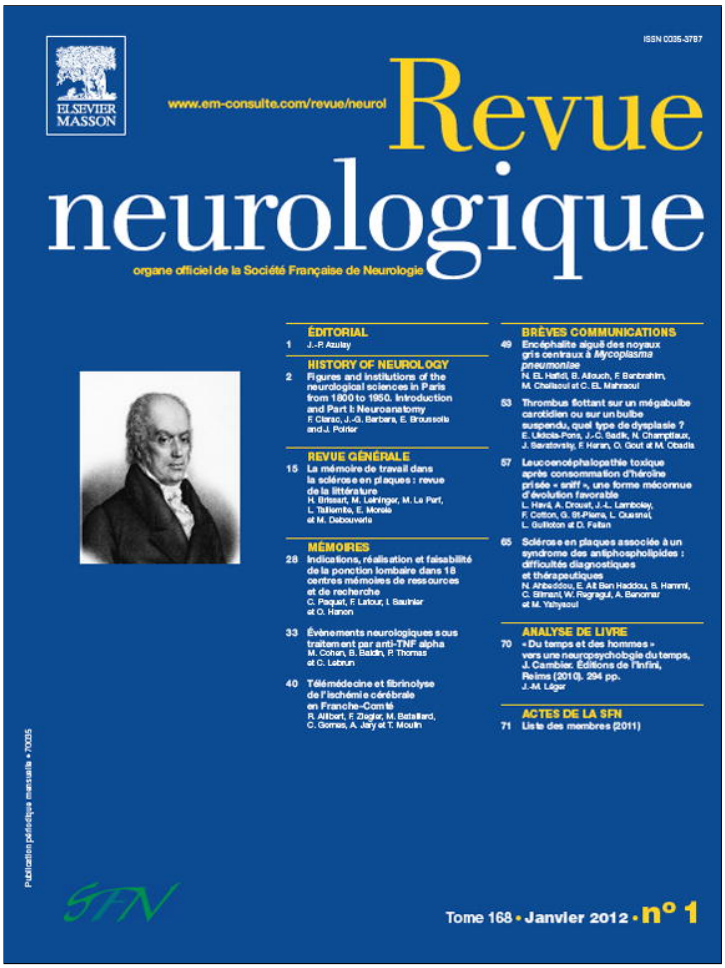

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History of Neurology

Figures and institutions of the neurological sciences in Paris from 1800 to 1950. Introduction and Part I: Neuroanatomy

Les figures et institutions des sciences neurologiques à Paris de 1800 à 1950. Introduction et partie I : neuroanatomie

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ABSTRACT

We present a short historical review on the major institutions and figures that contributed to make Paris a renowned centre of physiology and neurology during the XIXth and the first half of the XXth centuries. We purposely chose to focus on the period 1800–1950, as 1800 corresponds to the development of brain science and 1950 marks the true beginning of neuroscience. 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 first of four parts of this review, which includes an introduction followed by the chapter on neuroanatomy and on anatomo-pathology, which includes biographical sketches of Félix Vicq d'Azyr, François-Xavier Bichat, Franz Joseph Gall, Jean Cruveilhier, Jules Bernard Luys, Paul Broca, Louis Ranvier, André-Victor Cornil, Albert Gombault, Jean Nageotte and René Couteaux.

RÉSUMÉ

Nous présentons une revue générale historique brève 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 sciences du cerveau et 1950 le réel développement des neurosciences. Notre présentation est divisée en quatre chapitres, correspondant aux principales disciplines ayant

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progressé et contribué le plus aux connaissances que nous avons sur les sciences du cerveau : anatomie, physiologie, neurologie et psychiatrie-psychologie. Le présent article est la première des quatre parties de cette revue générale, qui inclut une introduction générale puis le chapitre sur la neuroanatomie et sur l'anatomo-pathologie, avec les biographies résumées de Félix Vicq d'Azyr, François-Xavier Bichat, Franz Joseph Gall, Jean Cruveilhier, Jules Bernard Luys, Paul Broca, Louis Ranvier, André-Victor Cornil, Albert Gombault, Jean Nageotte et René Couteaux.

1. Introduction

During the last decades, neuroscience research has experienced a tremendous growth in many fields of interest, notably in the anatomical, physiological, neurological or psychiatric domains. However, most of today's young scientists and physicians do not have sufficient historical background of these fascinating disciplines. Numerous authors from many parts of the world contributed to the development of the neurosciences and particularly neurology (Clarac and Boller, 2010; Clarac and Ternaux, 2008; Finger, 1994, 2000; Haymaker and Schiller, 1953; Rancurel et al., 2004). As early as the XIXth century, special credit should be given to German speaking universities from Central Europe, institutions in Great Britain and North America, French and Italian neurological schools, and also medical universities from Belgium, the Netherlands, Scandinavia, Southern Europe, Russia and subsequently from South America, Asia and Africa during the XXth century.

We took the opportunity of the XVth annual meeting of the international society for the history of the neurosciences, held in Paris in June 2010, to prepare a historical work in order to make a short presentation of the major institutions and figures who contributed to make Paris a renowned centre of physiology and neurology between 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 brain sciences and 1950 marks the rise of neuroscience.

The beginning of the XIXth century in France was characterized by a remarkable improvement of the medical and physiological knowledge. This was due to the influence of several combined factors. First, the XVIIIth century enlightenment and the *mouvement encyclopédique* (encyclopedic movement), with an emerging scientific approach of philosophy (positivism and materialism). Second, the French Revolution, with marked restructuring of the French hospital system (establishment of internship/residentship and externship in 1802) and of the academic organization (re-foundation of the three *Écoles de santé*–Medical faculties–in 1794). Third, the simultaneous presence of exceptional figures as François de Fourcroy (1715–1809), Pierre-Jean Georges Cabanis (1757–1808) and Philippe Pinel (1745–1826) to name but a few among the pioneers.

In 1830, there were numerous hospitals in Paris, in which 5000 medical students were working and where more than 20,000 patients were treated. Three medical faculties were developed at that time, in Paris, Montpellier and Strasbourg, respectively. The other major cities such as Lyon, Marseille, Bordeaux, Lille or Toulouse only had medical schools, which did not become faculties of their own right before the end of XIXth century and the beginning of the XXth century.

To put it shortly, the XIXth century in France, in what regards the scientific domain, was deeply marked by two major conflicting ideologies. As illustrated by Cabanis in his *Rapport du physique et du moral* (Essay on body and mind) published in 1802 in which he considered that ''*le cerveau sécrète la pensée comme le foie sécrète la bile*'' (the brain secretes the thought, just like the liver secretes bile) (Cabanis et al., 1802), the materialists claimed that the human psyche was to be understood uniquely with the help of physiology. They adopted the positivism of Auguste Comte (1798–1857) and his denial of the spiritualist psychology. Just like Émile Zola's (1840–1902) *Docteur Pascal*, they were convinced that the advances of science would bring happiness to the world (Zola, 1893). On the opposite, conservatives–who had the support of the royalist side and religious authorities–followed the ideas of Descartes and defended the body-mind dualism.

We have limited this presentation to Paris and its surroundings because the French capital, unlike in other cities, have long been the focal point of the country. After the reigns of Louis XIV and of Napoléon, everything was centralized in Paris, thus giving only a minor role to other cities. This explains why many of the figures we are going to evoke in this article ''went up'' to Paris, in search of a successful career. Our presentation will be divided into four chapters, matching the four disciplines which have progressed and contributed the most to the knowledge we have of the brain sciences: anatomy, physiology, neurology, and psychiatry-psychology.

2. Part I. Neuroanatomy

In the late XVIIIth century and all along the XIXth century, anatomical and postmortem pathological studies did a considerable growth in Europe. They were performed by physicians who however were not specialized to any specific organ. Nevertheless, a greater number of scientists oriented their interest to the study of the brain and spinal cord. Besides the macroscopic analysis, histological studies gained enormous power in the second part of the XIXth century. This was due to the improvement of microscopes and to the development of histological fixation and staining techniques notably the silver staining which made possible to visualize the nervous cells and axons. Undoubtedly, this breakthrough can be credited in a large part to German speaking universities. Anatomical studies concerning the nervous system were mainly dedicated during the XIXth century to the histology of

the nervous cells and to the cerebral cortex. We present below some historical aspects, citing the giants, and indicating also the contribution of the Paris school.

During the first half of the XIXth century, two French anatomists François Leuret (1797–1851), psychiatrist and student of Jean-Etienne Esquirol (1772–1840), and zoologist Pierre Gratiolet (1815–1865) took major steps forwards in our knowledge of the cortex. The fundamental data from their work *Anatomie comparée du système nerveux* (Comparative anatomy of the nervous system) allowed an accurate localization of the different areas of the brain. Leuret defined *lobes* and *gyri* as primary points of comparative anatomy on which are based the psychic functions (Leuret, 1857a, 1857b). Gratiolet complemented the results of his colleague by describing five lobes (frontal, parietal, temporal, occipital and insular) in each cerebral hemisphere, and the optic radiations that allow the connexion between the thalamus and the visual cortex (Gratiolet, 1861). In 1840, the French psychiatrist Jules Gabriel François Baillarger (1809–1890) brought to light six cortical layers, in turn transparent or opaque, while working on thin sections of the cortex with a microscope (Baillarger, 1840). This stratification has been adopted and enhanced outside France by Robert Remak (1815–1865) (Remak, 1838, 1841, 1847) and Albert von Kölliker (1817–1905) in 1841 and 1850, respectively (Eulenburg et al., 1900; Kölliker, 1850). These works on the brain led to intense arguments between the localisationists, who claimed that each area of the brain had its own function, and the unitarians who thought that the whole brain achieved all the functions.

Concerning the nervous cells, they were first considered separately with the cell bodies in the nervous centers and the fibers in the nerves which were named neural tubes, Remak tubes or ''axis cylinders''. The great step concerning these researches was that made by Otto Deiters (1834–1863) when he discovered the ''laws governing the relations between cells and fibers in central organs''. Such a position must be replaced in the more general context of the German cell theory after the work by Theodor Schwann (1810–1882), Matthias Schleiden (1804–1881), and the extension in the field of pathology by Rudolf Ludwig Carl Virchow (1821–1902). The Berlin Virchow's Institute became a world famous research center for microscopic studies. The term ''motor cell'' (''*motorischen Zellen*'') was first used by histologists such as von Koelliker in his book, *Mikroskopische Anatomie, oder, Gewebelehre des Menschen*. Followers of cell theory can be found in every nations referring to the studies of the German school, as the French Jean-Martin Charcot (1825–1893) Louis Ranvier (1835–1922) and André-Victor Cornil (1837–1908). Indeed, with Louis Ranvier and its great anatomical influence, anatomy and histology became very potent disciplines in France. A real school was started in Paris, and continued with René Couteaux (1909–1999), Jacques Taxi and André Calas.

The complete description of the nervous cellular organisation was done in the second half of the XIXth century. The nerve cell, which was termed the *neuron* in the 1890s by Heinrich Wilhelm Gottfried von Waldeyer-Hartz (1836–1921) after the work of Santiago Ramón y Cajal (1852–1934), Wilhelm His (1831–1904) and August Henri Forel (1848–1931), appeared to have the same essential characteristics as all the other cells of the living beings despite its particularities.

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 brain anatomy and pathology from the late XVIIIth to the XXth centuries: Félix Vicq d'Azyr, François-Xavier Bichat, Franz Joseph Gall, Jean Cruveilhier, Jules Bernard Luys, Paul Broca, Louis Ranvier, André-Victor Cornil, Albert Gombault, Jean Nageotte and René Couteaux.

3. Félix Vicq d'Azyr (1746–1794)

Born in Normandy, Vicq d'Azyr (Fig. 1) (Farrell and McHenry, 1987; Goldblatt, 1986; Hannaway, 1994; Mandressi, 2008; Mercado et al., 2004; Parent, 2007; Sournia, 1994; Stafford et al., 1992; Van Gijn, 2009) studied medicine in Paris and was the protégé of Antoine Petit (1722–1794), a professor of anatomy at the former *Jardin du roi* (King's garden), current *Jardin des plantes* (Paris botanical garden). Vicq d'Azyr, a person of poor health, returned to Normandy in 1773, where he studied fish. After the publication of his work, and with the support of two of his masters, Marie Jean-Antoine-Nicolas de Caritat, Marquis de Condorcet (1743–1794) and Louis Daubenton (1715–1799), he became a member of the *Académie des sciences* (French Academy of sciences) in 1774. In the same year, he was given the responsibility of analyzing a severe ''cattle epizootic'' by the *contrôleur des finances* (finance Minister) Anne-Robert Turgot (1727–1781) (Meynell, 1998). He travelled across the French provinces and made suggestions to avoid the propagation of this epidemic. His report led Jacques Necker (1732–1804)–the successor of Turgot–to create the *Société royale de médecine* (royal society of medicine), in charge of analyzing diseases and their treatments throughout the kingdom, society of which he became the perpetual secretary and Joseph-Marie-François Lassone (1717–1788) the president. Vicq d'Azyr contributed fundamentally to the study of anatomy and especially human brain anatomy (Vicq d'Azyr, 1779, 1780, 1784, 1786a, 1805). In 1786, Vicq d'Azyr published

Fig. 1 – Picture of Vicq D'Azyr.
Portrait de Vicq D'Azyr (Académie nationale de médecine).

his *Traité d'anatomie comparée et de physiologie* (Treatise on comparative anatomy and physiology), a remarkable anatomy and physiology treatise illustrated by sections of the human brain of a quality and exactitude never attained before (Vicq d'Azyr, 1786b, 1786c). He presented the deep brain structures and was the first one to describe the *locus coeruleus*, the *locus niger* and the mammillothalamic tract, also known as bundle of Vicq d'Azyr. We owe him the concept ''homology'' in biology. During the French Revolution, he presented a decisive plan to reform the teaching of medicine in France, and encouraged François de Fourcroy to have the three *Écoles de santé* (Medical faculties) re-created, in Paris, Montpellier and Strasbourg voted by the convention in 1794 (Peumery, 2001).

4. François-Xavier Bichat (1771–1802)

Bichat (Fig. 2) was born in Thoirette in the Jura French *département* (county) and trained in medicine in Lyon under the guidance of the young surgeon Marc-Antoine Petit (1766–1811). He joined the army of the Alps as a surgeon during the French Revolution. In 1794, he collaborated with Pierre Desault (1738–1795) at the Hôtel-Dieu hospital in Paris, until the sudden death of Desault which left Bichat alone, when aged 24. He compiled and published in a single piece of work, the lessons taught by his two masters and was appointed chief surgeon at the Hôtel-Dieu hospital, when he was only 29. In 1796, he founded the *Société médicale d'émulation* (medical society of emulation), one of the most prestigious scientific associations of that time. Bichat investigated the pathology of diseases (Albury, 1977; Anonymous and Bichat, 1968; Anonymous, 1971; Baudet, 1969; Binet, 1959; Breathnach, 1981a; Elaut, 1969; Fye, 1996; Godlewski, 1968; Haas, 1994; Haigh, 1975, 1984; Heywood, 1979; McIntyre, 2004; Prichard, 1979; Shoja et al., 2008). Gaspard Laurent Bayle (1774–1816), René Théophile Laënnec (1781–1826) and Guillaume Dupuytren (1777–1835), three students of Bichat, members of this society, founded the famous anatomoclinical school of Paris (Anonymous, 1968). At the same time, Bichat began to give private lectures on anatomy and operative surgery. He published several major treatises such as *Le Traité des membranes* (A Treatise on the membranes), in July 1799 (Bichat, 1799). He soon after attempted to explain the passage from life to death with anatomical, physiological and pathological analyses, by observing the way the different organs of the human body interact, in *Recherches physiologiques sur la vie et la mort* (Physiological researches on life and death) in which he opposed the notion of *vie de relation* (animal life) to the one of *vie végétative* (organic life) (Bichat, 1800). In his *Traité d'anatomie générale appliquée à la physiologie et à la médecine* (General anatomy applied to physiology and medicine) published in 1801, he defined the notion of tissue by dividing organs into 21 elementary tissues, by dissection and without using a microscope (Bichat, 1801).

Fig. 2 – Picture of Bichat.
Portrait de Bichat (©BIU Santé).

5. Franz Joseph Gall (1758–1828)

German physician and anatomist, Gall (Fig. 3) first studied medicine at the university of Strasbourg and then at the university of Vienna. He became a professor and a brilliant neuroanatomist (Critchley, 1965; Ellis, 2008; Kaitaro, 2001; Lechtenberg, 1992; Lesky, 1970; Livianos-Aldana et al., 2007; Macmillan, 1992; Pardue, 1998; Rawlings and Rossitch, 1994; Simpson, 2005; Van Wyhe, 2002; Young, 1968; Zola-Morgan, 1995). Gall invented a new method of dissecting the brain, which helped him to make great progresses in the understanding of brain function (Gall, 1808, 1822a, 1822b, 1823a, 1823b, 1825, 1832; Gall and Spurzheim, 1810). He supported the idea that psychic functions have a concrete localization within the brain. He was expelled from Austria and he subsequently came to France where his theories met a great success, despite being invalidated by the *Académie des sciences*. Gall coined the term cranioscopy, name he gave to his method of attempting to associate the different gyri of the surface of the cortex with psychic properties, but his main disciple Johann Christoph Spurzheim (1766–1833) renamed it phrenology in 1810 (Spurzheim and Gall, 1809), term still used today. He distinguished 27 mental faculties at the surface of the brain, which he stratified into three groups:

- the first one is shared by all the vertebrates and is located in the posterior and lower parts of encephalon;
- the second, found in higher vertebrates, is located in the inferior part of the anterior lobes;
- the third group is proper to humans and is located in the upper part of the anterior lobes (prefrontal area). Despite the examination of hundreds of brains and skulls, phrenology does not have a scientific backing, as the correlations it pretends to establish between anatomy and behavioural observation remain very subjective. Harshest criticism of phrenology originated from Marie Jean-Pierre Flourens (see neurophysiology chapter).

6. Jean Cruveilhier (1791–1874)

Jean Cruveilhier (Fig. 4), was born in Limoges in the center of France (Androutsos and Vladimiros, 2006; Anonymous and

Fig. 3 – Picture of Gall.
Portrait de Gall (©BIU Santé).

Fig. 4 – Picture of Cruveilhier.
Portrait de Cruveilhier (Académie nationale de médecine).

Eponym:, 1976; Bakay, 1989; Flamm, 1973; Pearce, 2003; Tainmont, 2009; Waring, 1968). He made a career in Paris with the support of the famous surgeon Guillaume Dupuytren (1777–1835) (Orcel and Vetter, 1976). In 1826, he reinstated the *Société anatomique* (*Anatomical society*) that had been dissolved in 1808, and was appointed *médecin des hôpitaux de Paris* (senior physician of Paris hospitals) and then became head of a department of medicine at La Salpêtrière hospital the same year. In 1825, he was appointed professor of anatomy at the Paris faculty of medicine and became in 1835 the first occupant of the recently founded chair of pathology. His three major works are *L'anatomie descriptive* (Descriptive anatomy) (Cruveilhier, 1834a, 1834b), the outstanding *Atlas d'anatomie pathologique du corps humain* (Atlas of human pathology) (Cruveilhier, 1828, 1829) and the *Traité d'anatomie pathologique* (Treatise on pathology) in five volumes (Cruveilhier, 1849). He was the first to describe cholesteatoma, also referred to as *tumeur perlée de Cruveilhier* (pearly tumor of Cruveilhier), and was also one of the first to give an anatomical description of the multiple sclerosis pathology, later individualised on the clinical level by Vulpian and Charcot.

Fig. 5 – Picture of Luys.
Portrait de Luys (Académie nationale de médecine).

7. Jules Bernard Luys (1828–1897)

Médecin des hôpitaux de Paris, head of a department of medicine at La Salpêtrière hospital and then at the Charité hospital in Paris, Luys (Fig. 5) studied two very distinct areas. He made crucial discoveries in the field of neuroanatomy, giving the first description of the centro-median nucleus of the thalamus and of the subthalamic nucleus (Fig. 6) (Luys, 1865). This nucleus was improperly coined by Luys *bandelette accessoire des olives supérieures* (accessory band of the superior olives) and later named *Luys's chen corpus* or *corpus Luysii* (Luys body) by August Henri Forel (1848–1931) in 1877 (Beck et al., 2008; Parent, 2002; Pearce, 2001). He also published the very first photographic atlas of the encephalon and an outstanding atlas representing drawings of sections of the brain (Luys, 1873). At the end of his career, Luys probably followed the trend of that time and decided to study the completely different field of mental pathology, and focused particularly on hysteria and hypnosis dedicating many works to these two conditions (Parent et al., 2002). He was a member of l'*Académie de médecine* (Academy of medicine), and one of the founders of the journal *L'Encéphale*.

8. Paul Broca (1824–1880)

Broca (Fig. 7) was born in a Protestant family, in Sainte Foy-la-Grande, a small town in the Gironde *département*, near

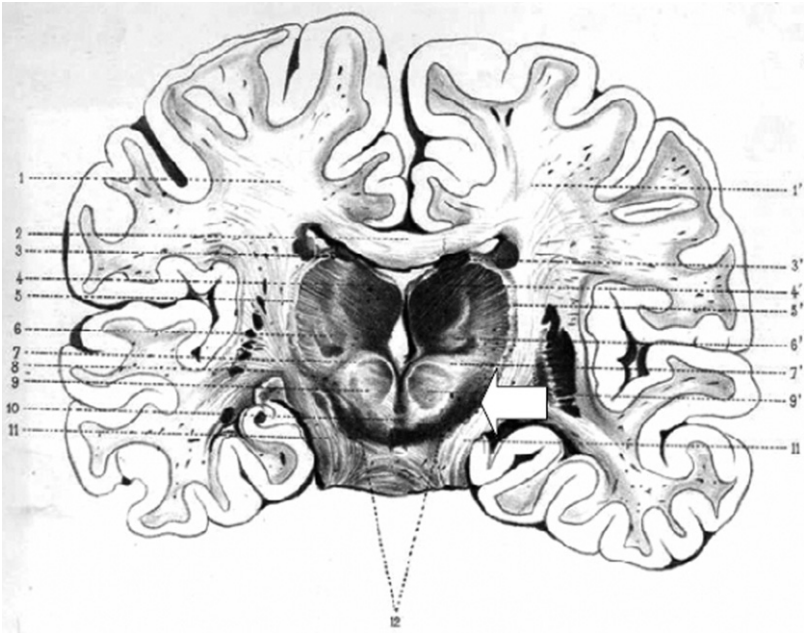

Fig. 6 – Reproduction of one of the drawings (Plate XXVI) which can be found in Luys' 1865 treatise on the anatomy of human brain, at the level of the subthalamic nucleus (see large arrow). Luys was the first to describe this brain region, which he improperly denominated "accessory band of the superior olives". This anatomical structure is not clearly labeled on this drawing, but can be recognized as the one prolonging (as the outer and upper part) the "susbtantia nigra", which is labeled n° 12.

Reproduction de l'un des dessins (Planche XXVI) qui peut être trouvé dans le Traité d'anatomie du cerceau humain de 1865 de Luys, situé au niveau du noyau sous-thalamique (voir la flèche large). Luys fut le premier à décrire cette région du cerveau qu'il appela de façon impropre « bandelette accessoire des olives supérieures ». Cette structure anatomique n'est pas indiquée de façon claire dans la légende de ce dessin, mais elle peut être identifiée comme la région prolongeant en haut et en dehors la « substance noire » (« locus niger ») étiquetée n° 12 (©BIU Santé).

Bordeaux, where several illustrious men (including Gratiolet) were born (Anonymous, 1980; Bendiner, 1986; Breathnach, 1981b; Cambier, 1980; Castaigne, 1980; Finger, 2004; Frédy, 1996; Huard, 1961; Jay, 2002; Monod-Broca, 1980, 2001, 2005, 2006; Rössner, 2007; Valette, 1980). He was successively *interne des hôpitaux de Paris* (intern/resident of Paris hospitals), surgeon of the hospitals, professor at the faculty of medicine of Paris and member of the *Académie de medicine*. Broca is mostly renowned as a scientist in the fields of neurology (Broca, 1853, 1866; D'Aubigné, 1980; Gusmao, 2002; Houdart, 1980), anatomy (Bonamy et al., 1866; Delmas, 1980; Denoix, 1980; Huard, 1980) and anthropology (Androutsos and Diamantis, 2007; Broca, 1862, 1871, 1873a, 1873b, 1873c, 1874, 1875, 1876, 1877a, 1879b; Clower and Finger, 2001; Pineau, 1980; Schiller, 1992). He made major steps in the study of cerebral localizations (Broca, 1877b, 1879a; Cowie, 2000; Stone, 1991). His name is associated to a speech disorder, Broca's aphasia, which he described thanks to the anatomoclinical observation of the foot lesions of the left ascending frontal convolution in his patient Leborgne (Alajouanine and Signoret, 1980; Broca and Nicolas, 2004). This Bicêtre'patient called ''Tan'' within the hospital because this was all he could say, apart from monosyllabic words and a curse. In a paper published in 1861 in *Bulletins de la Société anatomique de Paris*, Broca presented a detailed account of his postmortem examination of Tan's brain (Broca, 1861). In 1865, Broca proposed that the area for language was lateralized (Broca, 1865; Harris, 1991, 1993; Huard et al., 1982; Lee, 1981; Schiller, 1983). The ''priority'' of Broca's observation, its accuracy and the name that should be given to the syndrome were all disputed in public discussions

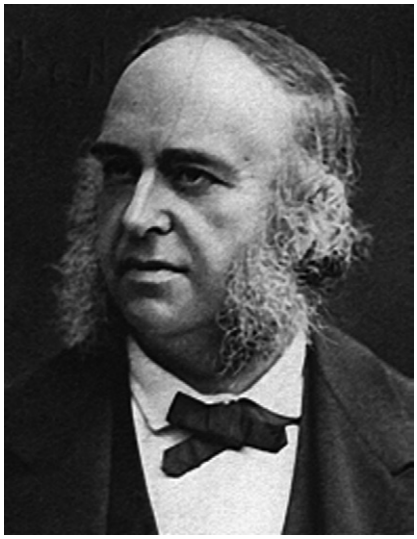

Fig. 7 – Picture of Broca.

Photographie de Broca (Académie nationale de médecine).

and papers (Brown and Chobor, 1992; Roch Lecours, 1999). In 1863, Gustave Dax (1815–1893) came forth with a report prepared by his deceased father, Marc Dax (1770–1837), one supposedly presented to the Montpellier medical society in 1836. There is no question that Dax's paper on the left hemisphere dominance for speech had been written in 1836, but there remains the nagging issue of whether it had been a public document (Buckingham, 2006; Cubelli and Montagna, 1994).

At the end of his life, in 1878, Broca described in great detail a region that forms the inner border of the brain. He analyzed it in different mammals' brains and called it the limbic region (Broca's great limbic lobe). Broca did not found its real function, and considered it associated with the olfactory system; we know today that it is linked with emotions (Broca, 1878).

Broca was the father of anthropology, and founded the *Société d'anthropologie de Paris* (Paris anthropological Society), the *Revue d'anthropologie* (Topinard and Broca, 1876) and *L'école d'anthropologie* (School of anthropology) in 1859, 1872 and 1876, respectively. Broca was a great humanist, a freethinker (he took part in the foundation of the *Société des libres penseurs* (Society of freethinkers). He was a republican hostile to the Empire, and became a senator. The surgeon Ulysse Trélat (1728–1890) ended his eulogy with the following words: ''Great and powerful intelligence, bright and serene soul, noble heart, what a rare and worthy trinity, magnificent union of everything that makes the true grandeur of the human being [...]''.

9. Louis Ranvier (1835–1922)

Born in Lyon, where he started his medical studies, Ranvier (Fig. 8) was admitted as an *interne des hôpitaux* de *Paris* in 1860. He became a professor and was given a chair of general anatomy in 1875 at the *collège de France* (the most prestigious scientific institution in France), where his teaching attracted considerable attention not only from anatomists and physiologists but also neurologists. Of particular interests were his techniques of axon staining used in the study of nervous degenerative processes in experimental pathology. Ranvier followed the experimental method taught by his master Claude Bernard (1813–1878), and always double-checked his morphological observations with the help of physiology (Barbara, 2006). His *Manuel d'histologie pathologique* (A manual of pathological histology) in collaboration with Victor Cornil (1837–1908) is still considered as a masterpiece (Cornil and Ranvier, 1869). His numerous findings were related to bone and connective tissues, muscle histology (Ranvier and Renaut, 1880) and, above all, to nervous fibre histology (degeneration, regeneration and nerve endings) (Barbara, 2007; Ranvier, 1889; Ranvier and Weber, 1878). He discovered the annular constrictions of the nervous fibers (narrowing or nodes) named after him, as well as the T-structure of the axons of spinal ganglia sensory neurons. He may have taught the Golgi method to Spanish scientists in Paris who brought it back to Madrid where Ramón y Cajal used it thereafter extensively. In 1897, Ranvier founded *Archives d'anatomie microscopique* with Édouard-Gérard Balbiani (1823–1899), the very first journal of microscopic studies. He was a member of the *Académie des sciences* and of the *Académie de médecine*. His main colleagues were Charles Malassez (1842–1909), Louis-Félix Henneguy (1850–1928), Édouard-Gérard Balbiani and Justin-Marie Jolly (1870–1953) who held a chair of histophysiology at the *collège de France* in 1925.

10. André-Victor Cornil (1837–1908)

Cornil (Fig. 9) had simultaneously a successful career in both medicine and politics (Anonymous, 1970). He was the second oldest of Charcot's residents (the first was Henri Soulier 1834–1921), a relentless worker, and was at the same time *médecin des hôpitaux de Paris* and professor of pathology. In 1882, he replaced Charcot who had taken over the chair dedicated to

Fig. 8 – Picture of Ranvier.
Portrait de Ranvier (©BIU Santé).

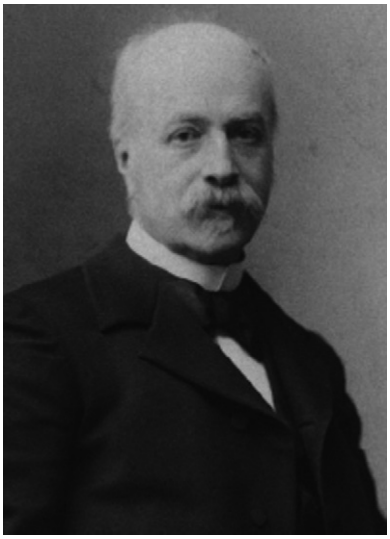

Fig. 9 – Picture of Cornil.
Photographie de Cornil (©BIU Santé).

the study of the nervous system. Cornil was a clinician but also, and mainly, a pathologist. He was passionate about postmortem examinations and histopathology (Cornil, 1863, 1864, 1865, 1879; Cornil and Babes, 1885). He wrote many papers and his *Manuel d'histologie pathologique* (A manual of pathological histology), which he wrote in collaboration with Louis Ranvier, is a remarkably clear condensation of all his observations (Cornil and Ranvier, 1869). His collaboration with Ranvier began with the small private histological laboratory they founded on *Rue Christine*, and went on at the *collège de France* and at the chair of Pathological anatomy. On the political level, Victor Cornil was a congressional representative of the Allier French *département* (County), senator-mayor of his small village Creuzier-le-neuf, regional councillor, prefect from the 6th to the 24th of September 1870, and vice-president then president of the regional council of Allier. He was an anti-monarchist and presided over the republican league in the *6th arrondissement* of Paris during the *Commune*.

11. Albert Gombault (1844–1904)

Gombault (Fig. 10) was resident of Charcot in 1872 and continued the work on amyotrophic lateral sclerosis (ALS). He analysed the case of Elisabeth P. who had a labio-glosso-laryngeal paralysis and died from respiratory asphyxia. He described severe alterations in the anterior pyramids and in the cellular bodies of the hypoglossal nucleus. He defended his MD thesis on ALS in August 1877 (Gombault, 1877). He was appointed *médecin des hôpitaux de Paris* in 1882 and head of a department of medicine at the *hôpital des incurables d'Ivry* (current Charles Foix, Jean Rostand hospital). He was a founding member of the *Société de neurologie de Paris* in 1899, *chef des travaux anatomiques* (chief of anatomical works) at the faculty of medicine and curator of the *musée Dupuytren*. His neurological, neuropathological and neurohistological works are still of importance today (Clarac and Lechevalier, 2006; Gombault and Philippe, 1895). With official authorization from the faculty of medicine, he founded an open course on histology in 1887. He studied saturnism in guinea pigs that had been fed during six months with food containing lead. If there were no clear behavioural disturbances, most nervous fibers showed marked defects of myelin. Using the teasing method, he dissociated the nervous trunks of the brachial plexus and of the sciatic nerve. The axons always stayed intact but the Schwann cell sheaths were severely affected. These lesions might heal to some extent if lead ingestion was discontinued. Subsequently he demonstrated similar lesions in humans with lead poisoning. His pictures were reproduced in Greenfields neuropathology, up to the 1976 edition. Gombault wrote the fifth part of the *Traité d'histologie pathologique* (Treatise on pathological histology, by Cornil and Ranvier), in collaboration with his beloved student Claude Philippe (1865–1903). He published several papers, but his name is more particularly associated with the *névrite peri-axile* (periaxial neuritis) of Gombault and Philippe (Gombault, 1880a, 1880b).

12. Jean Nageotte (1866–1948)

As a resident in 1889, Nageotte (Fig. 11) defended his thesis on tabes dorsalis while working at the laboratory of Fulgence Raymond (1844–1910), at Lariboisière hospital (Nageotte, 1893). He was named *médecin aliéniste des hôpitaux de Paris* (*psychiatrist of Paris hospitals*) at Bicêtre hospital, then at the Salpêtrière hospital, and was head of Joseph Félix Babinski's (1857–1932) department for pathological and histological exams, where he designed a new brain microtome for the laboratory. He did several important reports on the human brain (Nageotte, 1911, 1913). In collaboration with Babinski, he described the Babinski-Nageotte syndrome of vascular lesion of the medulla in 1902 and published works on cerebrospinal fluid cytology (Babinski and Nageotte, 1902). He succeeded to Louis Ranvier and took over the chair of comparative histology (which had originally been created for Ranvier), when the latter left in 1937. Despite his achievements, Nageotte was never elected to

Fig. 10 – Picture of Gombault.
Portrait de Gombault (©BIU Santé).

Fig. 11 – Picture of Nageotte.
Photographie de Nageotte.

the *Académie des sciences*. In 1911, he paid a tribute to his teachers in the summary of his works, and especially to Albert Gombault of whom he had been a resident, to Louis-Charles Malassez (1842–1909), who accepted him in his laboratory and to Babinski. Nageotte did considerable research on the microscopic anatomy of the connective tissue (Nageotte, 1922, 1936, 1939) and of the nervous system and published a very detailed book entitled *La structure fine du système nerveux* (Fine structure of the nervous system) in 1905 (Nageotte, 1905). He then dedicated his research to myelin and physicochemical properties and published a book in 1937 entitled *Morphologie des gels lipoïdes, myéline, cristaux liquides, vacuoles* (Morphology of lipoid gels, myelin, liquid crystals and vacuoles) (Nageotte, 1937). He was the teacher of René Couteaux. Following an accident Nageotte was struck down by hemiplegia and became progressively deaf.

13. René Couteaux (1909–1999)

Couteaux (Fig. 12) was *docteur en médecine* (MD), professor of histology and cytology at the Paris faculty of sciences and a pioneer in the anatomical and ultrastructural knowledge of synapses (Couteaux, 1941). He began his studies on the neuromuscular junction in 1935. On the biochemical level, he co-established with David Nachmanson (1899–1983) the concentration of the acetyl-cholinesterase activity in the neural area of muscle fibers even after denervation. Thanks to Janus green B staining, Couteaux defined the postsynaptic membrane, the subneural organization and the motor end plate and published his results in his PhD thesis in 1947 (Couteaux, 1947). After hearing a speech from Sanford Palay (1918–2002) at Caracas congress in 1957, from 1960 onwards, Couteaux decided to study the presynaptic portion of the synapse (Couteaux and Pécot-Dechavassine, 1970b). In 1970, he managed to obtain characteristic images of the exocytosis by opening synaptic vesicles (Fig. 13) (Couteaux and Pécot-Dechavassine, 1970a; Tsuji, 2006).

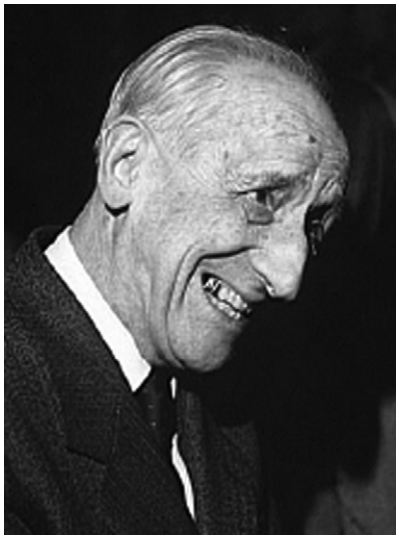

Fig. 12 – Picture of Couteaux (personal collection).
Photographie de Couteaux (collection personnelle de Jacques Poirier).

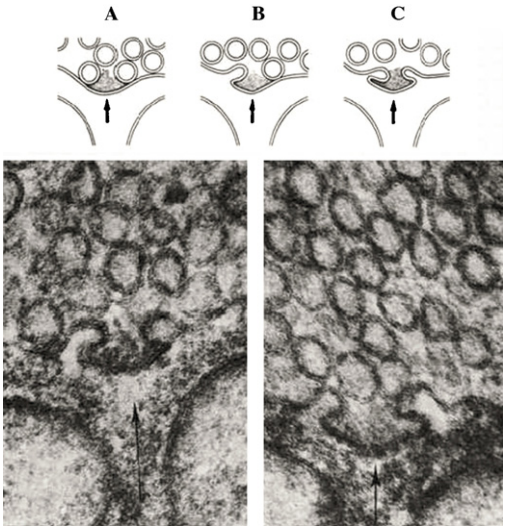

Fig. 13 – Exocytotic opening of the synaptic vesicles into the synaptic cleft at the level of the active zone (arrow) of the frog neuromuscular junction (magnification, × 205000). Reproduced with kind permission of Académie des sciences. From R. Couteaux and M. Pécot-Dechavassine (1970) comptes rendus hebdomadaires des séances de l'Académie des sciences, Série D: sciences naturelles, 271, 2346–2349. (Académie des sciences–institut de France.)
Ouverture par exocytose des vésicules synaptiques dans la fente synaptique au niveau de la zone active (flèche) de la junction neuromusculaire de la grenouille (agrandissement × 205000). Reproduit avec l'autisation de l'Académie des sciences. R. Couteaux and M. Pécot-Dechavassine (1970) comptes rendus hebdomadaires des séances de l'Académie des sciences, Série D : sciences naturelles, 271, 2346–2349. (Académie des sciences–institut de France).

Disclosure of interest

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

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