frequent complaints in neurology consultations and, as we have seen, a very similar entity exists in such other countries as China.[21,22] This suggests that the taxonomy of the disorder evolved over the course of the 20th century into similar disorders in Western medicine. Potentially, in line with criticism from other authors,[19] neurasthenia became a miscellaneous category for numerous subjective symptoms reported by patients with different profiles. However, fatigue as the cardinal symptom of the disorder is essential in CFS, and one analysis demonstrated how the majority of patients currently diagnosed with CFS also meet diagnostic criteria for neurasthenia.[23]

A recent occurrence has led to the return of neurasthenia. After the COVID-19 pandemic, large numbers of patients presented a constellation of symptoms that have been grouped together under the name PCS or long COVID.[25-27] Fatigue is also the cardinal symptom of this new disorder, and the clinical picture (Table 1) largely resembles that seen in patients with neurasthenia in the 19th century. This has led to increased interest in the aetiology of the disorder. The discussion on the biological basis of neurasthenia continues to be debated, despite the associated psychosocial factors. The similarities between neurasthenia, CFS, and PCS are clear. In the latter two disorders, an association has been reported with chronic inflammatory factors induced by viral infections.[28] While the original cases of neurasthenia reported by Beard were not associated with any prior infection, some authors have stressed that the epidemiological model, with rapid onset and subsequent resolution, resembles that of various postinfectious syndromes.[20] Currently, some authors believe that various clinical conditions, such as CFS, fibromyalgia, breast implant illness, and PCS, are sufficiently clinically and biologically similar to be grouped together under the so-called autoimmune autonomic nervous system imbalance.[29] We may suggest that the concept of neurasthenia would include patients with these types of disorders in the late 19th century, although we regrettably lack further evidence beyond the descriptions included in historical records.

The present study has certain limitations. Transcription of Charcot's letter was a challenge. Furthermore, as a significant part of Jean-Martin Charcot's private correspondence is not known, it is challenging to develop a global view of the professor's real clinical practice. In any case, the letter represents a reliable source on this practice, which is consistent with information described in the literature.[4,14,30] The analysis of private correspondence is highly relevant in the study of the history of medicine, and constitutes a source of information on the development of science. Many of these sources are in private hands, outside the academic sphere, and cannot be accessed digitally. Scientific societies and government bodies could develop digital repositories to help private collectors to share this documentation with researchers.

Neurasthenia has been studied as a model of a disease that has disappeared. However, the clinical description of the disease and the evolution of the concept in historical records suggests that, in fact, it has merely changed in taxonomic terms. Patients with similar symptoms may

today be diagnosed with CFS, fibromyalgia, or the recently described PCS. The pathophysiology of all three syndromes continues to be debated, and may involve socioeconomic, psychological, and biological factors. In any case, our colleagues in the 19th century had the subtlety and diligence to identify this profile of patients presenting accumulated suffering and disability. As George Miller Beard pointed out: "Volumes are written on typhoid and other fevers; but in this country these neuroses, although not fatal, cause more distress and annoyance that all forms of fever combined."[11]

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Conflicts of interest

The author has no conflicts of interest to declare.

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