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BOOK REVIEW

An improbable genius?

> . . . il croyait avoir découvert la panacée universelle, la liqueur de vie destinée à combattre la débilité humaine, seule cause réelle de tous les maux, une véritable et scientifique fontaine de Jouvence . . . [. . . he believed to have discovered the universal panacea, the vital liquor destined to combat human mental deficiency, the only real cause of all evil, a true and scientific fountain of youth . . . Zola, 1893, p. 54]

BROWN-SÉQUARD: AN IMPROBABLE GENIUS WHO TRANSFORMED MEDICINE
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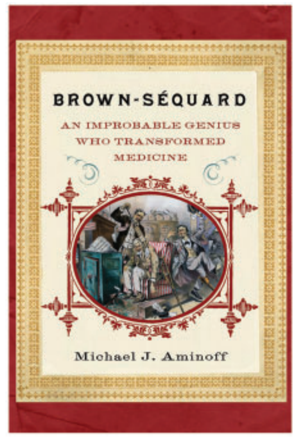

This citation may have been applicable to the subject of the present book, Charles-Edouard Brown-Séquard (1817–94). But if a physician's fame (or notoriety) were to be determined by how often he or she is depicted in novels, another neuroscientist (to use a modern term)—his contemporary, Jean-Martin Charcot (1825-1893)—would certainly be champion. Charcot not only figured in many contemporary novels (numerous French and, furthermore, Tolstoj, Stoker, Bjørnson, Kinck, Frich, Munthe, Péres Galdós, amongst others), but may even be found in recent novels (Enquist, Thuillier, Hustvedt, Eco). Obviously, scientific and medical events are often reflected in novels. Of interest during the period of consideration is the reflection of positivistic philosophy and its influence on medicine, completing the introduction of the scientific method by around the middle of the 19th century. It inspired the French author Emile Zola (1840–1902), considered the founding father of the naturalistic literary movement that was founded in Paris (1877) and influenced many novelists of the period. In the last volume of his Rougon-Macquart series, 20 novels describing various aspects of French society during the Second Empire (1852–70), Zola stages a physician that I have always assumed to be Brown-Séquard. Throughout the series two families are followed through five generations. Zola describes how the actions of the characters are determined by the environment and the hereditary taint that runs through the family and may present in several ways, including alcoholism, a tendency to kill and other nasty traits. Several socio-medical themes of the period are used, including the degeneration ideas of Bénédict Augustin Morel (1809–73) and Valentin Magnan (1835–1916). We know, however, that Zola was an admirer of another physiologist of the period, who was in many aspects Brown-Séquard's rival and predecessor at the Chair of Medicine at the Collège de France, Claude Bernard (1813–78). Zola identified himself with Bernard in particular in the concluding 20th volume *Le Docteur Pascal* (1893), which he called a scientific novel. Indeed, the main themes of the novel are experimental medicine and the study of heredity. When Zola discussed the book with his colleague, novelist Edmond de Goncourt (1822–1896), the latter scribbled in his *Journal*: 'In fact, the book . . . is the last where I will stage a scientist. This scientist, I'll attempt to let him be like Claude Bernard . . .'. As the book was published in 1893, but placed in the period of the Second Empire, this might explain why Zola had Bernard in mind, but was inspired by Brown-Séquard.

In *Le Docteur Pascal*, country physician Pascal Rougon has made a genealogical tree of his own family with the purpose of studying heredity. He notes all kinds of interesting details about his family members, proving that degenerative taints are inherited. Zola stages Rougon not just as a physician but also as a scientist. He extracts sheep brains and injects the extracts into patients. Although considering himself to be successful at the beginning, he finally turns to the injection of water, recognizing the placebo effect. One day, experimenting with organ extracts, he is criticized by his family members: '. . . il est encore à sa cuisine du diable!' [. . . he is still in his devilish kitchen . . .], referring to his home laboratory. The passage calls to mind Brown-Séquard's last scientific

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endeavour which was to extract material from testicles and inject it into himself and his patients in the belief that it would rejuvenate elderly people. In cooperation with his assistant Jacques-Arsène d'Arsonval (1851–1940), he produced the drug and offered it to colleagues, without charge, in order to let them try it on their patients. His first presentation was before the Société de Biologie de Paris in 1889, 2 years before George Murray (1865–1939) presented his ideas on how to treat a case of myxoedema with an extract from a sheep's thyroid at a meeting in England. Probably as a consequence of Brown-Séquard's claims, he was ridiculed, among others by a senior colleague, who said it would be just as sensible to treat a case of locomotor ataxia with an emulsion of spinal cord. Although Brown-Séquard made several serious studies, public reception was unfavourable and the project harmed his reputation. Nevertheless, his importance to the evolution of endocrinology was mentioned by surgeon Theodor Kocher (1841–1917) in his Nobel lecture (1909) and his ideas about internal secretion are still recognized.

Whereas the optimistic expectations of the scientific method in medicine during the first decades of the second half of the 19th century were indeed reflected by similar sentiments in novels, deception features more by the end of the century. The naturalistic movement was succeeded by several others in another of which Brown-Séquard is again depicted. The French novelist Joris-Karl Huysmans (1848–1907), originally a faithful follower of Zola, depicted him in *Là-bas* (1891, English translation: *Down there*). The novel may be considered a transition from his naturalistic period to the episode in which he became a mystic Christian, and is a charge against medicine in general: 'Puis maintenant, chaque médecin se spécialise; les oculistes ne voient que les yeux et pour les guérir, ils empoisonnent tranquillement le corps'. [...nowadays, every physician specialises himself; the eye specialists only see eyes, and in order to cure them, they quietly poison the body.] He describes a young woman whose paralytic symptoms could not be cured at the Salpêtrière—where Charcot successfully studied neurological disorders and struggled with hysteria—but was cured after treatment by an exorcist. Elsewhere in the book, the author describes the medical use of organ extracts, in particular from testicles, by Brown-Séquard. 'D'un autre côté, le docteur Brown-Séquard rajeunit des vieillards infirmes, ranime des impuissants avec des injections de parties distillées de lapins et de cobayes.' [At the other side, doctor Brown-Séquard rejuvenates disabled old men, enlivens the powerless with injections of distillated parts of rabbits and guinea pigs]. In a conversation with a physician (Des Hermies), the fictional character in the novel (Durtal) compares this with the elixirs for long life and the love potions sold by the sorcerers. He also criticizes hypnotism: 'Quelle bizarre époque! reprit Durtal, en le reconduisant. C'est juste au moment où le positivisme bat son plein, que le mysticisme s'éveille et que les folies de l'occulte commencent.' [What bizarre age, resumes Durtal, showing him out. It is just at the moment that positivism is at its summit, when mysticism awakes and the folly of the occult starts]. The citation nicely characterizes the sentiments of the 'fin de siècle' atmosphere in Paris society (Koehler, 2001).

However, before Brown-Séquard studied this much criticized subject, he had undertaken so many other projects. These are all described by Michael Aminoff, who authored a previous book on this remarkable polymath physician and physiologist: *Brown-Séquard. A visionary of science* (Aminoff, 1993). In the present book, he adds more biographical details, additional material on Brown-Séquard's investigations, and provides more historical background. It is astonishing indeed how this restless scientist took up so many scientific questions that crossed his path and thereby furthered knowledge. He showed the importance of the adrenal glands; the influence of acute brain injury on the function of the lungs; disagreed with others with respect to the cerebral localization concept; and, of course, became famous for his studies on spinal cord hemi-sections, with ipsilateral paresis and hypaesthesia and contralateral analgesia, which earned the eponym 'Brown-Séquard syndrome'.

When a new technical device for investigating the brain or a neurological disease is discovered, scientists all over the world start applying the instrument to the study of numerous illnesses. Likewise, when a new theory of physiology or pathophysiology is introduced, the idea is applied to a large number of situations. One such theory is the concept of vasomotor nerves that emerged in the mid-19th century. It is no surprise that Brown-Séquard played his part in this story. He and Bernard have been compared with 'the fox and the hedgehog' [after Isaiah Berlin's (1909–1997) idea to divide scientists into two categories], the first running after every interesting object that crosses his path, the other meticulously studying one subject until it has been completely explained. Early in their careers, the term 'vasomotor nerves' had been introduced by Benedikt Stilling (1810–79), who, like Brown-Séquard, had studied the spinal cord. Stilling, however, was not the first, as Thomas Willis (1621–75) had noticed small nerves surrounding blood vessels subserving constriction. Experimental observations that eventually elucidated the mechanism and function of the vasomotor nerves were carried out in the 1850s. In November 1852, Bernard found that section of the cervical sympathetic resulted in increased blood flow, rise in facial temperature and constriction of the pupil, the latter phenomenon he attributed to the discovery by François Pourfour du Petit (1664–1741; publication of 1727). At first, however, Bernard did not understand the observed phenomena as, in his understanding, the sympathetic was considered the producer of the 'chaleur animale' [animal warmth]; therefore, he expected the contrary, notably cooling of the face, and was quite surprised. In the same year (August 1852), Brown-Séquard, a republican and having left France after the coup d'état by Louis Bonaparte (1778–1846), later the emperor Napoleon III, of December 1851, published the results of his animal experiments during his stay in Philadelphia. He had galvanized—probably he meant faradized, as he used an induction coil, invented by the Berlin physiologist Emil du Bois-Reymond (1818–1896)—the cervical sympathetic of several animals and noticed constriction of the blood vessels in the ear and diminished temperature of the facial skin. On another occasion, Brown-Séquard had observed with his friend Tholozan (*nk*), after immersing one hand in very cold water, that the temperature of the non-immersed hand fell considerably, whereas that of the mouth had barely decreased. He interpreted the phenomenon in terms of excitation of the afferents, which resulted in reflex activity by vasoconstriction in both hands and therefore he is considered to

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be the first to provide a description of a vasomotor reflex. In contrast to Bernard, he interpreted the effects of section as well as of stimulation in the right way. Bernard did not acknowledge that Brown-Séquard preceded him in this and only started to use the term vasomotricity many years later (1862).

The understanding of the action of the vasomotor nerves influenced ideas in several other areas in medicine, including epilepsy, and in particular the theories on the pathophysiology of migraine. One of many famous migraine sufferers in the 19th century was Du Bois-Reymond, who had suffered from the affliction for about 20 years. His paper 'Zur Kenntnis der Hemikrania' [On the knowledge of hemicrania], has become a classic in migraine literature (Du Bois-Reymond, 1860). The paper was published following a presentation for the 'Gesellschaft für Natur- und Heilkunde' [Society for Natural Science and Surgery] in Berlin in March 1859 and translated into French probably at the request of Brown-Séquard, editor of the *Journal de la Physiologie de l'Homme et des Animaux* [Journal of Physiology of the Man and Animals, founded in 1858, at his own cost]. Du Bois-Reymond recognized the importance of the discovery of the vasomotor nerves and interpreted the phenomena he observed during his own attacks: 'It responds to each beat of the temporal artery. The latter feels, on the affected side, like a hard cord, whilst the left is in its normal condition. The countenance is pale and sunken, the right eye small and reddened.' He supposed that after the attack, the smooth muscle fibres would become exhausted from the lasting tonic cramp, followed by dilatation of the blood vessels, resulting in redness and warmness of the area around the ear. He intended to measure the temperature of the ear during the attack, expecting it would be lower than on the healthy side. He realized that the redness of the eye did not fit into this concept and supposed that the muscles of conjunctival blood vessels were prostrated earlier. He assumed the origin of the migraine attacks was in the cilio-spinal centre, considered it a disease of the spinal cord and gave the condition a new name, notably 'hemikrania sympathicotonica' [sympathicotonic migraine]. He made a comparison with epilepsy, referring to an article by compatriots Adolf Kussmaul (1822–1902) and Adolph Tenner (*nk*), two physicians often referred to with respect to the reflex theory of epilepsy, who attributed this complaint to changes in cerebral blood supply. With respect to the pathophysiology of epileptic seizures, they adhered to the idea of spasmodic constriction of all cerebral arteries. In migraine, Du Bois-Reymond argued, the mechanism was basically the same, only the intensity and the extension being different (Koehler, 1995). Immediately following the French translation, Brown-Séquard, who, at the time, was moving his practice and research from Paris to London, where he worked in the newly founded National Hospital for the Paralysed and the Epileptic, published his comments: 'Remarques sur le travail précédent' [Remarks on the preceding work]. He did not agree with Du Bois-Reymond's explanation, arguing that the symptoms were due to 'paralysis' of the sympathetic and proposed the contrary, 'hemicrania sympathicolytica'. (Peter) Latham (1832–1923) unified both theories not much later and in 1868, the theory resulted in the application of ergot for migraine (Koehler and Isler, 2002).

Another topic that interested researchers throughout the 19th century was that of cerebral localization. Although the first ideas arose early in the century with the work of Franz Joseph Gall (1758–1828) and Jean-Baptiste Bouillaud (1796–1881), it was not until Broca's localization of aphasia in 1861 that more solid proof of the concept was established. However, not everyone was convinced, in particular German researchers who were still reluctant as it had only been based on clinical cases. Lesion and electrical stimulation experiments thus far had not resulted in any confirmation. They attached greater value to results from experimental–physiological methods that eventually emerged from the electrical stimulation studies by (Gustav) Fritsch (1837–1927) and (Eduard) Hitzig [(1839–1907), 1870] and (Sir David) Ferrier [(1843–1928), 1873]. As mentioned above, Brown-Séquard did not agree with contemporaries in respect to the modern concept of cerebral localization. From his clinical observations and experiments, he concluded that reality was more complex. Based on the phenomena of inhibition and 'dynamogénie' (his term, which may be equated to excitation), constituting a dynamic system in which reflex mechanisms played a part not only in the spinal cord but also in the brain, he built an alternative hypothesis. He defended his localization concept on several occasions, for instance in the 1870s, when he crossed swords with Charcot, before the Société de Biologie in Paris. Instead of a cluster theory of localization, he defended his theory of 'réseau de cellules anastomosées' [network of anastomized cells], a kind of network theory, in which scattered cells subserving the same function are connected by nerve fibres. With this model, he was able to explain the fact that damage in several locations of the central nervous system may produce the same effect, and, to account for observations that some functions remain unimpaired despite extensive brain injury. Although his arguments were not always valid, because they were sometimes based on imprecise observations, his dynamic model influenced 'anti-localizers' such as (Friedrich) Goltz (1834–1902), but also (John) Hughlings Jackson (1835–1911) and probably (Constantin) von Monakow (1853–1930) and (Sir Charles) Sherrington (1857–1952), and still has some merit today (Koehler, 1996). Although one cannot claim that Brown-Séquard played a role in the development of modern network theories, one may wonder how interested he would have been reading about the relatively recent laws to which all kind of networks obey (Stam and Reijneveld, 2007).

A theme that is often found in biographies about researchers of the time is self-experimentation. A well-known example is Henry Head (1861–1940), who studied cutaneous sensation for which he had one of the radial nerve branches of his left arm severed and sutured by surgeon (James) Sherren (1872–1945). Subsequently, he investigated recovery by having (William) Rivers (1864–1922) test the sensory function in the arm over the subsequent 4 years. The paper was published in one of the early volumes of *Brain* (Rivers and Head, 1908). Brown-Séquard was another well-known self-experimenter studying the composition of gastric juice by swallowing sponges connected to strings and, later in his career, the strength of his muscles by injecting the testicle extracts mentioned above. If we think this only happened in the early days of experimental medicine, I call to mind more recent self-experimentations by Barry J. Marshall, who infected

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himself with *Helicobacter pylori* as part of a series of studies with J. Robin Warren for which they were awarded the Nobel Prize in Physiology or Medicine (Van der Weyden *et al*., 2005). Moreover, Brown-Séquard tested all kind of functions during the periods he endured on ships, crossing the ocean so many times. Mostly, he used experimental animals in his research. He must have had in mind someone such as the early 'physiologist' Albrecht von Haller (1708–1777), a century earlier, who informed the reader in the introduction to his *Dissertation on the sensible and irritable parts of animals* that he had examined 190 animals since 1751, 'a species of cruelty for which I felt such a reluctance, as could only be overcome by the desire of contributing to the benefit of mankind' (Von Haller, 1755/1936). Indeed, Brown-Séquard was once warned by his friend Thomas Huxley (1825–95) not to come to a meeting in Liverpool as anti-vivisectionists, who, more than in other countries, were very active in England and were expected to cause trouble if Brown-Séquard showed up.

Several biographies on Brown-Séquard have been published since his death in 1894 (Rouget, 1930; Olmsted, 1946; Role, 1977; Koehler, 1989; Aminoff, 1993). The present biography adds important material to previous books and places it in a larger context. Moreover, Aminoff made his book more accessible to a broader public, explaining terms in the text and providing brief biographical details on persons in footnotes. In the last chapter, the author provides a well-balanced criticism of Brown-Séquard's work, recognizing the exactness of his early studies (spinal cord, adrenal glands and vasomotor nerves) and questioning the unfocused work and lack of clarity at the end of his career. But, despite this criticism, he believes that Brown-Séquard, 'based on inspired intuition', anticipated 'many later developments in neurology and endocrinology', a statement that is well supported by the contents of the book; explains the appearance of the character in contemporary novels; and provides an affirmative answer to the question above this essay.

P. J. Koehler
Department of Neurology, Atrium Medical Centre, Heerlen, The Netherlands
E-mail: pkoehler@neurohistory.nl

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