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Cover: This composite image depicts Jean-Martin Charcot with HAL 9000's iconic glowing red eye replacing his right eye. The juxtaposition symbolizes the historical evolution of neurology as a discipline of vision—from the *Iconographie Photographique de la Salpêtrière* (1876), which codified the anatomo-clinical method through photographic observation, to contemporary artificial intelligence, which mirrors Gestalt-like reasoning in pattern recognition. The figure not only underscores both the promise and the epistemological challenges posed by AI in neurology, but also serves as a way of celebrating the 150th anniversary of the *Iconographie Photographique de la Salpêtrière*, reminding us of neurology's enduring foundation in visual perception and diagnostic pattern recognition.

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While several journals currently explore the history of neuroscience, each tends to reflect specific disciplinary orientations. In contrast, *The Charcot Journal* offers a more integrative and dynamic platform—one that fosters dialogue among historians, neuroscientists, clinicians, and scholars from the humanities and social sciences. It is distinguished by its commitment to interdisciplinary inquiry, the inclusion of underrepresented perspectives, and a focus on the evolving cultural and ethical dimensions of neuroscience.

By encouraging cross-disciplinary engagement, this journal aims to illuminate the historical foundations of neurology through critical contributions that bridge medicine, philosophy, cultural studies, psychology, and the history of science.

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The Eye of Neurology: From the *Iconographie Photographique de la Salpêtrière* to Artificial Intelligence

Francesco Brigo¹

¹ Innovation, Research and Teaching Service, Teaching Hospital of the Paracelsus Medical Private University (PMU), Azienda Sanitaria dell'Alto Adige, Bolzano, Italy.

Corresponding Author:

Francesco Brigo - ORCID: 0000-0003-0928-157

E-mail address: dr.francescobrigo@gmail.com

What could be more immediate than visual perception? We see something before us—here and now. Perception is nourished by the present; it lives in the instant. And yet, this immediacy is deceptive. Culture shapes biology, and what we perceive is influenced by what we *know* we perceive. As Charcot famously said, *to know is to recognize*. Our vision is not purely anchored in the present—it is filtered through the lens of the past.

This historical anchoring of perception becomes evident when we consider how our attention is directed. If today we attend to certain details and see in a particular way, it is because those who came before us taught us to look that way.

A striking example of this is the *Iconographie Photographique de la Salpêtrière*, first published in 1876 (Bourneville and Regnard 1876). As we celebrate its 150th anniversary, this landmark work reminds us that neurology is, above all, a discipline of vision. It also illustrates how our way of observing the signs of disease has been shaped over time by neurologists who laid the foundations of a diagnostic method rooted in pattern recognition—a process that closely resembles *Gestalt* reasoning.

Here, the transition from visual observation to cognitive interpretation becomes central. According to the *Gestalt* principle in psychophysiology, the whole is greater than the sum of its parts. What emerges is not simply given, but constructed through the dynamic interaction of elements.

This principle finds a powerful echo in the evolution of neurological method. Neurology—and medicine more broadly—has systematized this cognitive process, translating it into a structured approach. This method represents one of the highest expressions of human intelligence: the ability to disentangle the complexity of disease, to recognize diverse patterns of clinical presentation, and to transform chaos into order.

Even more fascinating is the circularity of this process: it is the brain itself that informs the way we study the brain. This recursive relationship underscores the depth of neurological inquiry.



At the heart of this method lies a hierarchical organization of information. By assigning different weights to each element, clinicians move from initial input to diagnostic output. The goal is to uncover hidden patterns beneath the dynamic and mutable surface of clinical phenomena. This is, in essence, the logic underpinning the correlation between signs, symptoms, and their neurological localization—the anatomo-clinical method systematized by Charcot.

One of Charcot's most renowned student, Sigmund Freud, captured this approach well. In describing his mentor's method, Freud emphasized Charcot's extraordinary ability to synthesize disparate, sometimes contradictory data, organizing it and assigning relative value to each piece until the initial chaos became structured. It is from this Gestalt-like reasoning that contemporary neurology emerges—an approach that also incorporates Bayesian logic, where conditional probabilities interact and evolve based on the quantity and nature of available information.

This brings us to a broader epistemological insight: neurology is founded on a method that enables the ordering of multiplicity and apparent chaos, allowing clinicians to identify meaningful aggregates—nodes around which understanding coalesces.

Today, this same logic is mirrored in the development of artificial intelligence. Facial recognition and image analysis systems powered by AI emulate the Gestalt-like mechanisms inherent in the human mind. Increasingly, such tools are being applied in neurology—not only in research but also in clinical practice. Examples include the automated analysis of neuroimaging, the detection of subtle clinical signs such as mild facial asymmetries or papilloedema, the interpretation of EEG recordings, and the recognition of movement disorder patterns (Auger et al. 2020; Sollee et al. 2022; Shi et al. 2024). Their remarkable performance—continuously advancing—underscores the AI potential of replicating human cognitive strategies.

But this also raises profound ethical, social, and epistemological questions. These are not peripheral concerns. They are urgent and central. As we move forward with technologies that mirror our cognitive processes, we must develop robust and effective responses. The stakes are high: these tools function in ways strikingly similar to us, and precisely because of that, their consequences remain largely unknown—and potentially unsettling.

I believe there is little doubt that we have entered—borrowing an expression from Michel Foucault (1926–1984), whose centenary is being commemorated this year, in what seems to be a year rich in anniversaries—into a new episteme (Foucault 1966). The large-scale adoption of artificial intelligence has brought about a radical and structural transformation in the horizon of thought and language within which we exist, with consequences that are unpredictable not only on the social, economic, and professional levels, but also in the very way we will conceive of the nature of the human being. Artificial intelligence, integrated into the transhumanist project, may well lead us toward a post-human reality—a prospect that is anything but remote (Ferry 2025).

In Stanley Kubrick's *2001: A Space Odyssey*, the artificial intelligence HAL 9000 is portrayed as a glowing red eye—an iconic symbol of machine vision and cognitive control. HAL's design evokes the idea that *to see is to know*, and reminds us how closely artificial systems can resemble human perception in their functioning.

Let us hope that this headlong race toward (or behind) technological progress, while strengthening the eye of artificial intelligence, does not cloud our own vision—nor obscure our clinical gaze—making us more blind.



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Testing Hughlings Jackson's proposed dietary treatment of epilepsy:

John Merson's cross-over trial of 1875

(History of Neurology)

Andrew J. Larner¹, Sarah Cooper², Max Cooper³

¹ Honorary Senior Research Fellow, Department of Translational Neuroscience & Stroke, Institute of Neurology, University College London, London, United Kingdom

² Department of Neurology, Royal Sussex County Hospital, Brighton, UK

³ Department of Primary Care and Public Health, Brighton and Sussex Medical School, Brighton, UK

Corresponding Author:

Andrew J. Larner - ORCID 0000-0003-0128-8010

E-mail address: ajlarner241@aol.com

Abstract

The results of randomised controlled clinical trials form the basis for the modern treatment of epileptic seizures. Elements of clinical trial design may sometimes be discerned in the therapeutic experiments of earlier generations. We review an investigation published in 1875 in which some features typical of a cross-over clinical trial were adopted. This trial of farinaceous versus nitrogenous diet in the control of epileptic seizures was explicitly based on the pathophysiological speculations of John Hughlings Jackson and was conducted by John Merson at the West Riding Asylum in Wakefield, West Yorkshire, England. This article examines the context, the setting, the investigator, the trial, and its aftermath.

Keywords: clinical trials; cross-over; diet; history of neuroscience; John Hughlings Jackson; John Merson.

Introduction

Randomised controlled clinical trials and the meta-analysis of such trials have underpinned many of the therapeutic advances in the management of epilepsy in recent decades, and trial data are central to the licencing and acceptance into clinical practice of new anti-seizure medications. However, any impression that clinical trials are a recent innovation, foreign to the clinicians of the past, is controverted by extensive evidence (Tröhler 2000; Chalmers 2001; Bhatt 2010). The trial of treatments for scurvy undertaken by James Lind (1716-1794) in 1747, possibly prompted by the proposal of Francis Haukesbee (1688-1763) in 1743 for an “experimentum crucis” to compare the safety and efficacy of new medicines (Cooper and Cooper 2025), is often regarded as the first controlled clinical trial. However, these older studies lacked the rigorous methodology of current trials. Hence, their outcomes were not free from many potential confounds, for which reason these investigations may perhaps be better conceptualised as therapeutic experiments rather than as clinical trials, at least as the latter term is now understood.

The aim of this paper is to present one such therapeutic experiment in patients with epilepsy, undertaken in the 1870s and based on the ideas of John Hughlings Jackson (1835-1911), the leading clinician studying epilepsy at the time (Greenblatt 2022). The study in question manifests some features typical of a cross-over clinical trial.

The context

No effective treatment for epilepsy existed before the 1850s when the first description of the use of bromides was published (Eadie 2012). Despite the efficacy of bromides, few people with epilepsy could access such medication. Seizures were thus essentially unmanaged, and hence refractory, with the result that many people with epilepsy could not be employed and were at risk of becoming destitute. In England and Wales, such individuals often fell into the Poor Law system of the workhouse and the lunatic asylum, as documented on more than one occasion by Charles Dickens (Larner 2012).

People with epilepsy formed a significant proportion of the lunatic asylum population in the nineteenth century, both those with psychiatric disorder or learning disability complicated by seizures (hence “insane epileptics” in the terminology of the time) and those not so afflicted (i.e. “sane epileptics”). There was a continuous expansion of asylum capacity throughout the nineteenth century necessitated by the increasing population of individuals deemed insane, with some asylums constructing wards dedicated specifically to the care of those “inmates” with epilepsy.

The setting

The late nineteenth century shift from moral to medical treatment of insanity was nowhere more apparent than at the West Riding Asylum (WRA) located at Wakefield in West Yorkshire, England. Under the medical superintendency of James Crichton-Browne (1840-1938) between 1866 and 1876, WRA was at the forefront of the investigation of brain disease. This was a consequence of the development of a dedicated pathological laboratory and the employment (without salary) of Clinical Clerks and Clinical Assistants who, along with the resident Assistant Medical Officers, could undertake research projects, generally at the suggestion and under the supervision of Crichton-Browne (Larner, forthcoming).

Many of these projects were subsequently published in the asylum’s house journal, the *West Riding Lunatic Asylum Medical Reports (WRLAMR)*. In addition, Crichton-Browne was able to persuade clinicians working outside WRA to contribute to the journal he edited, most notably Hughlings Jackson, who published no less than four papers on epilepsy therein (all were subsequently included in the publication of Jackson’s *Selected Writings*; Taylor et al. 1931, 77-

89, 90-111, 119-134, 135-161). One judgment of posterity has opined that “By far the most important writings in the *WRLAMR* are those by J Hughlings Jackson” (George and Trimble 1992, 248).

Despite his characterisation of epileptic seizures as a consequence of “discharging lesions”, Hughlings Jackson’s conception of epilepsy was not explicitly electrical, indeed his ideas were fundamentally chemical in nature (York and Steinberg 2006, 13). In 1873, Jackson’s speculations on the cause of epileptic seizures were aired in the pages of the third volume of *WRLAMR*:

There are, I submit, two ways in which nutrition may be imperfect - in quantity and in quality. I believe that nerve tissue in discharging lesions is over-nourished in the former sense and worse-nourished in the latter (Jackson 1873, 326).

I believe, then, that the highly unstable nervous matter of disease (in a ‘discharging lesion’) differs in composition, but not in constitution, from the comparatively stable grey matter of health. The alteration in composition is of course such that the nervous substance formed is more explosive. (Jackson 1873, 326).

The following is a speculation as to the kind of alteration of composition. One striking constituent of nervous matter is phosphorus. [...] My speculation is that in the abnormal nutritive process producing unstable nervous matter the phosphorus ingredient is replaced by its chemical congener, nitrogen. [...] If nitrogen be substituted as supposed, we can easily understand that the substance produced would be more explosive. [...] The nutrition is, therefore, assumed to be defective not in quantity but in quality, in those functional alterations I call ‘discharging lesions.’ (Jackson 1873, 327).

This formulation had clear therapeutic implications, as Hughlings Jackson realised:

I think these speculations have a practical bearing on the dietetic treatment of epileptics. I advise epileptics not to eat much meat (not much nitrogenised food), nor, indeed, much of anything. (Jackson 1873, 327).

This recommendation was to influence one of the junior doctors at WRA who was undertaking clinical research.

The investigator

John Merson (1846-?1936) was a graduate of the University of Aberdeen (MA 1866 MB CM 1870; Johnston 1906, 365) who came to Wakefield as Assistant Medical Officer and Pathologist in 1873, having already spent three years as Assistant Medical Officer in the Northumberland County Asylum. During his time at WRA, in addition to his clinical duties Merson attended the annual medical meetings, termed *conversazione*, held at the Asylum. At the events of both 1873 and 1875, he supervised a table displaying photographs of current and former patients taken in the asylum’s dedicated photographic studio. He was promoted to the degree of MD at the University of Aberdeen in 1874.

Merson undertook various research studies whilst at WRA, resulting in three publications in *WRLAMR*: “The urinology of general paralysis” in 1874; “On the influence of diet in epilepsy” in 1875; and “The climacteric period in relation to insanity” in 1876. It is the middle of these papers which is of particular interest here.

The trial

Rationale

Merson's opened his paper with a very clear explanation of his objectives and their rationale:

The primary object of this Essay is to record the results of a series of observations on a number of patients suffering from epilepsy, undertaken with the view of determining the relative value of a nitrogenous and a farinaceous diet in the treatment of that disease. These observations were suggested by a paper in the third volume of the West Riding Asylum Medical Reports on the 'Investigation of Epilepsies,' by Dr. Hughlings Jackson, in which the author brings forward certain speculations regarding the nature of the morbid alteration in the nutrition of brain tissue, underlying the epileptic condition. [...] they lead Dr. Hughlings Jackson to the conclusion that a farinaceous diet is more suitable in the epileptic condition than a nitrogenous. It was for the purpose of testing the value of this opinion that I undertook the series of investigations which it is the object of this paper to record. (Merson 1875, 1).

After a lengthy digression on the law of the conservation of energy, Merson then addressed the relevance of diet to brain function:

compounds containing nitrogen in one form or other make up a large proportion of the entire brain substance, a fact that leads us naturally to expect that the nutrition of this organ may be most readily affected through the increase or diminution in the nitrogenous principles of the food. The phosphorised [*sic*] matters of the brain are also marked out by their multiform chemical relations as likely to play an important part in the production of nervous activity, and in this relation the amount of phosphorus in the food becomes an important consideration. (Merson 1875, 10).

Thus, a consideration of the possible interaction of diet and epilepsy treatment was reached:

In considering the question of diet in its bearing on the treatment of epilepsy, we have first to enquire into the probable nature of the abnormal condition of brain matter existing in that disease, and then to determine whether this condition is likely to be influenced by the quantity and quality of the food. (Merson 1875, 11).

In addressing this issue, Merson directly quoted those passages from Hughlings Jackson's 1873 *WRLAMR* paper given above.

Participants and interventions

The study participants and the interventions were then explained:

Twenty-four chronic epileptic patients were selected and subjected to observation under two different kinds of diet, the one consisting largely of nitrogenous matter, and the other containing no animal food, but consisting of milk, arrowroot, potatoes, butter, oatmeal, and bread. Though the terms are not strictly accurate, I shall distinguish the former as *nitrogenous* and the latter as *farinaceous*. (Merson 1875, 13 [*italics in original*]).



Although not explicitly stated, it seems that all 24 participants were men since, speaking of the diet, Merson noted the “quantity allotted to each man per day” (Merson 1875, 14).

As for the conduct of the trial:

The patients under observation were engaged in light occupation in the wards, and walking exercise in the airing grounds when they were inclined. The amount of actual mechanical energy expended was therefore very small.

Previous to commencing the above dietary each patient was accurately weighed, and his physical and mental condition noted. Twelve of the patients under observation were then put on nitrogenous diet, the other twelve on farinaceous, and this arrangement was continued for four weeks, during which time their physical and mental conditions were closely observed from day to day, and the number of epileptic seizures accurately noted. At the end of four weeks the weights were again taken and the diet changed, those previously on nitrogenous diet being transferred to farinaceous, and those on farinaceous to nitrogenous. After another period of four weeks, during which the condition of the patients was from time to time noted and compared with that which had been observed in the previous period, the weights were again ascertained, and the patients allowed to resume their ordinary dietary. (Merson 1875, 15).

Hence, all patients experienced both the nitrogenous diet and the farinaceous diet, one month on each (hence one group AB, the other group BA), in other words a cross-over arrangement.

Outcomes

Merson considered not only the frequency of seizures as an outcome measure but also the effect on “mental condition” and “general physical condition”. In terms of the patients’ mental condition, the results of the dietary interventions were noted:

In a considerable number of those who took nitrogenous food during the first month, it was observed that soon after commencing that diet they became much more dull and stupid than they had previously been, would sit in a dreamy, listless manner for a great part of the day, were very slow and languid in their movements, and took little notice of what was going on around them.

As soon as the diet was changed to the farinaceous, it was remarked that the condition of mental hebetude began to pass off, and in some of the cases the change was very remarkable.

A similar condition was observed in some of those who began with farinaceous food. Several patients who, during the period of farinaceous diet, had been observed as more lively and intelligent, became languid and stupid when the food was changed to the nitrogenous. (Merson 1875, 16).

However:

no connection could be traced between this condition of mind and the number of fits (Merson 1875, 16).

As regards the patients' general condition:

The general physical condition does not appear to have been appreciably affected by one diet more than the other. Under both diets there was a slight tendency to lose weight during the first month, and this is in accordance with what has often been observed, that under a regulated diet of any kind there is a tendency to lose weight. During the second month most of the cases remained stationary in weight or gained slightly. (Merson 1875, 18).

Concerning seizure frequency, the key outcome variable:

as regards the number of fits in individual cases, there is a slight balance in favour of the farinaceous regimen. (Merson 1875, 15).

This was the outcome that Hughlings Jackson's considerations had predicted. But matters were not clear cut:

out of twenty-four cases observed there was in fourteen a decided decrease in the number of fits during the period of farinaceous diet; the average number of seizures for the farinaceous period in these fifteen [*sic*] was 20.7, as compared with 28.3 for the nitrogenous period. Of the remaining ten cases, four had the same number of fits under each diet. There are, therefore, only six left in which the advantage is on the side of the nitrogenous regimen [...] I think then that, after making due allowance for the short period of observation and the limited number of cases observed, there is still a certain indication that the actual number of fits is less under a farinaceous dietary than under a nitrogenous. (Merson 1875, 21-22).

Merson's conclusions regarding the outcome of the trial

Merson's conclusions as to the effects of nitrogenous versus farinaceous diet on epilepsy were as follows:

The results obtained during those two months of observation are not such as to justify the conclusion that either of the two diets used possessed any decided advantage over the other in the treatment of epilepsy. (Merson 1875, 15).

He was aware of (some of) the limitations of his study:

It must be allowed, however, that the time over which these observations extended was too short to warrant any decided conclusion as to the advantage of the one diet over the other. (Merson 1875, 19).

But nevertheless:

On a review of the whole evidence furnished by these observations, I think, after making due allowance for all circumstances likely to tell in the opposite direction, that there are fair grounds for the conclusion that a farinaceous diet is likely to be more useful in the treatment of epilepsy than a nitrogenous; but in order to get satisfactory results, observations would have to be extended over a longer period than was at my disposal in the present instance. I hope, however, to continue these observations, and at some future time may record the results of my further experience. (Merson 1875, 23).

The aftermath

The particular dietary approach to the control of epileptic seizures investigated by Merson, on the basis of Hughlings Jackson's pathophysiological speculations, does not seem to have had any followers or imitators. No "results of my further experience" were published by Merson. We are not aware of any comment on, or citation of, Merson's work by Hughlings Jackson. A later superintendent at WRA, William Bevan-Lewis (1847-1929), commented in his seminal work, *A text-book of mental diseases* (1889), that the study was "based upon too limited a number of instances, to warrant final acceptance" (Bevan Lewis 1889, 220).

Some twenty years after the trial was conducted, James Crichton-Browne recalled that:

whatever the effect of a liberal diet of animal food may be upon the healthy understanding, there can be little doubt that it is prejudicial to the mental power of epileptics. Just twenty years ago one of my colleagues, Dr. John Merson, carried out at the West Riding Asylum in a masterly way a series of observations bearing on this point. He placed two groups of epileptic patients on a nitrogenous and farinaceous diet respectively for a fixed period, and then for a like period he changed the dietary of the two groups, giving those patients who had had a farinaceous diet a nitrogenous one, and those who had had a nitrogenous diet a farinaceous one. The patients on whom he experimented were of a chronic and confirmed class – patients in whom long-continued epilepsy had resulted in mental deterioration; and yet even in them marked results were obtained. In fourteen out of twenty-four cases there was a decided decrease in the number of fits during the farinaceous diet, and in a very considerable number of cases it was observed that soon after the nitrogenous diet was commenced mental dulness [*sic*] and stupidity supervened, the patient passing into a state of hebetude, which only disappeared when a farinaceous diet was again resorted to. (Crichton-Browne 1895, 75).

This favourable recollection, twenty years after the events, along with the positioning of Merson's paper as the first article in the fifth volume of *WRLAMR*, might possibly suggest that Crichton-Browne had faith in and was invested in the study, likewise his further recollection published another 30 years later (Crichton-Browne 1927, 41).

As for John Merson, he had become the designated Deputy Medical Director at WRA by the time of Crichton-Browne's departure in 1876. Elected to membership of the Medico-Psychological Association (forerunner of the Royal College of Psychiatrists) in 1877, Merson was appointed Medical Superintendent of Hull Borough Asylum in 1878. In this role, Merson was adjudged "competent" but he "reduced the provisions supplied to patients [...] and stopped the issue of beer", undoubtedly a cost-cutting measure and one not calculated to endear him to the patients, but perhaps influenced by his findings with respect to farinaceous versus nitrogenous diets in asylum patients. "He came to Hull as a bachelor but soon announced his forthcoming marriage to a widow with children who had been Matron at Wakefield", one Harriet Castledine (Bickford 1983, 31-32).

Merson superintended the move from the Old Asylum in Hull's Argyle Street to the new purpose-built asylum at De La Pole Farm in 1883. A few years later Daniel Hack Tuke, a prominent figure in psychological medicine in these years, judged that it was "Dr. Merson [...] to whom the satisfactory state of the existing asylum is really due" (Hack Tuke 1889, 15). Merson remained in post at Hull Borough Asylum until 1924 but seems not to have undertaken any further research studies or authored any publications throughout his long incumbency. He

did, however, make medical news in 1897 when it was reported that he was “rendered unconscious by a violent blow to the back of the head with a cricket bat, by one of the inmates. His condition for some time caused much anxiety, but he is now making slow but steady progress” (Anon. 1897). A later account, erroneously attributing the incident to 1898, stated that “Dr. Merson was umpiring [...] when a patient he had given out attacked him so violently that he was concussed, and on sick leave for months” (Bickford 1983, 71). The attack was also mentioned, along with other similar incidents befalling asylum personnel, in a subsequent general reference to the “risks of asylum life” (Anon. 1898).

At a dinner held by the Royal Medico-Psychological Association in honour of Crichton-Browne in 1931, the former WRA Superintendent acknowledged that Merson was still living (Anon. 1931, 658). Six years later Merson’s name appeared in the Association’s obituary column (Royal Medico-Psychological Association Yearbook 1937, xl), but no dedicated obituary has been identified.

Discussion

Merson’s paper gives an interesting glimpse into clinical practice in the mid-1870s. The design of his investigation is in marked contrast to other studies of therapeutic agents for epileptic seizures undertaken at WRA around this time, such as Crichton-Browne’s account of nitrite of amyl (Crichton Browne 1873) and John Wallis’s on chloral hydrate (Wallis 1875), both of which were no more than case series. Merson’s study had greater sophistication, sequentially switching the patients between the two interventions being compared. Whether this approach stemmed from Merson himself or was suggested by Crichton-Browne cannot be ascertained from the available documentary evidence. Crichton-Browne’s work on conium for the treatment of mania at WRA has been considered in the light of a controlled evaluation, albeit flawed, of drug treatment (Adams 2010), but it did not include a cross-over comparison.

From our current perspective, with the benefit of hindsight (but hopefully not the condescension of posterity), it is evident that Merson’s study was subject to many observer and selection biases: small number of participants ($n = 24$, 12 in each group); no power calculations; no matching for age, sex, seizure frequency or type; no randomisation; no blinding; no pre-specification of outcome measures; brief trials (one month on each diet); no wash-out period before cross-over; subgroup analysis to derive averages for those subjects (fourteen? fifteen?) with a “decided decrease in the number of fits during the period of farinaceous diet”; etc. However, even though small in size and methodologically limited according to current standards, the cross-over design of Merson’s trial might nevertheless have helped to reduce intra-subject variability and minimize covariate imbalance, thus improving the robustness of the findings.

In addition to the aforementioned methodological concerns, there was no consideration of whether or not participants, unknown to Merson, might have breached the study protocol: the absence of “animal food” in the farinaceous diet might possibly have prompted some participants to seek out or even pilfer other (non-trial) patients’ meat. Subsequent studies of a dietary intervention for seizure management, specifically the ketogenic diet, are known to have been subject to difficulties with compliance and discontinuance due to dietary intolerance (Ruan et al. 2022).

Hence Merson’s conclusion that “the actual number of fits is less under a farinaceous dietary than under a nitrogenous” cannot be considered robust. Perhaps understandably, then, Merson’s trial does not feature in historical overviews of methods to control selection bias in therapeutic experiments (Tröhler 2000; Chalmers 2001). We do not find Merson’s trial mentioned in the James Lind Library (<https://www.jameslindlibrary.org>; accessed 02/09/2025).



Merson was explicit that the rationale for his study was the current thinking of Hughlings Jackson on the pathophysiology of epilepsy, thus contradicting a later judgment that characterised his work as “based on older thinking” (George and Trimble 1992, 248). Although a cross-over design may be detected in earlier therapeutic experiments, indeed dating back to the seventeenth century (Cooper and Cooper 2024), there is no evidence that Merson was aware of these prior reports.

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Girolamo Fabrici d'Acquapendente (1533-1619)

The Dawn of Color in Anatomy

(History of Medicine)

Giorgio Zanchin¹

¹ Padua University Medical School

Corresponding Author:

Giorgio Zanchin

E-mail address: giorgio.zanchin@unipd.it

Abstract

This article examines Girolamo Fabrici d'Acquapendente (1533–1619) and his pioneering *tabulae pictae* (“painted anatomical tables”). As professor of anatomy at Padua and mentor to William Harvey (1578-1657), Fabrici advanced embryology and venous anatomy, laying foundations for Harvey’s discovery of blood circulation. His collection of over 200 hand-painted plates, preserved in the Marciana Library, introduced color as a vital tool for anatomical teaching, surpassing the monochrome engravings of Vesalius in lifelike realism. The tables reveal striking attention to tissue qualities and three-dimensionality, particularly in the neuroanatomical series *De Anatomia Capitis Cerebri Nervorum*. Though no explanatory text survives, indirect testimonies highlight Fabrici’s reverence for the brain as both a scientific and metaphysical marvel. Rediscovered in the twentieth century after centuries of obscurity, the *tabulae pictae* affirm Fabrici’s enduring legacy at the intersection of anatomy, art, and philosophy.

Keywords: *Tabulae Pictae*, Fabrici d'Acquapendente, nervous system, anatomy, manuscript

Introduction

The title *The Dawn of Color in Anatomy* may appear somewhat romantic, yet it accurately reflects a relevant historical event. It evokes the moment in which anatomical representation transcended mere line and form to embrace the expressive and naturalistic power of color. The focus of this study is the *tabulae pictae*, the “painted anatomical tables,” and their author, Girolamo Fabrici d’Acquapendente (1533–1619).

Before addressing these works, it is necessary to outline briefly who Fabrici was and his place within the genealogy of the great anatomists of sixteenth-century Padua.



Figure 1. Portrait of Girolamo Fabrici d’Acquapendente (1533–1619).

In that illustrious lineage, Fabrici (Figure 1) occupies the fourth position, following Andreas Vesalius (1514–1564), Realdo Colombo (1516–1559) - the first to describe the pulmonary circulation - and Gabriele Falloppio (1523–1562), celebrated for his numerous neurological contributions and for the anatomical structure that bears his name, the Fallopian tubes.

Fabrici succeeded Falloppio as professor of anatomy at the University of Padua. He was born in the small papal town of Acquapendente, in the province of Viterbo, where a monument in the main square still commemorates him. Curiously, every extant portrait - including that on his monument - depicts him as an elderly man; no youthful likeness appears to have survived. Fabrici moved to Padua under the patronage of a noble Venetian family, the Lippomano, where he pursued his studies with distinction. His academic career was brilliant: in 1566 he became professor of anatomy and developed a flourishing surgical practice. His scientific output was abundant, as attested by the catalogue of his principal works, yet his essential contributions to the progress of medicine - and particularly to neurology - are elegantly summarized in an anonymous Latin distich, modelled on one originally dedicated to Virgil:

“Acquapendente gave me birth; in Padua I found rest. My fame I entrusted to the theater, to the anatomical tables, to studies of the fetus and of the valves of the veins.”¹

Indeed, Fabrici's studies and illustrations mark the first systematic research on embryology since the investigations of Aristotle (384–322 BCE). Published in 1600, his *De Formato Foetu* (*On the formation of the fetus*) represents a milestone in embryological knowledge.

¹ “*Aacula me genuit/ Tenet Urbs Patavina/ Teatri sum, Tabulis, Foetu/ Clarus et ostiolis*”.

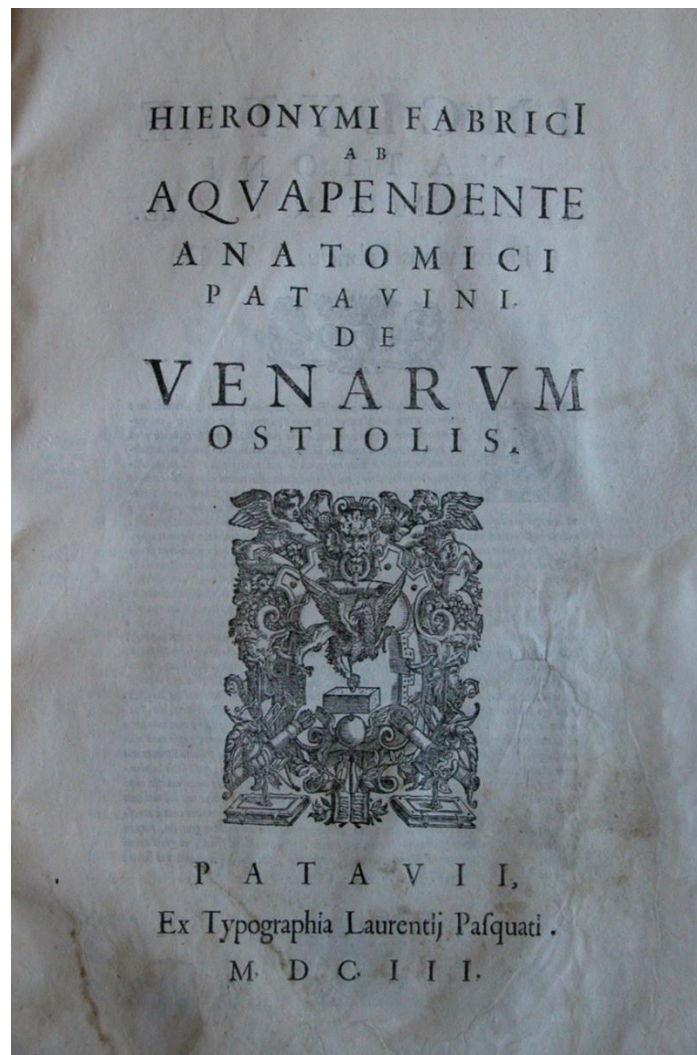


Figure 2. Frontispice of the *De venarum ostiolis*. Courtesy of the Pinali's Library-Ancient Section.

Yet his most influential work appeared three years later, in his treatise *De Venarum Ostiolis* (On the valves of the veins) (Figure 2). This treatise profoundly advanced anatomical knowledge. On the basis of Fabrici's meticulous description of venous valves, his student William Harvey (1578–1657) would later formulate the theory of blood circulation in his *Exercitatio anatomica de motu cordis et sanguinis in animalibus* (1628). Harvey (Figure 3) studied in Padua: in the Palazzo Bo, the historic seat of the University of Padua, Harvey's coat of arms remains visible (Figure 3), a testimony of his role in the administration of the university, a practice then common among students, who often participated directly in its governance.

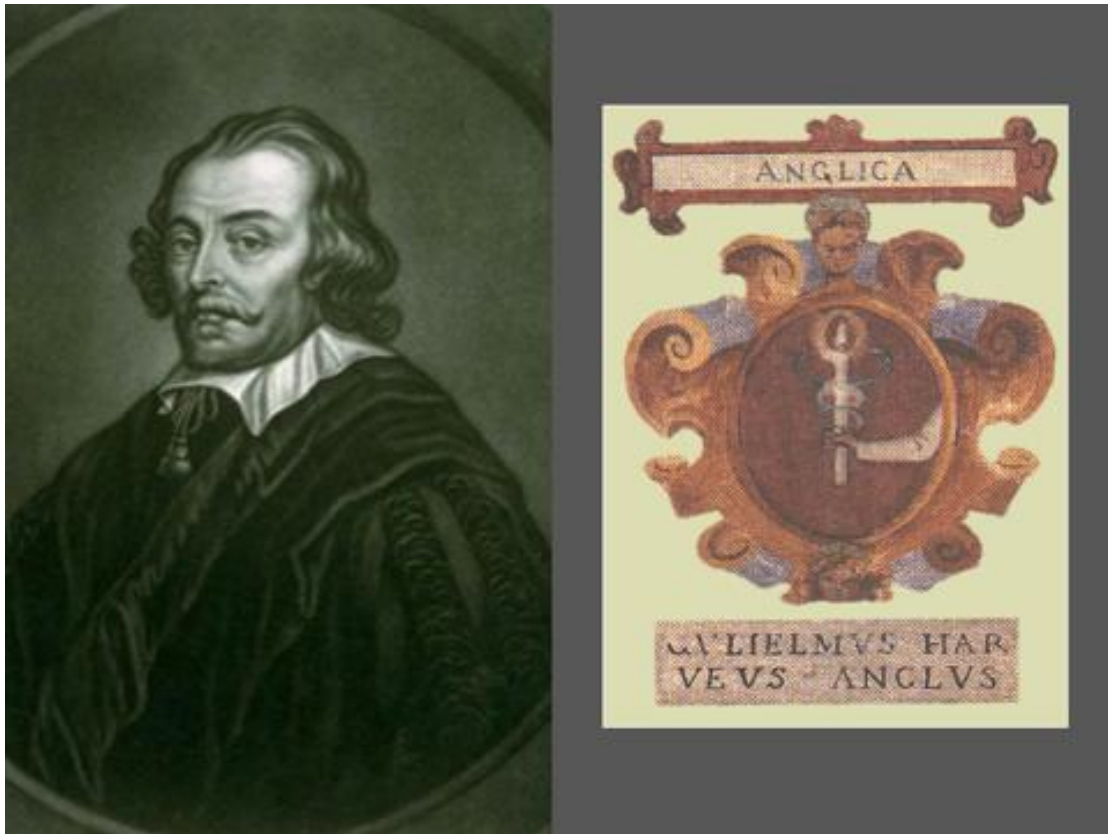


Figure 3. Portrait and coat of arms of William Harvey.

Harvey graduated in 1602, having attended Fabrici's courses in anatomy within the *Teatro Anatomico* (Figure 4). This theater, the first permanent anatomical theater in the world, inaugurated in 1495, was designed according to an elliptical plan that allowed for maximum visibility and active participation of the students. The architecture reflected a pedagogical principle central to the Paduan school: the student must *see* and *judge* what the teacher demonstrates, not accept it uncritically. The Padua theater subsequently served as a model for similar institutions throughout Europe, notably the one at Leiden, built by a Dutch pupil of Fabrici, Peter Paaw.



Figure 4. The Anatomical Theatre of Fabrici d'Acquapendente (1595). Palazzo Bo, Padova.
Centro Multimediale di Ateneo, Università degli Studi di Padova.

The *tabulae pictae* - i.e painted anatomical tables - constitute another of Fabrici's enduring achievements. Conceived as a colored atlas intended to illustrate the human and animal structure in the most natural way, the collection of 167 hand-painted pictures, preserved in the Marciana Library, is divided into eight volumes, accordingly to the anatomical subject:

- *De Anatomia Venarum Figure Varie*, Rari 110 [11 tables]
- *De Anatomia Ossium Figure Varie*, Rari 111 [22 tables]
- *De Anatomia Capitis Cerebri Nervorum Figure Varie*, Rari 112 [21 tables]
- *De Anatomia Animalium Figure Varie*, Rari 113 [55 tables]
- *De Partibus externis Figure*, Rari 114 [2 tables]
- *De Anathomia Thoracis et Parcium in Thorace Contentarum*, Rari 115 [5 tables]
- *De Anatomia Musculorum Totius Corporis. Figure varie*, Rari 116 [31 tables]
- *De Anatomia Abdominis et Parcium in Eo Contentarum*, Rari 117 [20 tables]

We find 44 more pictures bound within three volumes, which are also part of the d'Acquapendente's heritage: *De venarum ostiolis* [8 tables] and *De locutione et eius instrumentis* [1 table], Rari 118; *De formato fetu* (24 tables), Rari 119; *De visione, voce, auditu* (11 tables), Rari 120. As a whole, in the Marciana Library there are 211 pictures. About 40 more have been identified elsewhere. They are painted with oil and tempera, unfortunately on relatively fragile paperboard instead of canvas. Their realisation is clearly by different hands, as there are evident differences in style. Some artists have been proposed, among them the Varotaris, father and son, but this is still an open debate.

Girolamo Fabrici d'Acquapendente wanted this as a sort of “reference book” of anatomical coloured preparations, depicted with great naturalism, possibly also as a support to his teaching, to be placed alongside the anatomically dissected part or to be used temporarily when this was not available. At the end of the 16th century, in a period in which the monochrome xylographies of Vesalius remained an example of pioneering naturalism, Fabrici deserves merit for having first established with his collection the outstanding relevance of the use of colour in anatomical images. Since the printing techniques of the time could not reproduce color, painting remained the only medium capable of achieving the lifelike naturalism Fabrici sought. Fabrici evidently valued these works highly: in his will, he bequeathed them to the Most Serene Republic of Venice as a token of gratitude for the intellectual and material support he had received during his career. Curiously, for centuries the paintings were considered lost. As early as the eighteenth century, the Swiss anatomist Albrecht von Haller (1708–1777) lamented their disappearance. Only in the early twentieth century did the anatomist Giuseppe Sterzi rediscovered them, confirming their preservation in the same Marciana Library where they had been protected for centuries after their gift by d'Acquapendente.

One might ask what need there was for these painted tables after the magnificent engravings of Vesalius and his followers. The answer lies in the dimension of color. Though Vesalius's woodcuts already displayed extraordinary realism, only color could reproduce the immediate, almost corporeal vitality of the dissected body. Critics have noted that Fabrici's tables demonstrate not only anatomical accuracy but also a remarkable sensibility for the natural appearance of the tissues - their dryness, softness, roughness, even the marks of manipulation - imbuing them with a kind of emotional realism. Fabrici also adopted copper engraving for some of his printed works, a technique that allowed greater precision than the woodcut methods available to Vesalius.

Of the eight series, the third – *De Anatomia Capitis Cerebri Nervorum* - is of particular interest to us. Consisting of twenty-one plates, it focuses on the nervous system. Even a brief examination reveals their superiority to earlier depictions where the neuroanatomical structures could not take advantage of Fabrici's use of color, which introduces a striking realistic sense of three-dimensionality (Figures 5-6).

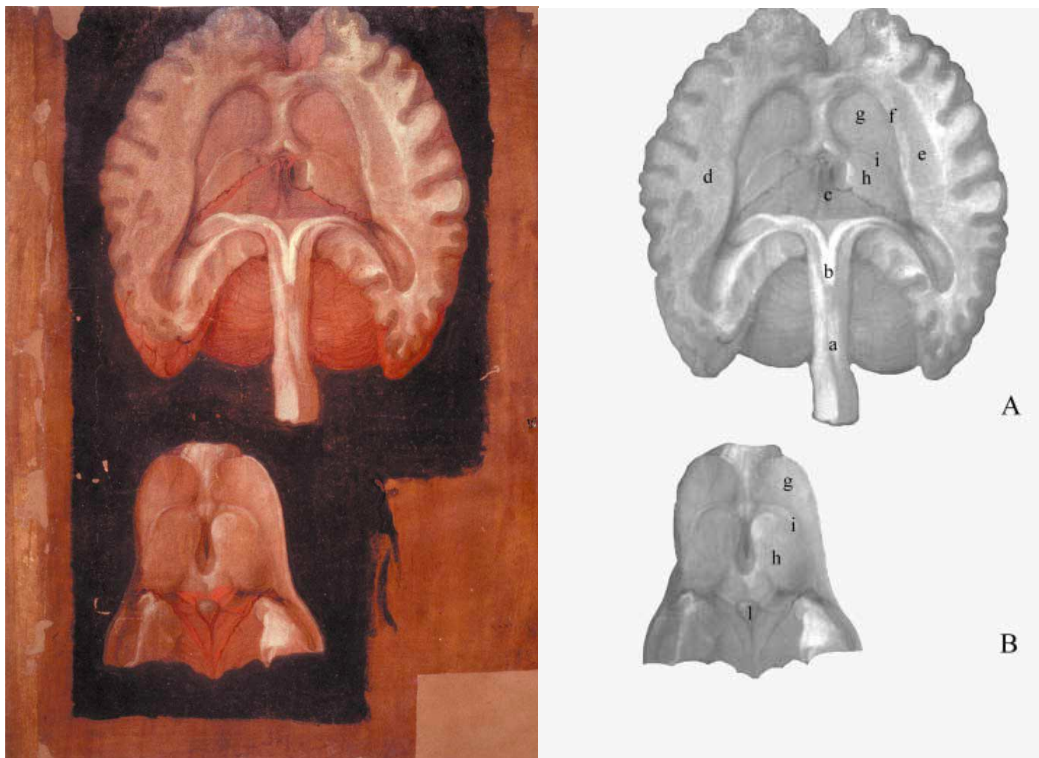


Figure 5. (A) On the superior part of the table: after the section of corpus callosum (a), also the fornix (b) has been cut on its anterior aspect and folded dorsally, whereas the tela choroidea (c) of the third ventricle has been left on site. On the right, the cerebral hemisphere has been sectioned rostrally and therefore the white matter (d) is clearly shown; on the left, a deeper section puts in evidence the nucleus lenticularis (e) and the capsula interna (f). Clearly visible are the nucleus caudatus (g), the thalamus (h) and the sulcus terminalis (i). This picture is utmost natural, particularly where it represents the chromatic features of the grey matter and of the white matter and its lucency.

(B) The inferior part of the table shows a close-up detail of the basal nuclei after the corpus callosum has been completely cut away. The epiphysis can be recognized (l). The nucleus caudatus (g), the thalamus (h) and the sulcus terminalis (i) are well represented, and their morphology is faithful.

Marciana, Rari. Table 112.8. Courtesy of the S. Marco's Library, Venice.

These works reveal Fabrici's artistic vision along with his pioneering scientific acumen. For instance, his representation of the cranial nerves emerging through the foramina of the skull (Figure 6) anticipates by nearly two centuries the clarity achieved in the great nineteenth-century anatomical atlases.

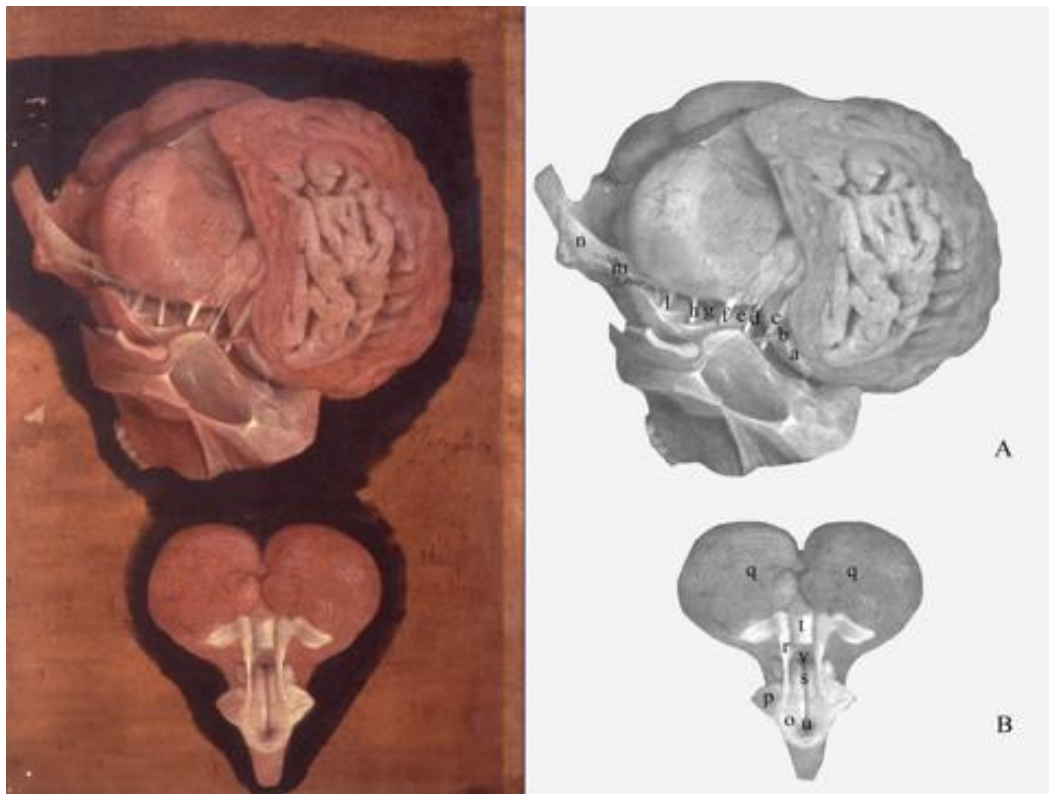


Figure 6. Above (A): A highly original left lateral view with a slight posterior obliquity of the relationship between the skull base and the base of the brain, with particular emphasis on the emergence of the cranial nerves and of the bony foramina into which they enter. The succession of cranial nerves is well represented and made recognizable by gently pulling the brain backwards and to the opposite side. Proceeding from the anterior part of the brain posteriorly, are highlighted: the first or olfactory nerve (a); the internal carotid artery (b); the second or optic nerve (c); the third or common oculomotor nerve (d); the fourth or trochlear nerve (e); the fifth or trigeminal nerve (f); the sixth or abducens nerve (g); the VII and VIII or facial and acoustic nerves (h); the IX, X, and XI or glossopharyngeal, vagus, and accessory nerves (l); the spinal component of the accessory (m); the first cervical root (n). The intracranial tract of the internal carotid artery (b) and its relationship with the optic nerve (c) are well represented, as is the vagus nerve (l). Below (B): View from the dorsal surface of the brainstem and cerebellum. The inferior (o) and middle (p) cerebellar peduncles have been sectioned; the cerebellum (q, q), maintained in connection with the superior cerebellar peduncles (r), has been elevated to simultaneously reveal the floor (s) and vault (t) of the fourth ventricle and the connections with the central canal of the spinal cord (u) and the mesencephalic aqueduct (v). Marciana, Rari. Table 112.10. Courtesy of the S. Marco's Library, Venice.

Unfortunately, no explanatory text accompanying the *tabulae pictae* has joined us. It remains unknown whether the depicted structures - so faithfully and often innovatively rendered - were ever described or interpreted in functional terms. Although Fabrici's testament and his heritage mention several unpublished manuscripts of neurological interest, none have been found. However, research has yielded an indirect testimony. A manuscript dated 1584, preserved at the *Accademia degli Intronati* in Siena, provides valuable insight into Fabrici's anatomical methods. It contains detailed notes by a careful student, describing the dissection of the brain - beginning from the surface and proceeding downward without detaching it from the skull - and accompanied by sketches with Latin nomenclature (Figure 7). The terminology often corresponds to modern usage.

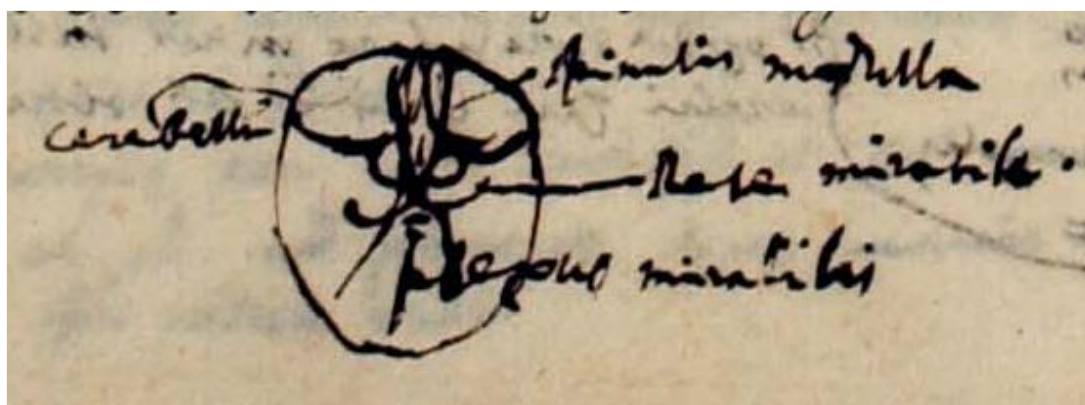


Figure 7. Fifth drawing of the “neurological section” of the manuscript *De anathomia quaedam excerpta sub excellentissimo Aquapendente anno 1584* (c. 69 verso). The drawing reads: *Spinalis medulla* (i.e. spinal cord); *Cerebellum*; *Rete mirabile*; *Plexus mirabilis*. Courtesy of the Biblioteca Comunale degli Intronati. Siena, Italy.

Although not written by Fabrici himself, one passage, clearly bears Fabrici’s own voice. Indeed, the following quotation, which refers to the Aristotelian cosmology, reveals the reverence with which he approached the study of the human body and specifically of the brain:

*“I am undertaking to describe a marvelous miracle of nature, the head.... the most divine of the parts [of the body] and connected with God because of its faculties. I am not astonished by the sky, by its splendor, light, vastness, movement, for it originates from pure celestial substance. I am instead overwhelmed by the head and the brain, which, although constituted of impure and corruptible matter, are nevertheless a site of the divine intellect...”*²

Fabrici d’Acquapendente thus emerges not merely as an anatomist, but also as a scientist who, at the dawn of modern anatomy, bridges the worlds of observation, art, and metaphysical inquiry; an investigator deeply fascinated and astonished by the brain, sharing with us the perpetual wonder which it inspires.

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This paper summarizes a lecture presented during the 55th National Congress of the Italian Society of Neurology held in Padova (24-28 October 2025). It refers, with modifications, to the following articles and to their bibliography:

Zanchin G, Panetto M, Hellman Dalla Francesca E. Echoes from the anatomical theater of Padua: Fabrici on the nervous system. *Vesalius* Vol.XXI, 2015;1:54-62.

Zanchin G, De Caro R. The nervous system in colour: the *tabulae pictae* of G.F. d’Acquapendente (1533 ca.-1619). *J Headache Pain* 2006;7:360-6.

² “Magnum naturae miraculum explicaturus sum ipsum caput [...] < , > caput est divinissimum membrum et per facultates in eo insitas est cum Deo connexum. Et ego certe non adeo miror coelum < , > eius splendorem < , > lumen < , > magnitudinem et cursum cum hoc ex purissima materia constructum sit < , > sed miror ipsum caput et cerebrum quod < , > cum sit ex corruptibili et impura materia < , > sit tamen sedes intellectus divini [...]”
De anathomia quaedam excerpta, c. 67 verso.



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From the Stars to the Gutter: The (Almost) Untold Story of a Neurological Genius

(History of Neurology)

Silvia Bencivelli^{1,2} and Simone Rossi²

¹ Science writer, Rome, Italy

² Siena Brain Investigation & Neuromodulation Lab (Si-BIN Lab), Department of Medicine, Surgery and Neuroscience, University of Siena, Siena, Italy

Corresponding Author:

Silvia Bencivelli

E-mail address: bencivelli@sciencewriters.it

Abstract

Charles-Édouard Brown-Séquard (1817–1894) is primarily remembered for the eponymous spinal cord hemisection syndrome. Yet his scientific contributions extended far beyond this single observation, encompassing groundbreaking work on sensory pathways in the spinal cord, the vital role of the adrenal glands, and the pioneering concept of “internal secretions” that foreshadowed modern endocrinology. His extraordinary career, however, was marked by profound personal restlessness—later attributed to a bipolar disorder—financial hardship, and perpetual professional instability across three continents. In 1889, at the age of seventy-two and at the pinnacle of his career as professor at the Collège de France, Brown-Séquard publicly announced that he had reversed the effects of ageing through self-injections of testicular extracts from dogs and guinea pigs. While this announcement inadvertently anticipated the field of hormone replacement therapy, it brought him immediate and devastating ridicule, effectively eclipsing decades of legitimate scientific achievement. His therapy, despite having had several distinguished aged followers (including Pasteur and Charcot), became the subject of satirical songs, cartoons, and dismissive commentary from the medical establishment. This article traces Brown-Séquard's remarkable trajectory from a childhood in Mauritius through his peripatetic career in France, England, and the United States, to his final hours, when he turned his own fatal cerebral haemorrhage into one last act of clinical self-observation. We argue that the derision provoked by his rejuvenation experiments has unjustly overshadowed his substantial and lasting contributions to the contemporary neurosciences.

Keywords:

Brown-Séquard; Brown-Séquard syndrome; history of neurology; endocrinology; organotherapy; spinal cord



June 1, 1889: the eminent Professor Charles-Édouard Brown-Séquard appeared before the Société de Biologie and confidently described his latest discovery:

I am seventy-two years old. My general strength, which has been considerable, has notably and gradually diminished during the last ten or twelve years. Before last May 15th I was so weak that I was always compelled to sit down after one hour's work in the laboratory. Even when I remained seated all the time, or almost all the time, in the laboratory, I used to come out of it quite exhausted after three or four hours' experimental labor, and sometimes after only two hours. For many years, on returning home in a carriage by six o'clock, after several hours passed in the laboratory, I was so extremely tired that I invariably had to go to bed after having hastily taken a very small amount of food. Very frequently the exhaustion was so great, that although extremely sleepy, I could not for hours go to sleep, and I only slept very little, waking up exceedingly tired (Dunbar 1889, 15–16).

He further explained that he had self-administered a treatment of his own design to counteract age-related physical decline. In line with his hypothesis on the “dynamogenic power” of substances released into the bloodstream by the testicles (Brown-Séquard 1889b), this new therapy consisted of subcutaneous injections of testicular extracts derived from dogs and guinea pigs.

In 1889, the concept of hormones was not yet understood; the word itself would only be coined in 1905 by Ernest Starling. Thus, on June 21st, 1889, when Brown-Séquard published the text of his speech in the *Comptes Rendus* of the Société (Brown-Séquard 1889a), he could only acknowledge that the scientific investigation into the composition of these extracts would be left to future researchers. The specific male hormone, testosterone, which we now know is primarily produced in the testicles and is responsible for many of the effects Brown-Séquard was observing, would not be isolated until 1935 by Ernst Laqueur's group (1880 – 1947) and then synthesised independently by Adolf Butenandt (1903 – 1995) and Leopold Ruzicka (1887 – 1976), who shared the Nobel Prize in Chemistry in 1939 (Nieschlag and Nieschlag 2019). What Brown-Séquard could do, however, was document and describe effects on himself:

The day after the first subcutaneous injection and still more after the two succeeding ones a radical change took place in me, and I had ample reason to say and to write that I had regained at least all the strength I possessed a good many years ago. Considerable laboratory work hardly tired me. To the great astonishment of my two principal assistants, Drs. D'Arsonval and Henocque, and other persons, I was able to make experiments for several hours while standing up, feeling no need whatever to sit down (Dunbar 1889, 16–17).

He then commented on the return of his muscular strength:

I have measured comparatively, before and after the first injection, the jet of urine in similar circumstances—that is, after a meal in which I had taken food

and drink of the same kind in similar quantity. The average length of the jet during the ten days that preceded the first injection was inferior by at least one quarter of what it came to be during the twenty following days. It is therefore quite evident that the power of the spinal cord over the bladder was considerably increased (Dunbar 1889, 17).

He made similar observations regarding the force of defecation. Next came the counterproof. On June 4th, he discontinued the injections:

For four weeks no marked change occurred, but gradually, although rapidly, from the 3rd of this month (July) I have witnessed almost a complete return of the state of weakness which existed before the first injection. This loss of strength is an excellent counterproof as regards the demonstration of the influence exerted on me by the subcutaneous injections of a spermatic fluid (Dunbar 1889, 19).

After this announcement, two things occurred. The first was the emergence of an unregulated market for rejuvenation elixirs that would persist for decades, anticipating the modern “lifestyle drug” industry and effectively framing ageing as a treatable disease for the first time (Eloy 1893). Among those “cured of old age” were poets, writers, politicians, athletes, and even scientists, including Louis Pasteur (1822 – 1895) (Celestin 2014).

The second consequence was the onset of isolation and the decline of Brown-Séquard’s reputation.

At the time, Brown-Séquard was a respected scientist (Berthelot 1900). Born in Mauritius in 1817, he had crossed the Atlantic Ocean over sixty times to deliver seminars and lectures attended by students from around the globe. He treated long queues of patients in his clinics in Paris, London, and New York, and had received multiple accolades for his scientific discoveries. By 1878, he was at the pinnacle of his career.

But his June 1st, 1889 announcement brought him ridicule: his therapy became the subject of popular songs, satirical plays, cartoons, and jokes. The Austrian medical journal *Wiener Medizinische Wochenschrift* wrote that Brown-Séquard’s actions were “the ultimate proof of the need to retire professors after the age of seventy.” The *Deutsche Medizinische Wochenschrift* dismissed his work as “a senile aberration.” Harvey William Cushing (1869 – 1939) referred to him as the “Ponce de León of endocrinology,” alluding to the Spanish explorer who, according to legend, stumbled upon Florida while seeking a fountain of eternal youth. Upon Brown-Séquard’s death, the French newspaper *L’Événement* wrote that he had been “the most ridiculed man of all time” (Celestin 2014).

This is likely why so little remains known about his scientific work and discoveries, which chiefly concerned the nascent fields of neuroscience and neurology. Beyond the eponymous syndrome involving the hemisection of the spinal cord, today’s specialists recall little of Brown-Séquard’s contributions. Yet his work was seminal in elucidating spinal cord pathways, requiring years of research under conditions that were often far from optimal.

Brown-Séquard’s scientific work began with his dissertation, *Recherches et Expériences sur la Physiologie de la Moelle Épinière* (Brown-Séquard 1846). In this work, he considered the spinal cord and brain separately and studied their reactivity. He then showed in detail how sensory

pathways travel in the white matter of the spinal cord: he first described that tactile and proprioceptive fibres enter the dorsal root and from the ipsilateral dorsal horn travel up through posterior columns to the Goll and Burdach nuclei, then cross and reach the contralateral thalamus after travelling through the medial lemniscus. On the other hand, nociceptive fibres cross immediately through the anterior commissure and travel up to the contralateral thalamus through the antero-lateral spinothalamic ascending systems. Decades later, these observations led to the definition of the so-called Brown-Séquard Syndrome (BSS), a rare neurological condition caused by damage to one side (hemisection) of the spinal cord. Different aetiologies may provoke BSS, including trauma, infections, tumours, multiple sclerosis, ischaemia, and, rarely, syringomyelia. Clinical manifestations of the hemicord syndrome are ipsilateral loss of motor function (weakness or paralysis) due to corticospinal tract damage and reduced or absent proprioception, vibration, and fine touch due to posterior column involvement. These ipsilateral signs are associated with reduction or loss of pain and temperature sensations contralateral to the lesion site, due to spinothalamic tract damage, which crosses—as Brown-Séquard had discovered—at spinal entry level.

It is worth recounting certain details of Charles-Édouard Brown-Séquard's personal history, an extraordinary yet ill-fated story marked by profound restlessness that later biographers have attributed to a bipolar disorder characterised by severe depressive episodes.

Born in Port Louis in 1817, three years after Mauritius came under British rule by the Treaty of Paris that followed Napoleon's defeat, Brown-Séquard acquired British nationality despite being of French descent. His mother, Charlotte Séquard, was French, while his father, Charles Edward Brown—an American sea captain of Irish origin born in Philadelphia—died at sea before his son's birth. Brown-Séquard took his father's given name (in a French-adapted form) and surname; later, he added his mother's French surname, Séquard, to underscore his cultural affiliation.

As a young man, Brown-Séquard showed an interest in poetry and a certain literary talent—he was reportedly called the “young Shakespeare of Port Louis.” At the age of twenty, he proposed to his mother that they travel to France so he could pursue his studies. His mother sold all their Mauritian holdings, including slaves, and set out with him.

However, events did not unfold as he had imagined. Once in Paris, Brown-Séquard submitted his writings to Charles Nodier (1780 – 1844) (Aminoff 2011), who advised him to abandon a literary career. Consequently, Brown-Séquard decided to study medicine, particularly the functions of the nervous system.

In 1842, the death of his mother triggered the first major depressive episode in Brown-Séquard's life. Nevertheless, he successfully obtained his medical degree in 1846. He subsequently embarked on scientific research in isolation, facing considerable hardships, particularly of a financial nature. Confined to his home laboratory, he dedicated himself entirely to his studies, often at the expense of basic needs such as food, sleep, and social interaction. During this period, he subjected his own body to various experiments, self-inflicting significant harm. Notably, he developed merycism, a rumination syndrome that would afflict him for the rest of his life. Merycism (from the Greek *merykazein*, to chew the cud) is a functional disorder characterised by the effortless, repeated regurgitation of recently ingested food, which is then re-chewed, re-swallowed, or expelled. Though historically associated with infancy and intellectual disability, it is now recognised as a condition that can affect adults. Additionally, during a cholera epidemic in Mauritius, he engaged in investigations into the disease's aetiology. It is likely that he became infected in this process and subsequently attempted to treat himself with an excessive dose of opium, leading to a near-fatal intoxication.

His lack of French nationality soon became a serious professional obstacle: for a long time, Brown-Séquard was unable to secure permanent positions in France, and therefore no steady income. On multiple occasions throughout his life, he travelled to the United States and to England, pursuing the dream of a university appointment. His restlessness, his fluctuating moods, and unfavourable circumstances—primarily political—impeded his career for decades. By the end of his life, he had amassed a very long record of journeys, relocations, and varying academic appointments, along with three widowhoods and three children: one died after only a few weeks, another suffered from severe mental health issues and alcoholism. The third, Charlotte, would become his only surviving descendant (Celestin 2014; Aminoff 2011).

Despite these challenges, Brown-Séquard managed to secure work and produced meaningful scientific contributions (Ott 1896). His research interests included the anatomy and physiology of the nervous system and its disorders, such as epilepsy. Thanks to his extensive knowledge of the spinal cord, he also hypothesised a form of “spinal epilepsy” (Olmsted 1946), a notion not subsequently supported by other investigations, that may instead correspond to what would now be recognized as ankle clonus, as highlighted by Jean-Martin Charcot (1825 – 1893) (Koehler 1994). He also studied rigor mortis. His third major area of inquiry involved identifying and clarifying the presence and role of what were then referred to as “internal secretions”—substances we now call hormones. Brown-Séquard conducted fundamental experiments on the adrenal glands, supporting the observations of Thomas Addison, who had described the chronic adrenal insufficiency syndrome that now bears his name (Williams 1949).

In 1878, Brown-Séquard finally obtained French citizenship and, just five days later, assumed the prestigious professorial chair at the Collège de France (Celestin 2014, 179). This position had previously been held by his mentor, François Magendie, and subsequently by his friend and rival, the eminent Claude Bernard, who had died earlier that same year at the age of 64. Although Brown-Séquard was only four years younger, he had just entered into his third marriage and was embarking on a more settled phase of his life. During this period, he received significant accolades: he was named Chevalier of the Légion d’Honneur, elected member of the French Academy of Sciences, and later served as President of the Société de Biologie. These honours solidified his reputation, and he gained increasing recognition as a leading figure in French science.

However, rather than consolidating his legacy and enjoying a well-earned retirement, Brown-Séquard embarked on a new line of experimentation—extracting enigmatic “testicular fluids” from guinea pigs.

Brown-Séquard’s life came to an end on April 2nd, 1894 (“Obituary” 1894), and he did not miss the opportunity to turn it into one last self-experiment. While suffering a cerebral haemorrhage, he recorded his symptoms:

“In the first place, my sight has become almost suddenly very poor – this is persistent: and another slight trouble, almost constant, but not absolutely so, exists; it is a complete loss of sight in a small part of the vision field constituting hemiopia, limited to a small part of the left of the two retinae. This is, of course, of cerebral origin, but it does not seem to be of organic origin, because it is not absolutely constant. Most likely, there is either inhibition or a vascular spasm, which destroys at time the power of sight in two small parts of the retinae. This began on Sunday. The next morning something worse occurred. My life, and all



that occurred for many months lately became suddenly a blank ...” (Celestin 2014, 224).

Within a few days, paralysis and aphasia appeared, followed by coma and, a day and a half later, death. On the last day of his conscious life, Brown-Séquard was able to write only a single word: “hyperesthesia.”

A more complete report in Italian language of Brown-Séquard’s personal and scientific life can be found in “*Tre colpi di genio e una pessima idea. Ascesa e caduta di uno scienziato squinternato*”, by Silvia Bencivelli, Bollati Boringhieri Editore, 2025.

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**WOSANZ's international online
Charcot bicentenary meeting
Saturday, 29 November 2025**
(Letter to the Editor)

Nadeem Toodayan,^{1,2} Zaheer Toodayan³

¹ Department of Neurology, Monash Medical Centre, Melbourne, VIC, Australia.

² School of Clinical Sciences at Monash Health, Faculty of Medicine Nursing and Health Sciences, Monash University, Clayton, VIC, Australia.

³ Department of Nuclear Medicine, Liverpool Hospital, Sydney, NSW, Australia.

Corresponding Author:

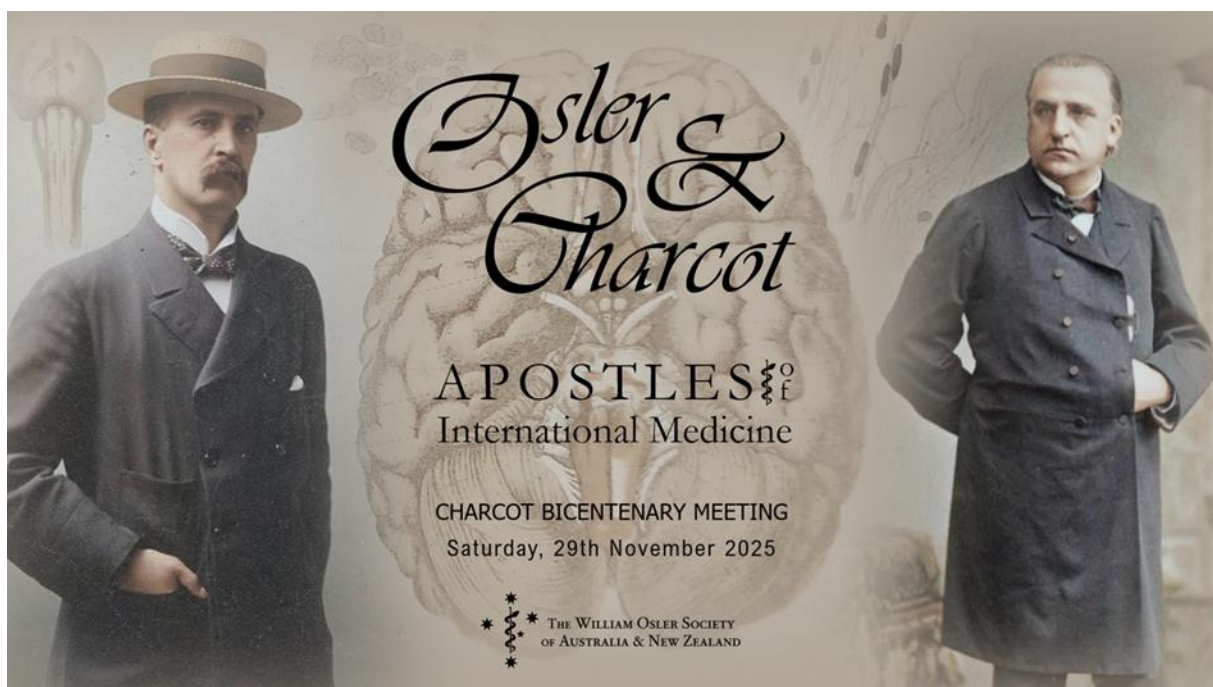
Nadeem Toodayan

E-mail address: nadeemtdyn@outlook.com

On Saturday, 29 November 2025, the William Osler Society of Australia and New Zealand (WOSANZ, est. 2019) hosted an international online Charcot bicentenary meeting to help globally commemorate the leading French neurologist and medical educator, Jean-Martin Charcot (1825-1893), on the two-hundredth anniversary of his birth. The meeting followed on from the ISHNs resoundingly successful Charcot bicentenary conference at the Paris Brain Institute in July of this year, and hosted two of the Paris speakers who re-presented their talks on Charcot's two-hundredth birthday to an international audience.

Charcot's official biographer – Chicago's respected Professor Emeritus Christopher G. Goetz – commenced the meeting with a scholarly overview of three of Charcot's most enduring legacies to twenty-first century neurology. First and foremost, there is Charcot's anatomo-clinical method, epitomised in his painstaking longitudinal studies of patients with debilitating chronic neurological illnesses at the Salpêtrière Hospital in Paris. By meticulously following the clinical course of his patients and correlating with pathological findings at autopsy, Charcot was able to delineate the clinical differences between such now well-recognised neurological pathologies as “multiple sclerosis” (intention tremor, ataxia) and “Parkinson's disease” (resting tremor, bradykinesia, stooped posture). Thus developed, antemortem diagnosis could be made “with absolute precision” in clinical neurology, Charcot taught, and this was particularly the case in conditions like “amyotrophic-lateral sclerosis” which Charcot also famously delineated and named. Secondly, Charcot importantly integrated new scientific discoveries into neurology, making use of various technological (e.g. timelapse photography in tic disorders) and artistic tools (e.g. wax models, ash gait trails) in his studies of diseases of the nervous system.

This same approach aligns with contemporary neurological practice, whereby modern scanners, various bedside aids, and chemical biomarkers enhance and extend the diagnostic capabilities of clinicians. Lastly, Charcot stressed the importance of heredity as a fundamental aetiological factor in the development of primary neurological disorders. A patient's inherited vulnerability – the “tache familiale” (familial mark) as Charcot called it – was a decisive factor in determining the clinical manifestations of primary nervous system pathology. Charcot was a meticulous and cautious clinician who frequently introduced new ideas with the double-negative French saying “si je ne me trompe pas” (“if I am not mistaken”). But in these three overarching legacies, Professor Goetz concluded, time has shown that Charcot was certainly not mistaken. Professor Goetz's well-received presentation provoked lively discussion amongst attendees with multiple interesting questions being treated to the Charcot scholar's perspective.



Charcot's studies at the Salpêtrière Hospital attracted international interest and were closely followed by William Osler (1849-1919) who examined Charcot's contributions to clinical neurology and internal medicine. At different times in his career, Osler critiqued Charcot's classification of chorea (1894) and views on hypnotism, but also promoted his neurolocalisation essays (1879), adopted his views on faith-healing, and championed his teaching style and clinics. Both Osler and Charcot attended the 1881 International Medical Congress in London where Charcot was an honoured guest, and on 17 June 1890, Osler visited Charcot's clinic at the Salpêtrière Hospital where he personally witnessed a demonstration of hypnotism – despite an extensive search conducted by the speaker (Nadeem), Osler's 1890 Paris notebook recording his observations of Charcot's clinic has not been found. Osler made liberal use of Charcot's teachings in his famous textbook of medicine (1892) and wrote a respectful obituary for Charcot in the September 1893 issue of the *Johns Hopkins Hospital Bulletin*. Through his friendship with Charcot's close pupil Pierre Marie (1853-1940), Osler had a French edition of his *Principles* published in Paris (in 1908), and in 1903, Osler's now famous Vernon plaque was styled after a similar 1883 medallion of Charcot seen at Marie's private residence. Jean-Martin Charcot was in Osler's eyes “a cosmopolitan teacher and leader” whose famous school of



neurology “gave great accuracy to the diagnosis of obscure affections of the brain and spinal cord” and “rendered clear and definite what was formerly the most obscure and complicated section of internal medicine.” “Who ever met with an English or American pupil of... Charcot, who did not love French medicine?”

Charcot’s crucial clinical and pathological research increased awareness of a number of invariably fatal neurodegenerative disorders (e.g. ALS) which remain largely untreatable even to this day. His own remarks on the futility of treatment for Huntington’s disease were quoted by Osler, who stressed that “its progression is fatal, and therapy is powerless to halt its progression, even for a moment.” In his own practice, Charcot avoided discussions about prognosis “in front of the poor patient” in cases of ALS, considering it “good and human” to let his patients live out their days without the burden of foreboding knowledge. “But [as for] the doctor, what is his role?”, Charcot pertinently asked his students. Professor Goetz emphasised Charcot’s answer as the single most important impetus for ongoing neurological research: “Let us always be searching, as it is the best way to find” Charcot said; “and, perhaps thanks to our efforts today, tomorrow’s verdict will not be that of today.”

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Did Charcot visit the West Riding Asylum at Wakefield in 1869?

(Letter to the Editor)

Andrew J Larner¹

¹ Department of Translational Neuroscience & Stroke, Institute of Neurology, University College London, London, United Kingdom

Corresponding Author:

Andrew J Larner - ORCID iD (0000-0003-0128-8010)

E-mail address: ajlarner241@aol.com

Neurology as a clinical discipline in Great Britain is generally understood to have emerged from 1860 onwards at the National Hospital for the Paralysed and Epileptic located in London's Queen Square (Shorvon and Compston 2019). However, a case may also be made for the West Riding Pauper Lunatic Asylum located in Wakefield, West Yorkshire, during the Superintendency of James Crichton-Browne (1840-1938) between 1866 and 1876, when neurology as an experimental science was established, principally through the work of David Ferrier (1843-1928) in the dedicated West Riding Asylum (WRA) laboratory (Adrian 1939, 433; Larner 2026).

What had prompted Crichton-Browne to construct a "Pathological Institute" with a laboratory and a photographic studio for the scientific study of brain disease in a remote county asylum? Although he was inclined to credit his Edinburgh teacher Thomas Laycock (1812-1876) as inspiration, it was pointedly remarked by another contemporary alienist, John Batty Tuke (1835-1913), that at WRA the "sciences are applied in a manner diametrically opposed to the theoretical method of Laycock" (Batty Tuke 1874, 109). Hence one must look for other templates for the research ethos exemplified by Crichton-Browne.

One possibility is the work of Charcot. This supposition is partly based on the circumstantial evidence that Crichton-Browne visited hospitals in Paris around 1862-3, immediately after he had first qualified, although it is not known if the Salpêtrière was included in his itinerary. Nevertheless, it has been suggested that Crichton-Browne's "choice of Paris influenced the rest of his career, for clinical observation in hospital or asylum wards and the performance of autopsies, on the French model, became Crichton-Browne's basic approach to psychological medicine" (Oppenheim 1991, 61-62).

Another date for a possible interaction between Charcot and Crichton-Browne, at a time when the latter's plans for WRA were still in development, is 1869, specifically in the context of the 37th Annual Meeting of the British Medical Association (BMA) held in Leeds, West Yorkshire, between 27th and 30th July 1869, an event which included a general invitation to the delegates



from Crichton-Browne to visit WRA. Charcot's name appeared in the list of "Members present at the Leeds Meeting" (BMJ 1869;2:279), but did he avail himself of the opportunity to travel to Wakefield?

Several accounts of the afternoon excursion on 28th July (by train from Leeds to Wakefield, then by omnibuses to the Asylum) appeared, initially in local newspapers (Anon. 1869a, b, c, d) and later in the medical press (Anon. 1869e, f). All of these reports noted that about 100 gentlemen were shown round the Asylum before enjoying a cold collation lunch, listening to music played by the Asylum string band, followed by speeches, then listening to the Asylum Church Choir before returning to Leeds. No report contains a complete list of the names of the attendees; the greatest detail is to be found in *The Wakefield Express* of 31st July: "Amongst the other guests were Sir William Jenner, Physician to Her Majesty [Queen Victoria] and the Royal Family, Professor Acland, of Oxford, Drs. [Harrington] Tuke, Maudsley, B.W. Richardson, Wood, of London; Dr. Sankey, of Cheltenham, Dr. Wilkinson, of Manchester, &c." (Anon. 1869c).

In addition, there is Crichton-Browne's handwritten entry in the WRA Medical Director's journal for the Quarterly Meeting held on July 29th 1869, which reads:

Having been requested by the President and Council of the British Medical Association which is now meeting at Leeds to permit a deputation of that body to inspect the Asylum I obtained the sanction of the Visitors [...] Spencer Stanhope, the Chairman of the last meeting, received them yesterday. A party of 100 gentlemen headed by Sir William Jenner, the Physician to the Queen, and including many of the most distinguished members of the medical profession in this country visited the Asylum yes[terday??] and expressed their admiration of its arrangements (Medical Director's Journal 1869, unpaginated [my transcription; ?? = uncertain]).

Hence, in not one of these various reports did Charcot's name appear. Absence of evidence is of course not equivalent to evidence of absence, but it seems improbable that had Charcot attended the WRA visit his name would have been omitted from all these sources. Moreover, had it occurred, Crichton-Browne was not the type to miss a publicity coup of this kind.

Nevertheless, it remains possible that Charcot and Crichton-Browne may have conferred at some time during the Leeds meeting: Charcot had good English, and Crichton-Browne probably reasonable French; he later published in a French medical journal (Crichton Browne 1876). It certainly does not rule out the possibility that the example of Charcot's methods as pursued at the Salpêtrière was instrumental in stimulating the developments at WRA which, principally through Ferrier, contributed to the origins of the experimental aspect of the profession of neurology in Great Britain, hence "the period when neurology became a science" (Adrian 1939, 433).

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