Origins of studies into brain neurophysiology

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The significance of brain for the vital functions system was indicated as early as in the ancient times. However, both its anatomy and physiology remained a matter of speculation for a long time. Hippocrates, in his ponderings about the hierarchic structure of the human body, indicated three organs – the liver, heart and brain – as the pillars supporting this structure. He stressed that the brain is the center of emotions and consciousness of a human being.

Aristotle, who was at variance with him, stated that the brain's role is to cool blood heated in the heart, to which he referred as a "habitat" for perception and sensations. This sparked off a discussion between supporters of each of these approaches to solving the mystery of life, which lasted for centuries. Its first chapter were studies into the anatomy and physiology of the brain and nervous system conducted in the 4th and 3rd century before Christ by scholars who co-founded the so-called Catechetical School of Alexandria, but most importantly by **Herophilos and Erasistratus**.

What is brain? What is its role with respect to the medulla oblongata and nerves running through the body? What integrates this entire system? These questions were asked by generations of life scientists and philosophers. In renaissance Italy, **Andreas Vesalius** and **Leonardo da Vinci** left behind precise drawings of the cerebral cortex along with their description, while **Realdo Colombo**, when studying ventricles of the brain, noticed a relatively small structure in the temporal lobe of the cerebral cortex and compared its shape to a seahorse – *hippocampus.*

In the 17th century, the Englishman **Thomas Willis** provided a description of the structure of the brain and spinal cord, as well as the connected anterior and posterior nerve branches, while the Italian, **Marcello Malpighi** – one of the forefathers of microscopic anatomy – presented detailed descriptions of the arrangement of grey matter and nerve fibers in the spinal cord. In turn, **Descartes**, speculating about the nature of animals and humans, established foundations for the modern understanding of reflexes; he perceived the brain as a precise control mechanism continuously connected with the soul, which nests in the pineal gland.

At the end of the following century, the Italian **Luigi Galvani** discovered electrical phenomena occurring in animal tissues, while the Austrian **Anton Mesmer** assured that "animal magnetism" can penetrate the entire spiritual and physical sphere of a human being. **Franz Gall** was also famous; while studying the brain structure, he demonstrated that particular psychological activities and vital functions are closely related with and determined by its surface structure, which became a foundation for phrenology – a discipline known not only in the field of science. Today, there are no doubts that this was the beginning of the theory behind the functional localization within the brain.

Gradually accumulated knowledge became the starting point for experimental programs that were conducted with increasing intensity as part of experimental physiology, a discipline developing since the beginnings of the 19th century. One of its forefathers was the French physician, **César Julien Jean Legallois (1770–1814).**

Legallois provided first evidence of the metameric organization of spinal cord, where each of its segments constituted a neuronal center for a particular functional region. At the same time, he speculated that there must be a separate "nervous force" that controls significant vital functions and originates both from the brain and the bone marrow.

Another Frenchman, **Marie Jean Pierre Flourens (1794–1867),** was an avid supporter of the localization theory. In a series of experiments involving triggered changes in the individual regions of the brain and spinal cord, he observed an impact on motor functions, spatial orientation, susceptibility to stimuli or changes in the behavior of animals. He demonstrated that the removal or serious damage of both brain hemispheres led to cessation of motor functions and elimination of the entire aspect of the sense-perception. Depriving an animal of the cerebellum triggered balance and motor coordination disorders. Cutting the spinal bulb deprived the subject of motor functions. Destruction of the brain stem resulted in death.

The discoveries made by the French surgeon and anthropologist, **Pierre Paul Broca (1824–1880)**, and the German psychiatrist and neurologist, **Carl Wernicke (1848–1905)**, provided further evidence confirming the existence of specific localizations for the individual brain functions. Meanwhile, two German physicians, **Gustav Theodor Fritsch (1837–1927)** and **Julius Eduard Hitzig (1839–1907)**, carried out a series of experiments in dogs meant to determine the potential relationship between external electrical stimulation and physiological functions of the brain. Hitzig, then a neurologist and psychiatrist at a garrison hospital, took an interest in the potential application of electrostimulation in clinical therapy. For this purpose, he designed an apparatus that he then used in the treatment of his patients. Checking the level and nature of the patients' reactions to stimuli generated by the apparatus, he observed that stimulation of the occipital region of the head invariably triggered eyeball movements. Intrigued by this phenomenon, he decided to carry out experiments in animals and selected rabbits as his subjects. Unfortunately, he did not succeed. Therefore, Hitzig turned to Fritsch, an anatomist and physiologist, for advice and help.

Joining their forces, both physicians decided to use low voltage current, that is – as it was described – barely sensible at the tip of the tongue. At the same time, they decided to perform these experiments in dogs. Already after the first trials, the scientists could state that stimulation of certain regions in the cerebral cortex results in a pronounced muscle reaction. At that moment, they could trigger extension and flexion of the dog's limbs, as well as pronounced movement of the mouth and neck muscles. This allowed them to draw a general conclusion that a part of the cortex is permanently related to movement functions, while other parts do not exhibit such a relationship. At the same time, these scientists observed that motor areas are generally located in the anterior part of the cortex. Thereby, the existence of the so-called *motor cortex* was proved.

Meanwhile in the United Kingdom, **David Ferrier (1843–1928)**, who was aware of the results obtained by Fritsch and Hitzig, conducted experiments in animal models that involved dogs, rabbits and guinea pigs since the beginning of the 1870s. This provided the English physician with significant reference material over a relatively short period of time. The results obtained were considered interesting enough for the Royal Society to grant Ferrier funds for extending the experimental program to include macaques. Shortly after, the scientist proved in a spectacular manner that stimulation of various animal species with the use of low voltage current allows to determine with high accuracy a detailed map of motor functions. If the pre-determined areas were surgically removed or damaged, a loss of functions that were previously triggered by stimulation occurred invariably. Ferrier was also able to demonstrate that intensive stimulation of the motor cortex regions resulted in a characteristic sequence of the neck, mouth and limb movements, which indistinguishably resembled the course of an epileptic seizure. This and other evidence supporting the localization model of neurophysiological functions of the brain were presented by the British scientist in a book titled ***The Functions of the Brain*** **(1876).**

Studies carried out by Fritsch, Hitzig and Ferrier led directly to establishing new directions for brain studies, among which especially two proved to be the most meaningful in the next decades. The first one was focused on the issue of electrophysiological phenomena, whereas the second was related to the cytoarchitectonics of the cerebral cortex. These provided the basis for a third one that was sought to explain the significant nature of the nerve cells – neurons.

Today, it is difficult to unequivocally determine who was the first to draw attention to the phenomenon of spontaneous electrical activity of the brain. This could be Ferrier's student, **Richard Caton (1842–1926)**, who attended the meeting of the British Medical Association in Edinburgh as soon as in 1875, where he proved that he recorded pronounced inclinations of the galvanometer in all observations he carried out. The external grey matter surface usually exhibited a positive potential. In turn, negative potential appeared when a deeper region of the grey matter became active. Caton stated that the above observations could prove the relationship between electrical phenomena and brain functions.

Over subsequent years, the British scientist continued his studies on various animal species, including apes, cats and rabbits, although with varied success; he was however gradually accumulating more and more evidence to support his hypothesis. In 1887, during the sessions of the Congress in Washington, he presented convincing evidence confirming the influence of light stimuli on changes in the recorded brain potential.

However, Caton's studies did not receive much recognition among physiologists.

In any case, there is no indication that **Adolf Beck (1863–1942)** was aware of the works of his British fellow. This talented experimenter, a student and assistant to **Napoleon Nikodem Cybulski** and later a professor at the University in Lviv, described in his report in October 1890 the spontaneous and induced electrical phenomena occurring in animal brains. He then determined that posterior cortical regions react to visual light stimulation, correctly located cortical regions sensitive to sound and also those exhibiting activity when different areas of the skin surface were irritated with electrical pulses. Beck wrote about the observed potential change occurring as a result of sensory stimulation. As he proved, evoked potential triggered inhibition of electrical waves transitions previously triggered by electrical stimulation of the sciatic nerve or by peripheral stimulation with light and sound stimuli. At the same time, Beck stated that individual sensory regions of the cortex do not have strictly outlined boundaries and often overlap. It is beyond any doubt that Beck was the first who described the phenomenon of desynchronization in the EEG trace.

The text written by Beck inspired a Viennese scientist, **Ernst Fleischl von Marxow (1846–1891)**, who, as soon as in 1882, observed that the stimuli exciting the sensory organs lead to changes in the potential distribution. For unclear reasons, he postponed the publication of results, a record of which he stored in an armored cabinet! He only reacted to the text written by the Polish physiologist. Thereby, a dispute over priority was initiated and finally ended by Caton who referred to his writings from the 1870s.

From today's perspective, the works of **Caton, Beck and Marxow** were of fundamental significance for further studies into brain neurophysiology.

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