

Neurosciences

# Charles-Édouard Brown-Séquard. An eventful life and a significant contribution to the study of the nervous system

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## Abstract

This is an account of the life of a 19th-century physiologist who was born in 1817 in Port-Louis (Mauritius Island, formerly 'Île de France') and died in Paris in 1894. His mother tongue, education and medical training were French, but as the 'Île de France' had become British a few years before his birth, he was a British citizen and therefore ineligible for a permanent position in a French institution. This explains, partly at least, his eventful life, during which he restlessly wandered during several decades between France, the United States, Great Britain and Mauritius, without ever finding a position that would satisfy him. This difficult period lasted until 1879 when, having finally acquired French nationality, he succeeded Claude Bernard in the chair of experimental medicine at the 'Collège de France'. Some of his contributions to the physiology of the nervous system are analysed: sensory pathways in the spinal cord, vasoconstrictor innervation, nervous inhibition and experimental epilepsy. **To cite this article:** *Y. Laporte, C. R. Biologies 329 (2006).*

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## Résumé

**Charles-Édouard Brown-Séquard. Une vie mouvementée et une contribution importante à l'étude du système nerveux.** La vie de ce physiologiste du XIX<sup>e</sup> siècle, né en 1817 à Port-Louis (île Maurice, précédemment île de France) et mort en 1894 à Paris, est décrite. Sa langue maternelle, son éducation et sa formation médicale étaient françaises mais, l'île de France étant devenue anglaise quelques années avant sa naissance, sa nationalité était britannique et il ne pouvait par conséquent être nommé à un poste permanent dans une institution française. Ceci explique, en partie du moins, sa vie mouvementée, durant laquelle il erra sans cesse pendant plusieurs décennies entre la France, les États-Unis, la Grande-Bretagne et l'île Maurice, sans jamais trouver de situation qui le satisfasse. Cette période difficile dura jusqu'en 1879, lorsque, ayant finalement acquis la nationalité française, il succéda à Claude Bernard dans la chaire de médecine expérimentale au Collège de France. Quelques-unes de ses contributions à la physiologie du système nerveux – voies sensibles dans la moelle épinière, innervation vasoconstrictrice, inhibition nerveuse, épilepsie expérimentale – sont analysées. **Pour citer cet article :** *Y. Laporte, C. R. Biologies 329 (2006).*

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## 1. Biography of Charles-Édouard Brown-Séquard

The 1<sup>st</sup> International Congress on the History of the Neurosciences was held in London in 1994. A special session was devoted to Charles Brown-Séquard to commemorate the 100th anniversary of his death, in Paris. Some of the papers presented at that session were later published in a special issue of the *Journal of the History of the Neurosciences* [1]. In France, Brown-Séquard's centennial went almost unnoticed but for the lecture I gave in 1996 at the Collège de France, where he held the chair of experimental medicine from 1879 until his death in 1894. The present issue of *Comptes rendus Biologies* gives me the opportunity to recall the eventful life of this engaging 19th-century physiologist and to analyse some of his contributions to the physiology and pathology of the nervous system.

Brown-Séquard was born in 1817 in Port-Louis on the island of Mauritius, previously the 'Île de France', which had become British only a few years earlier. His father, Charles Edward Brown, was an Irish-American naval officer who died before his son's birth. His mother, Charlotte Séquard, was French, and educated her son exclusively in French. As the young Brown was very bright, his mother, in spite of very modest means, embarked for France in 1838 with her 20-year-old son to complete his education.

The first thing Charles Brown did in Paris was to show Charles Nodier, a writer with some notoriety, some essays and poems he had written. Nodier destroyed all the illusions Charles might have had about his literary talents, and advised him to read law or medicine. A few months later, Charles Brown, having successfully obtained the 'baccalauréat ès lettres', began his medical studies. He was barely in his second year when Dr Martin-Magron, a physiologist who ran a private laboratory in Paris, invited him to work with him on the nervous system.

The sudden death of Charles' mother – she had eked out a living for the two of them by running a boarding house – put him into such a state of depression that he dropped his studies and impulsively returned to Mauritius. This was the first instance of the many abrupt decisions Brown-Séquard took during his life. But he soon missed his life in France, and he was back in Paris by the end of 1843, on borrowed money, and lived there for several years in conditions of extreme poverty. He served as 'externe des hôpitaux' under Trousseau and Rayer, who later never failed to help him.

In 1846 he defended his M.D. thesis, entitled "*Research and experiments on the physiology of the spinal cord*" [2]. This work was the last publication in which

he used his father's name only. To honour his mother's memory, Charles Brown added her name to his patronym and thereafter became known as Brown-Séquard. In 1848 he joined several well-known physiologists and anatomists to form the 'Société de biologie'.

In 19th-century France, foreigners could not get a permanent position in any French public institution, which explains – partly at least – the very unstable life of this British citizen of French education and medical training. For nearly thirty years he kept trying to find a stable position outside France which would give him both satisfactory personal status and proper facilities for carrying out experimental physiology. That long difficult period began in 1852 when he decided to move to America, although he was at that time barely able to speak English. This decision may have been influenced by the political situation in France because, as he was openly hostile to the coup d'état of Louis-Napoleon Bonaparte, he feared the consequences of his republican convictions.

The early days in America were difficult, and to survive he had to become an obstetrician. Soon however, helped by warm letters of introduction from prominent French physicians (especially Broca), he returned to his interest in physiology and gave private courses in Philadelphia, New York and Boston which were well received by senior physicians as well as students.

In 1853 he married Ellen Fletcher and returned to Paris, possibly to claim priority for the discovery of the vasoconstrictor nerve fibres, which he had published in an American journal [3]. In 1854 he was back in Port-Louis, where he distinguished himself in fighting a cholera epidemic using very large amounts of laudanum. That same year he accepted a chair of physiology and medical jurisprudence at the Medical College of Virginia in Richmond, but he soon became disappointed, resigned and returned to Paris in 1855. The next year he was giving a series of lectures in Boston, and in 1858 a course on neurology in London at the Royal College of Surgeons.

In 1859 the City of London built a new hospital devoted to the care of neurological illness, the 'National Hospital for the Relief and Care of the Paralyzed and Epileptic', located in Queen's Square. Brown-Séquard successfully applied for one of the two positions of physicians attached to that hospital. In London, where Brown-Séquard was already considered an expert on epilepsy, he had a highly successful private practice as a neurologist. However, after only four years, he resigned his hospital position, abandoned a rich practice and fled to Paris, because he had suddenly realized that his very

success in medical practice was preventing him from carrying out experimental work.

Then in 1864 Harvard Medical School offered him a chair of Physiology and Pathology of the nervous system but, after his wife's death, he returned to Paris in 1867 and gave a course in comparative and experimental pathology at the 'Faculté de médecine' in 1869. More despondent than ever, he resigned this appointment and, once more, moved to New York, where in 1872 he married Maria Carlisle, his 13-year junior. During the 1870 Franco-Prussian War, his close and powerful friend Louis Agassiz unsuccessfully tried to organize another chair for him at Harvard. In 1874 he gave a course on 'nervous force' at the Boston Lowell Institute as a tribute to Agassiz, who had died a year before. Unfortunately, after two years of marriage, his young wife died after giving birth to a girl, Charlotte. In the following months he gave a series of lectures in New York, Boston, Dublin and London. In 1876 Emma Dakin, much appreciated for her stabilizing influence, became his third wife.

After a surprising and unsuccessful attempt to resume medical practice in London, Brown-Séguard was once more in the United States when news reached him of the death of Claude Bernard. He returned to Paris immediately to prepare his candidacy for the vacant chair, as he knew that a request for French citizenship would be accepted, and he published an account of his scientific writings, a *Notice de titres et travaux*, which shows that among 300 original papers, 182 dealt with the physiology and pathology of the nervous system, 22 with experimental epilepsy and 12 with the physiology and pathology of vision.

In May 1878, having at last acquired French nationality, he succeeded Claude Bernard in the chair of experimental medicine at the Collège de France. As Aminoff writes [4], 'Brown-Séguard's travelling days were over, his academic dignity restored, his home finally established in France'.

Brown-Séguard wrote several books; he founded the *Journal de la physiologie de l'homme et des animaux* in 1858 and, with Charcot and Vulpian, the *Archives de physiologie normale et pathologique* in 1868. In 1873 he published the *Archives of Scientific and Practical Medicine and Surgery*. He was elected to the Royal Society in 1881 and to the 'Académie des sciences' in 1886. He died in 1894 and was buried in the Montparnasse cemetery, where his grave is surmounted by a small obelisk.

## 2. Sensory pathways in the spinal cord and the Brown-Séguard syndrome

At the time Brown-Séguard began work in Martin-Magron's laboratory on the spinal cord in various species, it was believed that all sensory fibres reached the brain through the posterior columns. By studying the effects on sensory perception of a variety of spinal-cord sections, Brown-Séguard demonstrated that this view was erroneous. He had observed that responses to sensory stimuli persisted after selective section of the posterior columns, and that after a transverse section of the cord sparing only the posterior columns, the animal did not react to painful stimuli. Furthermore, transverse hemisection of the cord was found to elicit, in addition to motor paralysis on the side of the lesion, a sensory loss on the opposite side, which he interpreted as showing the decussation of some nerve fibres activated by sensory stimuli to the opposite side of the cord. This interpretation was consistent with the effects of mid-line sagittal sections of the cord over a few segments, which elicited a loss of painful sensations in both sides at that level. Brown-Séguard's ideas were not well received, and it was at his own request that a committee was established by the 'Société de biologie' to examine his claims. The Committee, whose chairman was Broca and which included Claude Bernard and Vulpian among its members, confirmed Brown-Séguard's observations. The clinical studies Brown-Séguard subsequently carried out supported his experimental observations.

Further clinical experience provided a more complete description of the motor and sensory alterations observed below damage limited to one side of the cord: on the opposite side, there is a contralateral loss of sensitivities to pain and temperature, whereas on the side of the lesion, the limb is paralyzed and both the appreciation of posture and passive movements of the limbs and discriminative touch are lost. Today we know that the crossed spinal tract severed by the hemisection is the spino-thalamic tract, whose cells of origin are activated by sensory fibres of small diameter, either myelinated (A $\delta$ ) or unmyelinated (C), whereas the dorsal column is essentially composed of the ascending branches of large-diameter afferent fibres that supply muscle, joint, and certain skin sensors. The ipsilateral paralysis is accompanied by a so-called pyramidal deficit resulting from the section of descending motor pathways.

The association of these sensory and motor symptoms is eponymously known as the Brown-Séguard syndrome.

In the light of certain facts, it is very doubtful that the sensory part of this syndrome can be accounted for simply by the section of some sensory fibres. First, the ipsilateral zone of hyperesthesia which is generally observed below the lesion can no longer be ignored or dismissed as a side effect of the experimental procedure. Second, Brown-Séquard himself had reported in 1880 [5] that when the cord undergoes a second hemisection below a first one, the contralateral anaesthesia is replaced by hyperesthesia, whereas the originally hyperaesthetic ipsilateral side becomes anaesthetic. Brown-Séquard recalled these observations in a very fair appraisal he gave [6] of the disturbing observation made in 1892 by the British neurologist Mott [7] that a monkey whose cord had been hemisectioned was able to locate a painful stimulus in the contralateral side. Brown-Séquard suggested that anaesthesia was due to a strong inhibitory effect exerted on some spinal structures rather than to the simple division of some spinal fibres, and that the hyperaesthesia was due to an excitatory action exerted on some other spinal structures. Brown-Séquard's explanation in terms of supraspinal control of spinal mechanisms was much later supported by Denny-Brown's work [8]. In a study where the extent of the sections was carefully controlled, he reported that a cord hemisection in monkeys did elicit contralateral analgesia with ipsilateral hyperesthesia only when it was *incomplete*, and had spared some spinal cord tissue near the midline. When an animal with such a lesion underwent a second more rostral hemisection that was *complete*, the initial contralateral anaesthesia disappeared. Denny-Brown interpreted these observations as showing that the contralateral sensory loss observed after incomplete hemisection of the cord was due to the release of an inhibitory action exerted on sensory spinal neurons by descending fibres situated in the ipsilateral anterior columns. To say the least, the time for a comprehensive understanding of the Brown-Séquard Syndrome has yet to come!

### 3. Vasoconstrictor innervation

In 1852 Brown-Séquard published in the *Medical Examiner of Philadelphia* [3], a description of the effects of electrical stimulation of the distal part of severed cervical sympathetic chains in various animals, especially in the rabbit: the blood vessels of the face and ear contracted and their temperature decreased. After stimulation ceased, the phenomena Claude Bernard had observed after sectioning the chains reappeared: vasodilation and hyperthermia. Brown-Séquard drew the conclusion that the sympathetic chain contains nerve fi-

bres that supply the smooth muscle fibres of the arterial walls, which contract when they are activated by these nerve fibres, thus reducing the diameter of the arteries and consequently the blood flow. On the other hand, as these nerve fibres are apparently tonically active in physiological conditions, their section results in the relaxation of the arterial wall and in an increase of the diameter of the arteries under the action of blood pressure; thus the blood flow increases and the temperature of the irrigated tissues, which in resting conditions is lower than that of the blood by several degrees, also increases.

Claude Bernard strongly challenged Brown-Séquard's conclusions. Influenced as he was by the very old idea that the sympathetic nerves that accompany the arteries preside over the organic reactions taking place in live tissues, he had assumed that sympathetic fibres were 'calorigenic'. A controversy took place between the two physiologists [9]. Claude Bernard maintained that the hyperthermia was due to a greater production of heat and not to the increase in blood flow, on the ground that there was no strict parallel between hyperthermia and vasodilation. Surprisingly, he argued that during the removal of the sympathetic cervical ganglion, vasoconstriction was observed, not vasodilation. Brown-Séquard replied that nerve fibres do discharge for a certain time during the removal of the ganglion (or even during the section of the chain) and consequently that during this time the true action of the fibres is revealed; that is why it is necessary to wait some time after the section to observe its consequences. Furthermore if any sympathetic nerve fibres were calorigenic, their section should reduce, not increase the temperature of the tissue.

Brown-Séquard was probably the first to describe a vasomotor reflex. He had noticed that after immersing one hand in very cold water, the temperature of the other hand fell substantially, whereas that of the mouth was barely lowered.

Some years later, a new controversy opposed the two men. In 1878, Claude Bernard had reported that opposite circulatory conditions could be elicited in the sub-mandibular-gland arteries of the dog by electrical stimulation of two nerves; that of the cervical sympathetic chain produced a strong vasoconstriction, whereas that of the tympanico-lingual nerve (chorda tympani) elicited a vasodilation so strong that the venous blood became as red as arterial blood. Claude Bernard interpreted these opposite actions as showing that the arteries of the gland were contracting or relaxing under the influence of nerve fibres in the sympathetic chain and in the chorda tympani respectively. This time, it was Brown-Séquard who challenged the exist-



tence of vasodilator fibres. For him, vasodilation had to be an indirect consequence of glandular cell activity, not the result of the relaxation of arterial muscle fibres by a direct inhibitory action of certain nerve fibres. The existence of vasodilator fibres was later confirmed, but modern physiology did also confirm Brown-Séquard's prediction in the sense that indirect vasodilation is now proven: after stimulation of the chorda, an enzyme is released by the activated secretory cells, which by acting on certain proteins produces bradykinin, a strong vasodilatory agent.

#### 4. Inhibitory and dynamogenic actions

The existence of inhibitory action in the central nervous system had been known since Setschenov showed in 1863 that stimulation of certain regions of the frog midbrain inhibits limb reflexes. However, Brown-Séquard is often credited with having put forward the notion that the activation of a region of the brain may exert at a distance an excitatory (dynamogenic) action on some nervous structures and an inhibitory one on others.

In a note published in French in the *Revue neurologique* in 1893, Sherrington – possibly after a visit to Paris at a time when Brown-Séquard was still alive – described an almost paradigmatical instance of reciprocal innervation that he had observed in Rhesus monkeys during the ocular movements elicited by stimulation of a frontal lobe. The extra-ocular muscles that are antagonists to the muscles whose contraction is responsible for a particular movement of ocular globes are inhibited [10]. In this note, Sherrington writes: “*M. Brown-Séquard a longuement insisté sur cette double action et dans ses écrits il parle d'activité inhibitrice de l'écorce*”.<sup>1</sup> The words: “he talks in his writings” appear to indicate some reticence, an impression undoubtedly confirmed by the fact that thereafter Sherrington would never mention Brown-Séquard's ideas, even in his Nobel-Prize lecture devoted to inhibition as a coordinating factor. Sherrington's reluctance is perhaps understandable when one considers the rather obscure evidence on which Brown-Séquard's perception of the inter-relations of inhibition and excitation rests. Even the report of the ‘Académie des sciences’ Committee that recommended him for the 1884 Lallemand prize is disappointing, being a list of many disparate instances of inhibition.

<sup>1</sup> “Mr Brown-Séquard was very insistent on this dual action and he talks in his writings of the inhibitory activity of the cortex.”

#### 5. Experimental epilepsy

When Brown-Séquard was studying sensory pathways in the spinal cord by practising various kinds of sections, he frequently observed that, a few weeks later, the operated animals presented tonico-convulsive seizures in the non-paralyzed parts of their body, including the face [11]. Brown-Séquard gave a great deal of attention to these attacks because he thought that as an experimental model of epilepsy they could serve for understanding the physiopathology of naturally occurring epilepsy and be useful for testing anti-epileptic drugs.

These attacks, mostly observed in guinea pigs, could appear spontaneously, but were usually triggered by stimulation of the skin, especially that of the face. During the attacks, which lasted 2–3 minutes, urinary and faecal incontinence took place, but vocalization was also observed, suggesting that unlike with grand mal seizures the animals had no loss of consciousness. Brown-Séquard was aware of the trophic changes that took place in the epileptogenous zone: loss of hair, changes in cutaneous sensibility and also accumulation of lice. He noted that the frequency of spontaneous seizures was curiously related to the amount of space available to the animals in their cages, increasing when it was limited.

Today the view sometimes put forward in the past that reflex epilepsy was nothing but an exaggerated form of scratch reflex is no longer supported, but the intriguing fact remains that delousing infested animals puts a stop to their seizures, even if all it shows is the importance of permanent local irritation by the parasites.

Brown-Séquard was convinced that experimentally induced epilepsy was transmitted to the offspring of the affected animals... and Charles Darwin himself manifested his interest in this instance of transmission of an acquired character!

In the domain of the neurosciences as in others, notably in what was to emerge much later as endocrinology (his demonstration that suprarenal glands are essential for life, and the astonishing episode of the rejuvenating action of animal-testicle extracts), Brown-Séquard will not be primarily remembered as an experimenter, but rather as a man endowed with an exceptional ability to conceive – well ahead of his time – basic physiological mechanisms. He was, as Aminoff so aptly called him in his excellent biography, a “visionary of science” [4].

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