Історія медицини

History of medicine

ISSN: 2411-6181(on-line); ISSN: 2311-9896 (print)
Current issues of social studies and history of medicine. Joint Ukrainian-Romanian scientific journal, 2017, №:2(14), P. 149-152
***UDK** 614.2:351.77*
***DOI** 10.24061/2411-6181.2.2017.58*

ІСТОРИЧНИЙ ОГЛЯД ЕЛЕКТРОФІЗІОЛОГІЧНИХ МЕТОДІВ ДОСЛІДЖЕННЯ

Валентин ШВЕЦЬ , Софія БОШТАН, Лілія БОРЕЙКО,
ВДНЗ України «Буковинський державний медичний університет»,
м. Чернівці (Україна),
bsofija@mail.ru

HISTORICAL OVERVIEW OF ELECTROPHYSIOLOGICAL METHODS.

Valentyn SHVETS, Sofia BOSHTAN, Lilia BOREIKO,
Higher State Educational Establishment of Ukraine
„Bukovinian State Medical University", Chernivtsi (Ukraine),

Швец Валентин, Бoштан София, Борейко Лилия. Исторический Обзор электрофизиологических методов исследования. Трудно переоценить значение для физиологии нервов, мышц и центральной нервной системы имели электрофизиологические исследования.

Впервые мысль о том, что в животном организме происходят какие-то электрические явления была высказана Л. Гальвани в 1786 г. Основанием для нее служил эксперимент, в котором Гальвани наблюдал сокращение мышцы. Несмотря на то, что упомянутые здесь исследования, являлись основополагающими, электрофизиология как самостоятельная область исследования оформилась лишь в середине 40-х годов XIX в. благодаря классическим исследованиям Э. дю Буа-Реймона. Обладая хорошей подготовкой в области физики, Э. дю Буа-Реймон значительно усовершенствовал электроизмерительную аппаратуру, провел весьма точные эксперименты и установил ряд закономерностей, характеризующих электрические явления в мышцах и нервах. В.Ю. Чаговець впервые в мировой науке применил теорию электролитической диссоциации Аррениуса для электрофизиологии, сформулировал ионную теорию происхождения биоэлектрических потенциалов (1903) и предложил конденсаторную теорию электрического раздражения живых тканей (1906). Резюмируя, нужно отметить, что, несмотря на примитивную технику исследования, выдающимся ученым того времени удалось создать основы современных знаний в этой области науки.

Ключевые слова. *нейрофизиология, электрофизиологические исследования, история электрофизиологии.*

Introduction. An electrophysiological study was difficult to overestimate for the physiology of the nerves, muscles and central nervous system. Electrophysiology is the direction of research in physiology, the subject of whose interests are electrical phenomena in living structures and it is the section of physiology that studies the electrical phenomena in the body in its various activities: voluntary and involuntary induced and spontaneous on the micro and macro range from research bioelectrical activity mediated by ionic processes in synapses and the membranes of individual cells and fibers, to analysis of the results of printing registration to assess the integrative functions of the whole organism. Currently electrophysiology itself is both methodical base of many branches of physiology and psychology, and medicine and biophysics[1].

The main material. The successes of electrophysiology throughout its history are inextricably linked with the current achievements of physics and technology and improvements in electrical measuring and electroregistration equipment. Any new achievement in this field was immediately accepted "for service" by electrophysiologists. One example can be the following fact, referring to the early period of electrophysiological studies[2].

The development of electrophysiology is traced from the early beginnings represented by the work of the Dutch microscopist, Jan Swammerdam, in the 17th century through the first notion of an aqueous transmembrane pore as a substrate of excitability made by Luigi Galvani in late 18th century to the invention late in the 20th century of the patch-clamp technique by Erwin Neher and Bert Sakmann.

For the first time the idea that some electrical phenomena occur in the animal body was expressed by L. Galvani in 1786. The basis for it was an experiment in which Galvani observed a contraction of the muscle when a two-metal arc was applied to it and a suitable nerve to it. Galvani's interpretation of his experience was refuted by A. Volta, who convincingly showed that the source of electricity was the contact of two different metals, and not living tissue, which in this case plays the role of a wet conductor. However, Galvani soon after confirming his idea made the experience of applying the sciatic nerve to the abdomen of the gastrocnemius muscle of the frog and saw that this was often accompanied by a contraction of the muscle. First electric potentials arising in the brain in response to stimulation of a sensory organ R. Caton investigated in 1875 he imposed a recording electrode directly on the cerebral cortex of the animal, the other - on the surface of the brain and cut using light as a stimulus lamps, observed changes in the potential difference between the electrodes. Caton also include the merit of opening an electroencephalogram (EEG) in the same experiments. By placing both electrodes on intact brain, he discovered the potential difference continuous

[1] Gary S. Aston-Jones, George R. Siggins Electrophysiology, URL: http://www.acnp.org/g4/GN401000005/
[2] Del Castillo J, Hime J, Pérez-Acevedo N.A "Short history of electrophysiology and its techniques", Section III, *Electrophysiological instruments and techniques*, P R Health Sci J, 1998, N. 17(1), P. 81-88.

fluctuations in the absence of stimulation. It was also EEG. For the first time evoked potentials (EP) in the cerebral cortex recorded by Neminskyy (1913.1925) with a string galvanometer. In 1797 the discovery of L. Galvani was confirmed by the German naturalist A. Humboldt.

In 1837, the Italian physicist and physiologist K. Matteucci discovered the difference in electrical potentials between the damaged and intact muscle parts. He also showed that with contraction, the muscle generates an electric current that can be the cause of the excitation of another neuromuscular drug.

In 1848 the German physiologist E. Dubois-Reymond, using more advanced means of experimental technique, confirmed the existence of a potential difference between the damaged and undamaged parts of the unexcited muscle or nerve, and also that the "fault current" decreases upon excitation. This "negative fluctuation" was subsequently called the "action potential". The work of E. Dubois-Reymond laid the foundation for modern electrophysiology.

In the history of world electrophysiology, the indisputably outstanding works of Russian physiologists of contemporaries E. Dubois-Reymond and his immediate followers are not reflected. This fact is difficult to explain by the ignorance of the Russian physiologists by the European physiologists, the unknown or unpublished work of these scientists by Russian scientists. In particular, it is impossible to name unknown works on electrophysiology of the Russian physiologist Ivan Mikhailovych Sechenov and a number of his contemporaries. In 1856-59 he worked in the laboratories of I. Müller (Berlin), E. Dubois-Reymond and F. Hoppe -Seyler (Berlin), O. Funke (Leipzig), K. Ludwig (Leipzig), G Helmholtz (Heidelberg)[3]. There he had a real opportunity not only to study the achievements of physiology, electrophysiology of that time, but also to critically evaluate these achievements. Later, in 1862 I.M Sechenov in his book "On Animal Electricity", advanced arguments against the generally accepted at the time of the concept of bioelectrogenesis E. Dubois-Reymond. He also criticizes this criticism in his lectures "On Animal Electricity" at the Military Medical Academy, for which he was awarded the Demidov Prize of the St. Petersburg Academy of Sciences (1863). A feature of the views of Western European scientists on the causes and mechanisms of electrical phenomena in living tissues was that they were based on elementary physical models. At the same time, living entities and phenomena were identified with inanimate ones, and the truth of physical prerequisites was not questioned. These concepts, much simplified in comparison with reality, about the nature of "living electricity" were called the theory. (On the same fundamentally incorrect methodological purely physical positions are many modern electrophysiologists who absolutize the modern physicochemical models of electrogenesis). Refuse then the Western physiologists from this deliberately incorrect rigid installation, and electrophysiology, even without changing the direction of its development, could get much better results. But for this it would be necessary either to recognize the ideas of I.M Sechenov about the nature of living electricity, or at least to use these ideas without specifying the name of their creator. And the idea of I.M Sechenov is simple and is reflected in the quote from the above-mentioned book: "The electrical phenomena of muscles and nerves are the products of their life." It would seem, what is special about this seemingly insipid phrase? A feature is that, unlike E. Dubois-Reymond, who "... a number of phenomena boiled down to the molecular structure of the organ that produces them ..." I.M. Sechenov considered these phenomena "products of life". Although, is it possible to reproach E. Dubois-Reymond and his contemporaries in that they did not see the difference between science, physics and life, if the majority of modern material scientists adhere to the same purely physical primitive views on the relations of reality and perceptions of it. Shumovskii's work (Shumovsky, Medical Gazette, "On Pairelectronic Phenomena in Muscles and Nerves", 1862) on the effect of cooling on resting currents was published in 1862[4].

Later, in 1862 I.M Sechenov in his book "On Animal Electricity", advanced arguments against the generally accepted at the time of the concept of bioelectrogenesis E. Dubois-Reymond[5]. He also criticizes this criticism in his lectures "On Animal Electricity" at the Military Medical Academy, for which he was awarded the Demidov Prize of the St. Petersburg Academy of Sciences (1863). A feature of the views of Western European scientists on the causes and mechanisms of electrical phenomena in living tissues was that they were based on elementary physical models. At the same time, living entities and phenomena were identified with inanimate ones, and the truth of physical prerequisites was not questioned. These concepts, much simplified in comparison with reality, about the nature of "living electricity" were called the theory. (On the same fundamentally incorrect methodological purely physical positions are many modern electrophysiologists who absolutize the modern physicochemical models of electrogenesis). Refuse then the Western physiologists from this deliberately incorrect rigid installation, and electrophysiology, even without changing the direction of its development, could get much better results.

But for this it would be necessary either to recognize the ideas of I.M Sechenov about the nature of living electricity, or at least to use these ideas without specifying the name of their creator. And the idea of I.M Sechenov is simple and is reflected in the quote from the above-mentioned book: "The electrical phenomena of muscles and nerves are the products of their life." It would seem, what is special about this seemingly insipid phrase? A feature is that, unlike E. Dubois-Reymond, who "... a number of phenomena boiled down to the molecular structure of the organ that produces them ..." I.M. Sechenov considered these phenomena "products of life". Although, is it possible to reproach E. Dubois-Reymond and his contemporaries in that they did not see the difference between science, physics and life, if the majority of modern material scientists adhere to the same purely physical primitive views on the relations of reality and perceptions of it. Shumovskii's work (Shumovsky, Medical Gazette, "On Pairelectronic Phenomena in Muscles and Nerves", 1862) on the effect of cooling on resting currents was published in 1862.

The first work in Russia, which initiated a purposeful explanation of the causes and mechanisms of the emergence and existence of electrical phenomena in living tissues, should be considered the work of V. Yu. Chagovts - junior contemporary I.M Sechenov.

[3] Verkhratsky A, Krishtal O.A, Petersen O.H. “From Galvani to patch clamp: the development of electrophysiology”, *Pflugers Arch*, 2006, N. 453(3), P. 233-247.

[4] Nilius B. “Pflügers Archiv and the advent of modern electrophysiology. From the first action potential to patch clamp”, *Pflugers Arch,* 2003, N. 447(3), P. 267-271.

[5] Kostyuk P.G., Winter V.L., Magura J.S., Miroshnichenko M.S., Shuba M.F. Biophysics, Kyiv, CUP "Kyiv University", 2008, 567 p.

This was his publication (1896) when he was still a third -year student of the Military Medical Academy. Subsequent work was carried out by him in the period from 1898 (dissertation) to 1906 (Essay on Electrical Phenomena on Living Tissues, Issue II. Electrophysiology of the Nervous Process, Petersburg), when he was an employee of I.R. Tarkhanova at the Department of Physiology of the Military Medical Academy.

V.Yu. Chagovets made a follower of the idea of I. Sechenov described above about the origin of electrical phenomena in living tissues. Through logical reasoning, clothed in clear mathematical calculations, he theoretically proved that the ultimate cause of the existence of the difference in the potentials of living tissue is its metabolism - the central phenomenon of life. At the same time, the values of electrical phenomena calculated on the basis of the theoretical model ("fault current") were surprisingly identical with the experimental data. By the way, V.Yu. Chagovets, who completely overthrew the views of E. Du Bois-Reymond and his Western European predecessors and followers, was dedicated to the memory of E. Dubois-Reymond, who two years earlier had left for another world. We will not find Chagovets in the works of Western scientists, and even in the works of those who were subsequently nominated as Nobel laureate in the field of electrophysiology[6]. Another important achievement of V.Yu. Chagovets in electrophysiology and physiology in general had a physiological interpretation of the empirical relationship between the previously "inexplicable" intensity and the duration of the effect causing excitation (the Goorweg-Weiss curve). V.Yu. Chagovets formulated (1906) a more adequate mathematical model describing these relations, and showed that the dependence of Goorweg-Weiss is a particular case of his model.

So the model of the relationship between intensity and duration of exposure, which is of great importance both in explaining the natural transmission of excitation, and in explaining the effect of electric current on the body, should rightly be called the Chagovets-Goorweg-Weiss model. A few years later in 1909 the French physiologist Louis Lapik proposed chronaxy as a quantitative point measure of the excitability of a living object. Significant, but unrecognized in the West, successes of Russian electrophysiology were associated with the works of Bronislav Fortunatovich Verigo (1860-1925), an employee of I.R. Tarkhanov in the Department of Physiology of the Military Medical Academy. In his thesis ("On the action of a discontinuous and continuous galvanic current on the nerve (an attempt to explain the physiological phenomena of an electroton", 1888), performed partly under the guidance of I.M Sechenov in his laboratory at the University of St. Petersburg, B.F Verigo laid the foundations of modern ideas about the accommodation of excitable tissues, the patterns of influence of subthreshold effects.

So in 1888 the German physiologist J. Bernstein[7] (Julius) invented a differential reotom, a device for studying the currents that accompany the excitation of living tissue. With his help, J. Bernstein estimated the time characteristics of the action potential: the latent period, the rise and fall time of the action potential. In 1875 the French physiologist E.J. Marey used a capillary electrometer to record electrical heart phenomena, and the Russian and Soviet physiologist A.F. Samoilov in 1908 applied this device to the study of skeletal muscle. In the seventies of the 19th century I.R. Tarkhanov uses the telephone as a device for detecting the currents of muscle action in humans and animals, and in 1884 the Russian physiologist N.E. Vvedensky used this experience in his studies of action potentials.

So, the first work, which initiated a purposeful explanation of the causes and mechanisms of the emergence and existence of electrical phenomena in living tissues, should be considered the work of V. Yu. Chagovets, performed in 1896 in the laboratories of Russian physiologists I.M. Sechenov and I.R. Tarkhanov in the Military Medical Academy and St. Petersburg University.

Later Yu. Bernshtein (1902) formulated the membrane-ion concept of the electrogenesis of living tissues, and in 1908 the model of bioelectrogenesis of V. Nernst was published[8]. All these ideas were developed by a number of other scientists (Hodgkin FL, Huxley AF, 1939, 1952, Boyle PJ, Conway EJ, 1941 and many others) and led to modern representations (the Goldman-Hodgkin-Katz model) on the origin of the rest potential And the action potential in the cells of excitable tissues.

Significant contribution to the development of electrophysiology was also made by Russian and Soviet physiologists Vasiliy Yakovlevich Danilevsky (1852-1939), Daniil Semenovich Vorontsov (1886-1965), Alexander Borisovich Kogan (1912-1989), Platon Grigoryevich Kostyuk (1924-1966), Mikhail Nikolaevich Livanov (1907-1970) and many others. Under the leadership of D.S. Vorontsov at the Institute of Animal Physiology started working eminent physiologists Platon G. Kostyuk (1924-2010) and Vasily Skokie (1932-2003). The work of these scientists associated with the first use of intracellular electrodes. During the 1952-1959 P.H. Kostyuk spent a large series of studies of excitation and inhibition in twoneurons (monosynaptic) reflex arc of the spinal cord. In these electrophysiological study, researchers for the first time in the Soviet Union were used intracellular microelectrode. In neurophysiology they were introduced in 1951 in the laboratory of British physiologist by D. Ekkls, and since 1958 have become the main tool for removal of intracellular responses of neurons in the central nervous system and study processes occurring in them. In conducting this research P.H. Kostyuk received accurate information relative to the duration of synaptic delay and single course exciting and inhibitory influences.

These results were summarized in the monograph "Reflex arc" (1959), which to date is a classic leadership not only on the physiology of the spinal cord, but the overall physiology of the neuron. The Presidium of the USSR in 1960 marked the work and the monograph prize of I.P. Pavlov. If P.H. Kostyuk more interested in studies of neurons in the central nervous system, on the advice of D.S Vorontsov V.I. Skok engaged in similar studies of neurons in the peripheral autonomic nerve ganglia.

This was expected that the most common electrophysiological properties of the central and peripheral neurons are quite the same and autonomic ganglia neurons advantage

[6] Kornreich B.G. "The patch clamp technique: principles and technical considerations", *J Vet Cardio,* 2007, N. 9(1), P. 25-37.
[7] Nilius B. "Pflügers Archiv and the advent of modern electrophysiology. From the first action potential to patch clamp", *Pflugers Arch,* 2003, N. 447(3), P. 267-271.
[8] Piccolino M. "Animal electricity and the birth of electrophysiology: the legacy of Luigi Galvani", *Brain Res Bull,* 1998, N. 46(5), P. 381-407.

lies in the fact that they are more accessible and interneuron connections they minimal[9]. In 1959 V.I. Skok was first performed intracellular removal of the natural electrical activity of neurons sympathetic and parasympathetic ganglia with preserved blood supply and nerve connections to the spinal cord.

Conclusions. It was found that the excitation of the nervous centres accompanied by electrical phenomena, then there is the idea of the ability to use electrophysiological methods to study the problem of localization of functions in the brain. This idea was expressed, and tried to justify his experiments B. F. Verigo (1889) and A. Beck (1890). Verigo, as if foreseeing the future development of the electrophysiology of the brain, wrote that the electrophysiological method of studying the problem of localization can have a "huge advantage over the other because of its complete objectivity". The subject of study in electrophysiology is also the activity of the nervous and other elements of their constellations, and individual organs and the whole organism under the action electrical current. Today actually electrophysiology is both methodological basis of many sections of physiology and psychology, and, in addition, medicine and Biophysics.

Швець Валентин. Бoштан Софія, Борейко Лілія. Історичний огляд електрофізіологічних методів дослідження. Вперше думка про те, що в тваринному організмі відбуваються якісь електричні явища була висловлена Л. Гальвані в 1786 р Підставою для неї служив експеримент, в якому Гальвані спостерігав скорочення м'яза. Трактування, дане Гальвані, було спростовано А. Вольтом, який переконливо показав, що джерелом електрики був контакт двох різних металів, а не жива тканина, яка в даному випадку грає роль вологого провідника. Незважаючи на те, що згадані тут дослідження, були основними, електрофізіологія як самостійна галузь досліджень оформилася лише в середині 40-х років XIX ст. завдяки класичним дослідженням Е. дю Буа-Реймона. Володіючи хорошою підготовкою в галузі фізики, дю Буа-Реймон значно вдосконалив електровимірювальну апаратуру, провів точні експерименти і встановив ряд закономірностей, що характеризують електричні явища в м'язах і нервах.

Успіхи електрофізіології протягом всієї її історії нерозривно пов'язані з поточними досягненнями фізики і техніки та вдосконаленнями електровимірювальної і електрореєструючої апаратури. Будь-яке нове досягнення в цій галузі негайно приймалося "на озброєння" електрофізіологами. Одним із прикладів може слугувати такий факт, що відноситься до раннього періоду електрофізіологічних досліджень. Коли Швейггер побудував мультиплікатор (1820), а Ампер відкрив, явище астазії магнітної стрілки (1821), флорентійський фізик Нобілі (1827), з'єднавши мультиплікатор і астатичну пару стрілок з ділянкою тулуба і лапкою жаби, виявив наявність електричного струму. Цей струм він назвав власним струмом жаби". Значну кількість фактів, які доводили справедливість відкриття Гальвані, отримав К. Маттеуччі (1837-1840), який використовував у своїх дослідах як мультиплікатор, так і "живий реоскоп".

В.Ю. Чаговець уперше в світовій науці застосував теорію електролітичної дисоціації Арреніуса для електрофізіології, сформулював іонну теорію походження біоелектричних потенціалів (1903) і запропонував конденсаторну теорію електричного подразнення живих тканин (1906). За пропозицією В.Ю. Чаговця завідувачем кафедри фізіології людини Київського медичного інституту було обрано Данила Семеновича Воронцова (1886– 1965). З 1945 по 1956 роки Д.С.Воронцов завідував відділом загальної фізіології інституту і одночасно працював професором кафедри фізіології тварин і людини. Упродовж цих років Д.С. Воронцов віддає свою енергію і величезний досвід справі виховання молодих фізіологів та розвитку фізіологічної науки в університеті. Під його керівництвом відділ загальної фізіології став одним із провідних центрів електрофізіології не лише в Україні, але і в Радянському Союзі. Під керівництвом Д.С. Воронцова в Інституті фізіології тварин розпочинали працювати видатні фізіологи Платон Григорович Костюк (1924–2010) і Василь Іванович Скок (1932–2003). Роботи цих вчених пов'язані з першим використанням внутрішньоклітинних електродів. Упродовж 1952–1959 рр. П.Г. Костюк провів великий цикл досліджень з вивчення процесів збудження і гальмування в двонейронній (моносинаптичній) рефлекторній дузі спинного мозку. Результати цих досліджень були узагальнені в монографії "Двохнейронна рефлекторна дуга" (1959), яка до теперішнього часу є класичним керівництвом не лише з фізіології спинного мозку, але і загальної фізіології нейрона.

Резюмуючи, слід зазначити, що, незважаючи на примітивну техніку дослідження, видатним вченим того часу вдалося створити основи сучасних знань в цій області науки.

Ключові слова: нейрофізіологія, електрофізіологічні дослідження, історія електрофізіології.

Швець Валентин *– д. біол. н., проф. кафедри фізіології імені Я.Д. Кіршенблата ВДНЗ України «Буковинський державний медичний університет». Коло наукових інтересів: фізіологія нирок, вплив важких металів на нирки, історія медицини. Автор 110 наукових праць, статей, співавтор 2 підручників, монографії.*

Shvets Valentyn *– Doctor of biological science, professor of the physiology department named after of Ya. D. Kirshanblat of Higher State Educational Establishment of Ukraine „Bucovinian State Medical University”. Research interests: effect of heavy metals on the kidneys, the history of medicine. Author of 110 scientific publications including 2 text-books and monographs.*

Боштан Софія *— асистент кафедри фізіології ім. Я. Кіршенблата ВДНЗ України «БДМУ». Коло наукових інтересів: історія медицини, історія фізіології, нейродегенеративні зміни на тлі розвитку цукрового діабету, патофізіологія цукрового діабету. Автор біля 10 наукових статей та публікацій.*

Boshtan Sofiia *— assistant of physiology department named after Y. Kirshenblata of Higher State Educational Establishment of Ukraine „Bucovinian State Medical University”. Co-author of 10 scientific articles. Research interests: history of medicine, pathogenic factors influence on the structure and function of the human nervous system and diabetes.*

Борейко Лілія *— к. мед. н., доцент кафедри догляду за хворими та вищої медсестринської освіти ВДНЗ України «БДМУ». Коло наукових інте ресів: історія медицини, історія медсестринства. Автор біля 90 наукових статей та публікацій.*

Boreiko Lilia *— PhD, Assistant of professor of Nursing and Higher Nursing Education department of Higher State Educational Establishment of Ukraine „Bucovinian State Medical University”. Co-author of 90 scientific articles. Research interests: history of medicine, history of nursing.*

Received: *29. 03. 2017*
Advance Access Published: *April, 2017*

[9] Neher E., Sakmann B. “The patch clamp technique”, *Sci Am*, 1992, N. 266(3), P. 44-51.