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History of Neurology

Figures and institutions of the neurological sciences in Paris from 1800 to 1950. Part II: Neurophysiology

Les figures et institutions des sciences neurologiques à Paris de 1800 à 1950. Partie II : neurophysiologie

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SUMMARY

We present a short historical review of the major figures and institutions that contributed to make Paris a renowned centre of physiology and neurology during the XIXth and the first half of the XXth century. We purposely chose to focus on the period 1800–1950, as 1800 corresponds to the actual beginning of experimental physiology of the nervous system – what is here referred to as "neuroscience"–and 1950 marks its exponential rise. Our presentation is divided into four chapters, matching the main disciplines which have progressed and contributed the most to the knowledge we have of the brain sciences: anatomy, physiology, neurology, and psychiatry-psychology. The present article is the second of four parts of this review which includes the chapter on neurophysiology with selected biographical sketches of François Magendie, Marie Jean-Pierre Flourens, Claude Bernard, Charles-Édouard Brown-Séquard, Étienne-Jules Marey, Alfred Fessard and Denise Albe-Fessard.

RÉSUMÉ

Nous présentons une brève revue historique générale sur les principales institutions et personnalités ayant contribué à faire de Paris un centre renommé de physiologie et de neurologie au cours du XIX[e] siècle et de la première partie du XX[e] siècle. La raison du choix de cette période allant de 1800 à 1950 s'explique par le fait que 1800 marque les débuts des neurosciences et 1950 leur développement exponentiel. Notre présentation est divisée en quatre chapitres, correspondant aux principales disciplines ayant progressé et contribué le

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Anatomie
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plus aux connaissances que nous avons sur les sciences du système nerveux: anatomie, physiologie, neurologie et psychiatrie-psychologie. Le présent article est la seconde des quatre parties de cette revue générale, qui concerne le champ de la neurophysiologie. Après un chapitre d'introduction est présentée une sélection de biographies résumées de François Magendie, Marie Jean-Pierre Flourens, Claude Bernard, Charles-Édouard Brown-Séquard, Étienne-Jules Marey, Alfred Fessard et Denise Albe-Fessard.

Introduction

The present article–which deals with neurophysiology - is the second of four parts of a short historical review of the major institutions and figures who contributed to make Paris a renowned centre of physiology and neurology during the XIXth and the first half of the XXth century.

The experimental physiological studies of the nervous system in France developed in the XIXth in France with François Magendie (1783–1855). His contribution and also controversies with the great British neurophysiologist Charles Bell (1774–1842) have already been described at length. The *Collège de France* in Paris was one of the most renowned places for physiological studies during all this period. In his famous 1865 *Introduction à l'étude de la médecine expérimentale* (Introduction to the study of experimental medicine), Claude Bernard (1813–1878) insisted on the major importance of experiments in medical sciences: « La méthode expérimentale, considérée en elle-même, n'est rien autre chose qu'un raisonnement à l'aide duquel nous soumettons méthodiquement nos idées à l'expérience des faits... L'expérimentation ou l'art d'obtenir des expériences rigoureuses et bien déterminées est la base pratique et en quelque sorte la partie exécutive de la méthode expérimentale appliquée à la médecine » (''Considered in itself, experimental method is nothing but a reasoning which helps us methodically to submit our ideas to the experience of facts... The experimentation, or art of obtaining rigorous and well-determined experiments is the practical basis and to some extent the executive part of the experimental method applied to medicine'').

Neurophysiology had close links with chemistry and physics. This is the case of Étienne-Jules Marey (1830–1904), a remarkable man whose main goal, as a physician, was to record biological phenomena in the best possible manner. He invented all kinds of devices, which allowed him to apprehend either slow or extremely fast phenomena. Marey did not develop most of his experiments and left this task to others.

Much later, Alfred Fessard (1900–1982) created the first major *laboratoire de physiologie nerveuse du CRNS* (National Center for Scientific Research laboratory of nervous physiology) in the 1950s; on the premises Marey had obtained nearly 50 years before, for his photographic studies.

Apart from Paris, several leading countries in Europe and North America took major steps in neurophysiology during the XIXth and the first half of the XXth century. Although the present paper is not focused on this topic, we will briefly mention some of the most important contributors. In Germany, Ernst Heinrich Weber (1795–1878) and Gustav Fechner (1801–1887) founded the psychophysical method. Wilhelm Wundt (1832–1920) became one of the pioneers in experimental psychophysiology. Johannes Peter Müller (1801–1858) did his famous experiments on sensory and perceptive senses. Several of his pupils did their own renowned research, notably Hermann von Helmholtz (1821–1894), Emil du Bois-Reymond (1818–1896), Theodor Schwann (1810–1882), Friedrich Gustav Jakob Henle (1809–1885), Carl Ludwig (1816–1895) and Ernst Haeckel (1834–1919). In Russia, Ivan Petrovich Pavlov (1849–1936) was professor of physiology in Saint-Petersburg. He invented the conditioned reflex for which he received the Nobel Prize in 1904. In the United Kingdom, Charles Sherrington (1857–1952) and Edgar Adrian (1889–1977) made major findings on the functions of neurons for which they received the Nobel Prize in 1932. Henry Dale (1875–1968) and Otto Loewi (1873–1961), formerly German, and then American citizens, received the Nobel Prize in 1936 for their discovery of the chemical function of acetylcholine in neurotransmission. In the USA, Walter Bradford Cannon (1871–1945) expended the experimental theories of Claude Bernard. In 1944, Joseph Erlanger (1874–1965) and Herbert Spencer Gasser (1888–1963) won the Nobel Prize for their work on the peripheral nerve fibers.

Following this introductory paragraph on the scientific context of the time, we will now present, without being exhaustive, a biographical sketch of several scientists who worked in Paris and greatly contributed to our knowledge of the physiology of the nervous system and especially the brain during the XIXth century and first half of the XXth century: François Magendie, Marie Jean-Pierre Flourens, Claude Bernard, Charles-Édouard Brown-Séquard, Étienne-Jules Marey, Alfred Fessard and Denise Albe-Fessard.

François Magendie (1783–1855)

Magendie (Fig. 1) was born in Bordeaux and studied medicine in Paris (Albury, 1977; Bloch, 1989; Breathnach, 1983; Clarac and Boller, 2010; Fenton, 1951; Haas, 1994; Lazorthes and Campan, 1984; Olmsted, 1952; Schiller, 1971; Shampo and Kyle, 1987; Stahnisch, 2009; Tubbs et al., 2008). He was appointed resident and defended his thesis in 1808 (Magendie, 1808). As an assistant in anatomy of Guillaume Dupuytren (1777–1835), he was involved in research on the spinal cord and spinal nerves. During the following decades, Magendie invested his time to the study of physiology (Gallistel, 1981; Gans, 1972; Magendie, 1816, 1817, 1834; Magendie and James, 1839; Saavedra-Delgado, 1991). He favoured the new trend in France of using instruments such as the sphygmomanometer, the thermometer or the aerometer. In 1809, he analyzed the poison contained in the strychnos (a tropical shrub) (Magendie, 1809), which enabled him to isolate strychnine in 1818. He introduced it as a medicinal drug, as well as emetine, morphine, iodides and bromides. His research was continued

Figure 1 – Picture of Magendie.
Portrait de Magendie (©BIU Santé).

Figure 2 – Picture of Flourens.
Portrait de Flourens (Académie Nationale de Médecine).

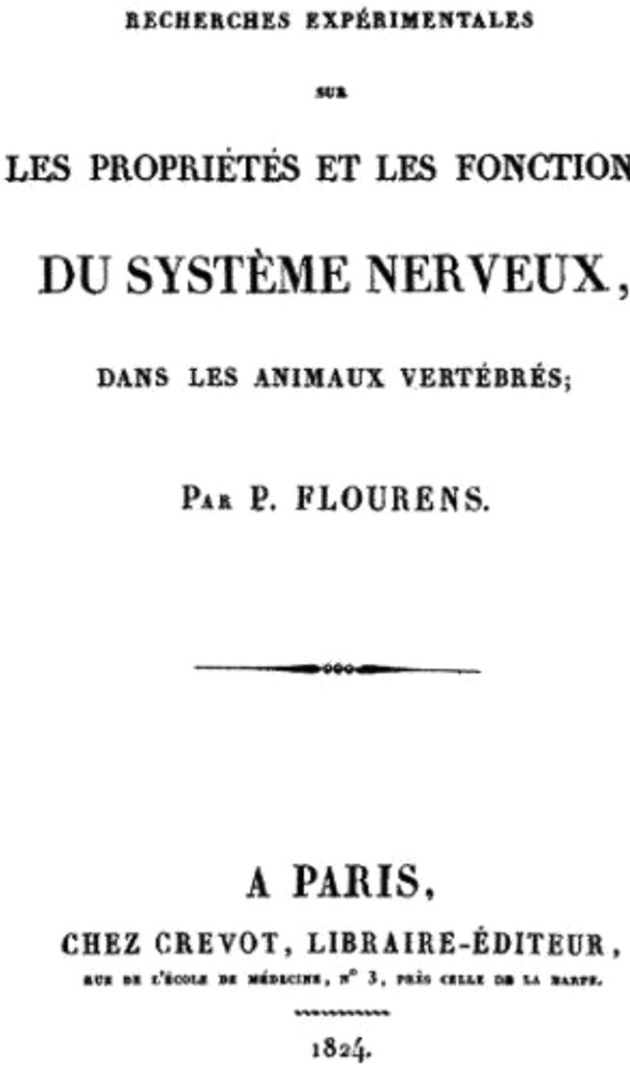
and corroborated shortly after by Henri Milne-Edwards (1800–1885). In 1821, he founded the first journal dedicated to physiology, the *Journal de Physiologie expérimentale*. Magendie is best known for the laws named after him and for his argument with Charles Bell (1774–1842), the famous British neurophysiologist (Jørgensen, 2003). In 1822, he dissected a litter of puppies and dissociated, in the spinal roots, the efferent motor conduction in the ventral root from the sensory afferent conduction in the dorsal root.

He was nominated *médecin des hôpitaux de Paris* in 1818 and headed a department of medicine at the *Hôtel-Dieu* hospital in 1830. In 1831, he became Professor at the *Collège de France*, where he met Claude Bernard, his assistant. Magendie explored the functions of the cerebellum and of the fourth ventricle and studied the pressure applied by the cerebrospinal fluid with a *sphygmomètre* (sphygmomanometer) designed by Jean-Louis Poiseuille (1799–1869) (Magendie, 1842; Stahnisch, 2008; Sourkes, 2002).

From a philosophical point of view, Magendie was a materialist and conceived the human intellect in a scientific manner escaping the comfortable religious belief of the divine nature and immortality of the soul. He thought scientists should study human intellect as if it resulted from a single organ, the brain, according to the general laws of physiology (Magendie, 1817).

Marie Jean-Pierre Flourens (1794–1867)

Flourens (Fig. 2) was born at Maureilhan in Hérault *département* (County) in the south of France and studied medicine in Montpellier, where he graduated in 1813 (Yildirim and Sarikcioglu, 2007). He was the assistant of Georges Cuvier (1769–1832), became a member of the *Académie des Sciences* in 1828 and then a professor of comparative anatomy at the *Collège de France* in Paris. He was elected at the *Académie Française* in 1840 in a contest with Victor Hugo. Flourens was an accomplished experimenter and developed the techniques of ablation and of selective stimulation of the brain, which enabled the study of walking, swimming and flying of numerous animal species, notably in birds, following and translating the work of the Italian anatomist Luigi Rolando (1773–1831) (Clarac, 2008; Flourens, 1823, 1825, 1844). He described his results in his famous 1824 book (Fig. 3) entitled: *Recherches expérimentales sur les propriétés et les fonctions du système nerveux chez les animaux vertébrés* (Experimental Studies of the Properties and Functions of the Vertebrate Nervous System) (Flourens and Rolando, 1824). Flourens was asked by Napoléon Bonaparte to assess the doctrine of Gall, which he initially followed and soon rejected. Many of his studies were made in this context, fighting the doctrine of localisation in the cortex. Flourens clearly showed the role of the cerebellum in motor coordination and the function of the ear labyrinth in equilibrium using ablation studies (Boling et al., 2002; Fine et al., 2002; Manto, 2008; Pearce, 2009; Tizard, 1959). He adopted the 1812 experiments of César Julien Legallois (1770–1814) and localized with more accuracy the respiratory centre that he located at the apex of the calamus on the floor of the fourth ventricle within the *medulla oblongata* (Pearce, 2009; Tizard, 1959). He defined *le nœud vital* (vital node) situated at the apex of the *calamus scriptorius* and no larger than a pinhead. He was one of the fiercest opponents to Franz Joseph Gall (1758–1828) and phrenology (Flourens, 1842, 1863; Flourens and Meigs, 1846; Blöde and Flourens, 2000). His ideas on the unity of the brain suggested its plasticity. In 1847, he described the effects of chloroform and ether on the nervous system at the *Académie des sciences*. He is also known as the master of the physiologist, anatomist and neurologist, Alfred Vulpian (1826–1887).



RECHERCHES EXPÉRIMENTALES

SUR

LES PROPRIÉTÉS ET LES FONCTIONS

DU SYSTÈME NERVEUX,

DANS LES ANIMAUX VERTÉBRÉS;

PAR P. FLOURENS.

A PARIS,

CHEZ CREVOT, LIBRAIRE-ÉDITEUR,

RUE DE L'ÉCOLE DE MÉDECINE, N° 3, PRÈS CELLE DE LA HARPE.

1824.

Figure 3 – Reproduction of the title page of the famous 1824 Flourens treatise.
Reproduction de la page de titre du célèbre traité de 1824 de Flourens.

Claude Bernard (1813–1878)

Claude Bernard (Fig. 4) was born in Saint-Julien in the Beaujolais area near Lyon. After an aborted career as a writer, he started medical studies and was appointed *interne des hôpitaux de Paris*. He became a *docteur en médecine* (MD) in 1843 and worked under the direction of Magendie at the *Collège de France*. He defined the role of the pancreas in digestion in 1846, by showing that it secretes a substance allowing the digestion of fats (Bernard, 1846). He later carried out the *expérience du foie lavé* (''washed liver experiment''), which described the transformation, storage and use of sugar within the body (Bernard, 1853; Kahn, 1996; Rodriguez de Romo and Borgstein, 1999; Swan, 1997). He also examined the functions of the autonomous nervous system (Reader, 2005) and discovered, in opposition to Charles Brown-Séquard (1817–1894), the function of the vasomotor nerves, responsible for blood flow regulation by contraction or dilatation of the blood vessels. In order to provide an explanation to the chemical balance that exists in every organism, he was the first one to suggest the concept of *milieu intérieur* (''internal medium'', that is to say the internal environment) (Conti, 2001; Wasserstein, 1996), better known as homeostasis and defined by Walter Bradford Cannon (1871–1945) in the 1930s (Cooper, 2008; Jeanrenaud et al., 1998).

Claude Bernard took over the chair of experimental physiology created for him at the Sorbonne University in 1854 (Bernard and Tripier, 1858a, 1858b; Griffin, 1993; Haas, 1996; McIntyre, 2001). He succeeded Magendie at the *Collège de France* after the latter's death in 1855, and became a professor at the *Muséum* (National Museum of Natural History) in 1868. He laid the foundations of experimental medicine in *L'Introduction à l'étude de la médecine expérimentale* (An Introduction to the Study of Experimental Medicine), published in 1865 (Bernard, 1858, 1865a, 1865b; Noble, 2008; Normandin, 2007; Tan and Holland, 2005). He then became a member of *Académie Française* and a person of international reputation. He died in 1878 and had a state funeral, thus becoming the very first Frenchman of science to receive such an honour. Claude Bernard was a great physiologist and professor who attracted

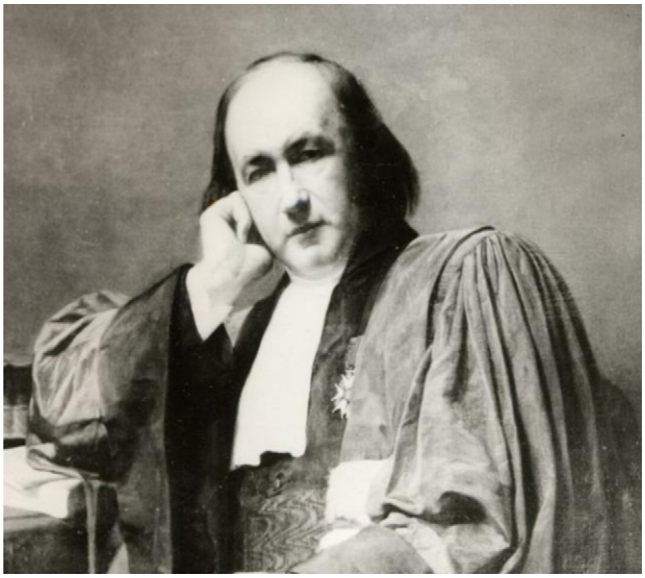


Figure 4 – Picture of Claude Bernard.
Photographie de Claude Bernard (©BIU Santé).

young students from all over the world including Russian anatomists and physiologists. He is mentioned in the novel by Dostoyevsky, *The brothers Karamazov*. He was highly praised and respected worldwide as a pioneer of experimental physiology and founder of the first great physiology school in France. However, historical analyses of his students and of early xxth century science reveal the limits of his epistemology and that of his faith in physiological determinism, his rejection of Darwin's theory and his rejection of statistics in biological sciences.

Charles-Édouard Brown-Séquard (1817–1894)

Born in Mauritius, to an Irish-American officer from Philadelphia and a French mother from Marseille, Brown-Séquard (Fig. 5) spent his life between France, England, Mauritius and the USA (Bonduelle, 2001; Dubb, 1995; Haas, 1998; Jay, 1999; Koehler, 2001; Laporte, 2006; Rengachary et al., 2008; Simonetti et al., 1994). He was a student of Armand Trousseau (1801–1867) and worked at the Charité hospital where he became the protégé of Pierre-François-Olive Rayer (1793–1867). He described what is known as the Brown-Séquard syndrome (Brown-Séquard, 1861; Tattersall and Turner, 2000), a lateral hemisection of the spinal cord (Aminoff, 1996; Brown-Séquard, 1855a, 1855b), in his 1846 medical thesis in Paris (Brown-Séquard, 1846) His second major contribution is related to the sympathetic nervous system (Brown-Séquard, 1854). In 1852, in collaboration with Claude Bernard he demonstrated the constriction of blood vessels of the ear after stimulation of the cervical nerve (Laporte, 1996).

With the support of Paul Broca (1824–1880), Brown-Séquard gained a position in Philadelphia but left for Mauritius to cure a cholera epidemic in 1854. He then moved from Mauritius to Boston in 1856 and decided to live at London's Royal College, where he inspired the young John Hughlings Jackson

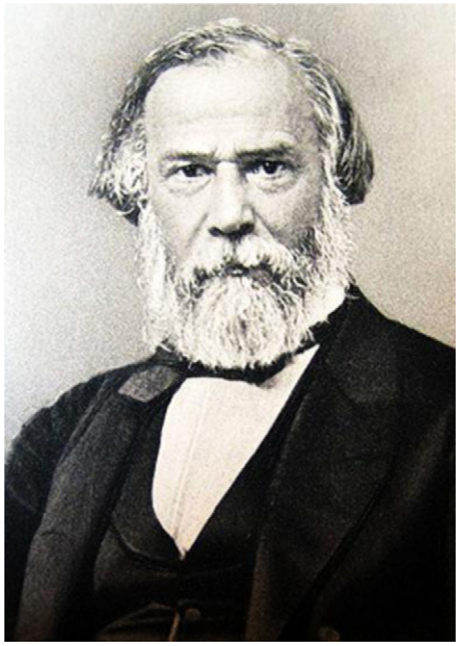


Figure 5 – Picture of Brown-Séquard.
Photographie de Brown-Séquard (©BIU Santé).

(1835–1911). Brown-Séquard took part in the founding of the London school of neurology at Queen Square. He succeeded Claude Bernard in Paris at the *Collège de France* after the latter's death in 1878 and was helped in his work by his student Arsène d'Arsonval (1851–1940).

Brown-Séquard did several major studies on the physiology and pathophysiology of the nervous system (Brown-Séquard, 1853, 1856b, 1865, 1868, 1871). With Jean-Martin Charcot (1825–1893) and Alfred Vulpian (1826–1887), Brown-Séquard founded the *Archives de physiologie normale et pathologique*, a scientific journal succeeding the *Journal de la physiologie de l'homme et des animaux* (Journal of Human and Animals Physiology) (1858–1863), edited under his direction. As an opponent of the cerebral localizations he debated with Charcot at the *Société de Biologie* (1875–1876) (Goetz, 2000). One of the other major contributions of Brown-Séquard was to show the importance of internal secretions and the role of adrenal glands. In 1856, he discovered adrenalin/epinephrine and published *Recherches expérimentales sur la physiologie et la pathologie des capsules surrénales* (Experimental Researches on the Physiology and the Pathology of Adrenal Capsules) (Brown-Séquard, 1856a). In 1889, he went as far as presenting a report claiming he had rejuvenated himself thanks to subcutaneous injections of animal testicular extracts. However extravagant this publication may seem, it undoubtedly stimulated the research on sex hormones (Rengachary et al., 2008).

Étienne-Jules Marey (1830–1904)

Marey (Fig. 6) was born in Beaune in Burgundy and studied medicine in Paris (Baron, 1983; Campan, 1978; Debru, 2004; Lefebvre, 2002; Lüderitz, 2005; McIntyre, 2005; Merlen, 1985). He was appointed *interne des hôpitaux de Paris* in 1854 and

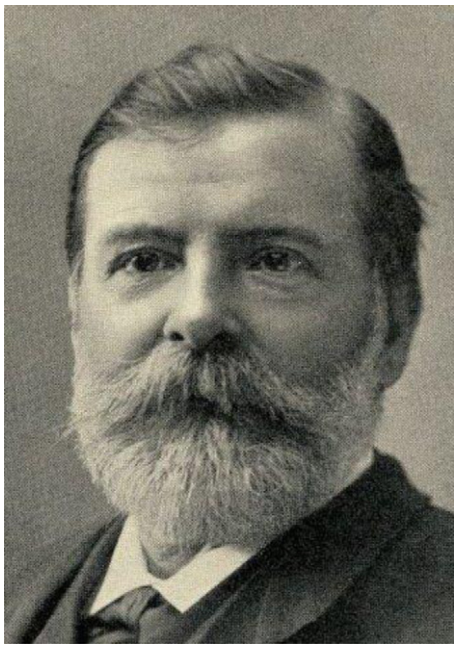


Figure 6 – Picture of Marey.
Photographie de Marey (©BIU Santé).

defended his medical thesis *Recherches sur la circulation du sang à l'état physiologique et dans les maladies* (Research on Blood Circulation in Normal and Pathological States) in 1859 (Marey, 1859). He was a physician but he did not practice much and turned to research (Marey, 1875). For the measure of different sort of physiological phenomena, Marey invented a great number of apparatus that have been used in France in the majority of physiological laboratories and by generations of students. He measured the electrical activity of the heart using a mercury Lippmann electrometer. One of his most important inventions was the sphygmograph: a device recording pulse waves measured by arterial catheterism in horses (Lawrence, 1978; Marey, 1860). This was presented to the *Académie des Sciences* in 1860. Marey published *Du Mouvement dans les fonctions de la vie* (On Movement in Life's Functions) in 1868 (Marey, 1868). He was appointed professor of physiology at the *Collège de France* in 1869 and dedicated his life to any possible movement. As many of these phenomena are invisible to the naked eye, he invented two techniques that foreshadowed the cinematograph (Michaelis, 1966; Silverman, 1996) and greatly influenced the academic art of the XIXth century and the beginnings of modern art: the graphic method (Fig. 7) and the chronophotography (Laporte, 1998; Mannoni, 2004). He published in 1873 *La Machine animale. Locomotion terrestre et aérienne* (Animal Mechanism: a Treatise on Terrestrial and Aerial Locomotion) (Marey, 1873; Marey and Demery, 1883). In 1874, the astronomist Jules Janssen designed the photographic revolver, intended to capture the movement of celestial bodies. Marey developed the chronophotographic gun in 1882 (Marey, 1882). Thanks to this famous invention he could photograph a bird's flight on 12 consecutive frames by the graphic method and chronophotography. In 1882, Marey created the *Station Physiologique du Bois de Boulogne* (Physiological Laboratory of Bois de Boulogne in Paris), funded by the French government, to which the Marey Institute was later added (Barbara, 2004). This institute was the basis for the new

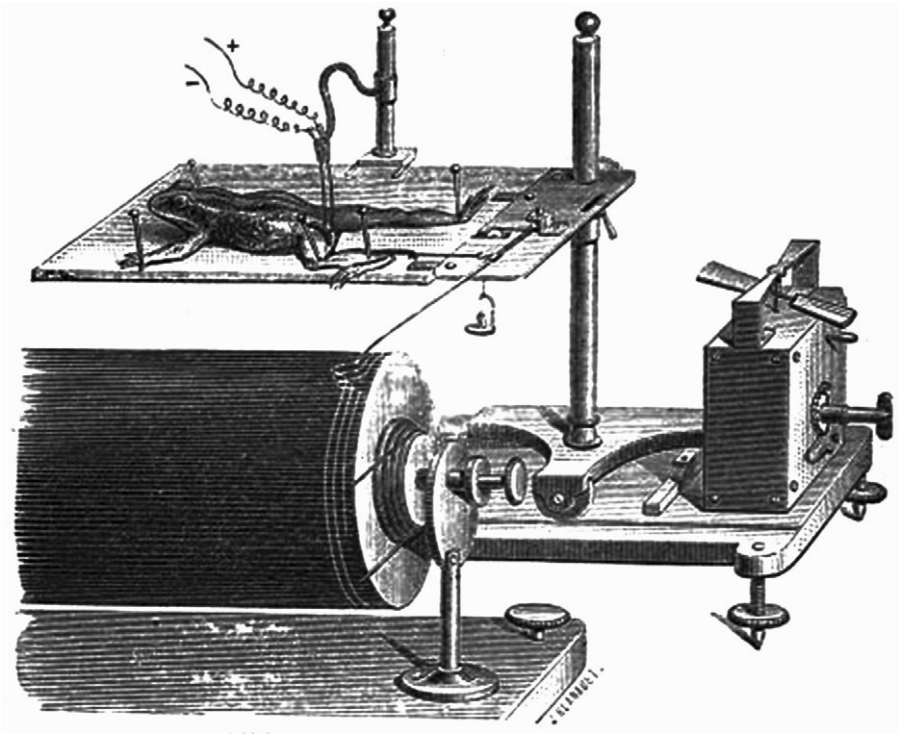


Figure 7 – Marey's myograph used in measuring muscle contraction in frog.
Myographe de Marey utilisé pour mesurer la contraction musculaire chez la grenouille (©BIU Santé).

research laboratory of electrophysiology created by Alfred Fessard before the Second World War (Barbara, 2010).

Alfred Fessard (1900–1980)

Alfred Fessard (Fig. 8) was both a physicist and a physiologist (Buser, 1982; Buser and Naquet, 1983). He was influenced by the psychologist Henri Piéron (1881–1964) and was a *préparateur* (assistant) in his psychophysiology laboratory of *l'Ecole Pratique des Hautes Etudes* (Practical School of Higher Studies), an institution of higher learning created in 1868, which offered post-graduates studies in a variety of highly specialized fields in Paris. He worked with Daniel Auger (1900–1940) at the Tamaris-sur-Mer marine biological laboratory near Toulon on the Mediterranean Sea coast. They carried out various electrophysiological recordings on preparations of invertebrates. There, Fessard met Angélique Arvanitaki (1901–1983) and discovered the giant neurons of the mollusc Aplysia. They studied the electrical activities of crustacean nerves. It was the subject of Angelique Arvanitaki thesis. Alfred Fessard's works of 1935, on the EEG, in collaboration with Gustave Durup showed the conditioning of the blocking of the alpha rhythm (Durup and Fessard, 1935). Fessard was influenced by the renowned British neurophysiology school and revived neurophysiology in France and tried to develop researches on both cellular and integrated levels (Fessard, 1936a, 1936b, 1939). He was appointed professor at the *Collège de France* and director of the Marey Institute. In 1939, he invited Siegmund Feldberg (1900–1993) and David Nachmansohn (1899–1983), two Jewish researchers escaping the Nazi government in Germany, to the marine biological laboratory of Arcachon (located on the Atlantic Ocean shore near Bordeaux). Together, they showed the cholinergic nature of the transmission in the electrical lobe of torpedo, an argument in favour of the chemical theory (Feldberg and Fessard, 1942). Since then, the international reputation of Fessard has never been contested.

Fessard became a member of the *Académie Nationale de Médecine* and of the *Académie des Sciences* and after World War II, assembled all the scientific and institutional conditions required to create a French school of neurophysiology of high international standard (Fessard and Posternak, 1950; Lapicque et al., 1950). He wrote an article on the neuronal networks and consciousness entitled *Mechanisms of Nervous Integration and Conscious Experience* at the international congress of Laurentides in 1953 (Fessard, 1954). He made his laboratory one of the most important scientific places in Europe, owing to the presence of renowned students and researchers such as his wife Denise Albe-Fessard, Pierre Buser, Jacques Paillard (1920–2006), Ladislav Tauc (1926–1999) and others (Albe-Fessard and Fessard, 1975; Bullock and Fessard, 1974; Fessard, 1976; Fessard and Lelord, 1973; Fessard et al., 1973; Morin and Buser, 1973). In the 1960s, Fessard took part in the foundation of the International Brain Research Organization (IBRO), and he became a member of its executive committee and of the governing council.

Figure 8 – Picture of Alfred Fessard and of his wife Denise Albe-Fessard.
Photographie d'Alfred Fessard et de son épouse Denise Albe-Fessard. (Fonds Jean Fessard with permission).

Denise Albe-Fessard (1916–2003)

Denise Albe-Fessard (Fig. 8), an emblematic figure of French neuroscience, obtained her diploma from *l'École de physique et chimie de la Ville de Paris* (Paris School of Physics and Chemistry) and was associated with the works carried out at Marey Institute from the beginning. In 1942, she married Alfred Fessard, who headed the CNRS Center of nervous physiology and electrophysiology. She defended her thesis on the electrogenesis of the electrical discharge in electric fishes, gymnotus, torpedo and ray in 1950 (Albe-Fessard, 1950). In the 1945–1950s, Denise Albe-Fessard and her husband carried on their researches on these particular electric fish at the marine biological laboratory of Arcachon (near Bordeaux), and in Rio de Janeiro with Carlos Chagas (1879–1934). Albe-Fessard was one of the first to succeed in recording intracellularly neurons of the cat cortex, after having refined her method on the nuclei of Torpedo (Albe-Fessard et al., 1961a, 1961b; Albe-Fessard and Kruger, 1962; Korn et al., 1966; Massion et al., 1965a, 1965b). In 1961, she began to collaborate with Gérard Guiot (1912–1998), a neurosurgeon at the Foch hospital in Paris metropolitan area and recorded, after craniotomy, the evoked potentials and the unitary neuron responses in the thalamus of parkinsonian patients who have had thalamotomy. In the mean time, she obtained new results on the mechanisms of pain and somatic representations in the human thalamus (Albe-Fessard, 1996; Albe-Fessard and Iggo, 1973; Albe-Fessard et al., 1963, 1966a, 1966b, 1967; Berkley, 2004; Guiot et al., 1962a, 1962b, 1964). She then focused her research on the thalamus and studied its intralaminar nerve nets in monkeys. Her activity at Marey Institute allowed several of her students to pursue a very successful career (Chalazonitis et al., 1978; Massion et al., 1962; Naquet et al., 1962).

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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