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REVIEW ARTICLE

The Erratic History of Electroencephalography

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ABSTRACT

The history of electroencephalography begins around 1850 with a supposition of Emil du Bois-Reymond concerning the transfer of information by electric currents over the nerve to the effector. Luigi Galvani in Bologna showed with his frog legs experiments 1786 indeed the existence of animal electricity. Richard Caton in Liverpool placed in 1875 as the first electrodes on the brains of rabbits and was able to record the electrical brain activity. Caton received little attention for his research and left with his animal experiment aversion the field. In contrast to Caton, Adolf Beck in Kraków, got a huge attention for his recordings of the electrical activities of the frog brain. The most interesting response to his important paper of 1890 came from Vasili Danilewski from Charkov, mentioning his unpublished doctoral thesis of 1877. He did his dog recordings before Beck, but one year after Caton who send him his abstract, remaining that he discovered before him electric brain waves. Colleagues of Danilewski such as Prádwicz-Neminski from Kyiv performed also adequate work in this field, but due to Stalin's dogmatic regime, electrophysiology became prohibited and disappeared in Russian. Jewish Adolf Beck, now professor in Lwów, experienced there in war time in 1940 dangerous times and ultimately the Nazi's came for him. His son succeeded to hand him a cyanide capsule to save him from the gas chamber. By the tragedies of the war in Poland and the split between East and West Europe, Beck and his work go lost. Hans Berger began in Jena with brain recordings in humans and in 1927 he exclaimed 'I can record brain actvity from an intact human skull'. This was replicated abd agreed upon by Edgar Adrian in 1934, and Berger received international fame, but not in Germany. The often authoritative Berger hated the Nazi's and was suspended by the regime. He came in a severe depression and ended his life by hanging in June 1941. In this heavy war time, electrophysiology moved to the USA. Frederic and Erna Gibbs at Harvard got, with their studies of epilepsy in 1934 a breakthrough in clinical electroencephalography, Alfred Loomis and Herbert Jasper used the electrical brain actvity to identify several stages of sleep. Later, Jasper performed in Montreal, with neurosurgeon Wilder Penfield, important research on focal epilepsies. After the second world war, around 1950, electroencephalography blossomed up, in the USA as well as in Europe. Recording electroencephalograms for studying the functioning of the brain and in particular investigating domains of sleep and epilepsy. It became common that almost every university and hospital had a resording device. That electroencephalography was a mature methodology, was demonstrated by great discoveries for example through the finding of REM sleep by Kleitman and Aserinski in 1953.

Prologue

The German physiologist Emil du Bois-Reymond [1] (1818-1896) affiliated to the University of Berlin (Prussia) hypothesized around 1840 that the transmission of an excitatory neuronal proces from a nerve to an effector could primarely take place through electric currents. He put forward the general conception that a living tissue, such as a muscle, might be regarded as composed of a number of electric fibers, and that the electric behavior of the muscle was produced by these units. In this way Du Bois-Reymond ultimately believed in animal electricity transmitting the messages from a sensor via the nerve to the muscle. In !849 the great Hermann von Helmholtz [2] (1821-1894) working in Königsberg measured in 1849 the speed at which a signal is carried along a nerve fibre. He used a dissected sciatic nerve of a frog and a calf muscle to which it is attached, and used a galvanometer as a sensitive timing devise. Von Helmholtz reported conduction speeds in the range of around 30 meters per second and supported the idea of animal electricity of his friend du Bois-Reymond. These two scientists, both pupils of Joannes Müller, the man of the 'law of the specific nerve energies', paved the way for electrophysiological studies.

Luigi Galvani [3] (1737-1798) worked already with peripheral nerves and musculature. After an incident when Galvani touched a frog nerve with a metal scalpel at the same time that a spark came, twitched the frog's body. He came, just as du Bois-Reymond and Helmholtz, to the conviction that the nerve worked as a conductor of electricity, like a wire from a generator. After much research Galvani showed the existence of animal electricity. But the suggestion that the brain transmits information by animal electricity from nerves to body, is miles away from the recording of electrical waves from the skull of living organisms, as is done in electroencephalography. It took years of intensive research, to cover this long and difficult pathway from the beginning in 1800 with the discovery of Galvani of animal electricity, and ended in 1950 by recording electrical waves of the skull of animals and humans by the method of electroencephalopathy, In six sections it is scheduled how the idea of animal electricity was transformed into a scientific instrument for brain measuring and diagnosis.

SECTION 1. LUIGI GALVANI: DISCOVERY OF ANIMAL ELECTRICITY

Luigi Galvani [3] (1737-1798) (Fig.1) was an Italian biologist and neuroscientist working at the University of Bologna as a professor of anatomy. He pioneered in the field of bioelectricity and discovered what he called 'animal electricity'. This was a famous finding, that arose from an accidental experiment showing that dead frog legs twitched when two pieces of different metal completed the circuit. Galvani believed that he had reanimated a body because the leg conducted electricity. On September 20 in the year 1786, when he hung some fresh frog legs on brass hooks from the iron railings of his garden, he unexpectedly discovered the powers of bimetallic electricity. Galvani looked upon the nerve as a conductor of electricity, like a wire from a generator and he believed that the muscles contained electricity secreted by the brain and distributed by the nerves to the muscles. Galvani interpreted that as an alternative form of electricity in living tissues and called that 'animal electricity'.

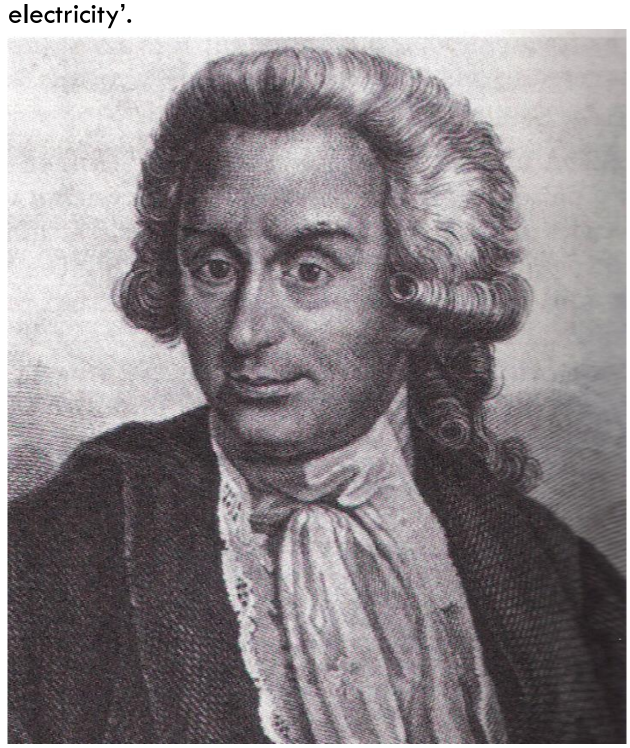

Fig.1. Luigi Galvani, a pioneer in the study of electrical phenomena in animals.

Initially Galvani's work became popular in the scientific field and that incited jealousy to a close colleague named Alessandro Volta [4] (1745-1827), a professor of physics at the University of Pavia. Volta doubted the interpretation of Galvani and did not believe the biological nature of the muscle contraction by animal electricity. He supposed that this contraction phenomenon was derived by the contact of two different metals, producing the electric effect. To prove this, Volta built a battery consisting of alternating disks of zinc and copper separated by cloth soaked in salty water. This 'voltaic pile' was the first electric battery, allowing streams of current, a marked improvement for scientists in electricity. Volta is credited as the inventor of the electric battery, which is seen as a major contribution to the science of physics. He invented the 'voltaic pile' in 1799 and reported the results of his experiments in 1800 to the president of the Royal Society. It made Volta famous and gave him a major influence. Both Galvani and Volta had no problems with the concept of bimetallic electricity, but the heavy debate between the two was the suggestion of Galvani that the electricity came from the animal itself (organic electricity), while Volta assumed that the bimetallic electric battery served as a source of current (anorganic electricity).

Galvani published his first frog contraction experiments in 1791. They had a major impact to the field. Galvani's conception of animal electricity was insightful, because he proposed that the brain conducted electricity in order to generate muscle movements. Indeed this position was not radically different from that of the ancients, who viewed the brain as a secreting gland of mysterious spirits. Galvani formulated the conception of his experiment by substituting 'mysterious spirits' simply by 'mysterious electricity'. The explanation of Galvani was initially the leading view and dominated in the community. After the invention and experiments with the 'pile' of Volta in 1800, together with the negative words of the influential Volta about Galvani's explanation of the concept of animal electricity, the situation slowly changed, The controversy between the former friends escalated completely and they became almost rivals. The controversy between the two rivals switched even to the community and the adherents of animal electricity were totally against the advocates of metallic electricity. Volta's view became more and more dominant over Galvani's opinion in this hot dispute. And when the work of Galvani was pushed into the field of quackery, or even into the sphere of dark science with mysterious fluids and spirits, it became even more worse, instead that it was the beginning of a new electrophysiological science. Galvani had to defend his claim concerning the existence of a distinct animal electricity more and more. Gradually, fatigue and frustration became too much for Galvani. and after personal tragedies, such as the death of his wife and the entry of Napoleon in North-Italy in 1796, he was completely fed up and decided to quit his defense. Academics were forced to take an oath of allegiance to Napoleon, but Galvani refused and had to leave his academic position. Volta, who was as a noble man a personal friend of Napoleon, was, perhaps, involved in the decline of Galvani. On December 4, 1798 Luigi Galvani died in poor and needy circumstances in obscurity. However, with the death of Galvani the nagging question of the active electrical contribution to animal muscles remained. The question concerning the existence of animal electricity was not solved.

Giovanni Aldini [5] (1762-1834) a nephew of Galvani who also lived in Bologna, took up his uncle's work after he died with the will to defend his reputation and to clear up the concept of galvanism. He began experimenting with dead frogs, but soon he was looking for something more exciting. Ultimately, he took human corpses with a more sophisticated nervous system, such as decapitated criminals and other dead bodies. When he applied electrical impulses to these corpses, all kind of muscles began to move. With these positive results for animal electricity, Aldini traveled extensively throughout Europe, spending much time to defend the concept of his uncle's animal electricity concept, against the incessant attacks of Volta. With Aldini's replication of Galvani's findings as well as the conclusions of later colleagues, such as von Helmholtz [2], in this field of science, it became an established fact that animal electricity did exist and the high honor for the discovery of animal electricity came posthumously to Luigi Galvani.

SECTION 2. RICHARD CATON: FIRST RECORDING OF ELECTRICAL BRAIN ACTIVITY

The discovery of animal electricity had a major influence on the shift from supernatural to mechanistic explanations of the functions of brain and body. Galvani made clear that the power for nerve conduction and muscle contraction was provided by internal animal electricity located in body organs, and not by mysterious spirits. The physician Richard Caton [6] (1842-1926) (Fig. 2) affiliated to the Royal Infirmary School of Medicine in Liverpool was intensely interested in electrical phenomena. Caton wondered whether electrical brain activity evoked by sensory stimulation, could be useful in localization studies. The existence of invisible brain potentials is required, but nobody had experienced or recorded this electrical activity. Despite this uncertainty Caton received a grant from the British Medical Association to explore animal electrical brain phenomena. To his surprise Caton succeeded quite fast in recording electrical brain activity, by unipolar electrodes placed on two points of the exposed external surface of a rabbit brain. Caton, primarily engaged in studying the localization of sensory functions, could now record effects of sensory stimulation on the electrical activity. He presented his findings to the British

Medical Association on August 24, 1875, and subsequently a short abstract of 20 lines appeared in the British Medical Journal.

Fig.2. Richard Caton, recorded electrical actvity from the brains of rabbits and monkeys in 1876.

Caton described in this report the spontaneous waxing and waning of the electrical activity recorded from the brain of rabbits and monkeys. He used the following words: 'In every brain hitherto examined, the galvanometer has indicated the existence of electric currents. The external surface of the grey matter is usually positive in relation to the surface of a section through it. Feeble currents of varying direction pass through the multiplier when the unipolar electrodes are placed on two points of the external surface, or one electrode on the grey matter, and one on the surface of the skull. The electric currents of the grey matter appear to have a relation to its function. When any part of the grey matter is in a state of functional activity, its electric current usually exhibits negative variation. Impressions through the senses were found to influence the currents of certain areas: e.g. the currents of that part of the rabbit's brain which Dr. Ferrier has shown to be related to movements of the eyelids, were found to be markedly influenced by stimulation of the opposite retina by light'.

From the wording of this abstract it appears that Caton was firstly interested in the localization of sensory areas, the primary goal of the study, but secondly into the characteristics of the electrical brain activity. The succeeding paper from 1877 confirms this. Caton extensively described In this longer publication identical experiments, but with a larger number of animals and almost with the same results. In this study the focus was more directed to the characteristics and features of the electric brain currents. He considered that the electric brain waves are biological in origin, because they varied with the degree of alertness of the animal, in terms of waking and sleep. Caton also proved that these electrical varying waves are vulnerable to anoxia and to anesthesia and are abolished by the death of the animal. Unfortunately, Caton was not able to show images of the recordings of his observations, since his detecting instrument was a slow Thomson's galvanometer, with a small mirror fixed on the instrument visualizing the electrical currents by a beam of light that was projected onto the chamber wall.

In 1887 Caton attended the Ninth International Medical Congress in Washington, USA, and read a paper on 'Researches on Electrical Phenomena on Cerebral White Matter'. He thought that his lecture was well received, but most of the audience did not notice the importance of the study. Indeed, Caton did not much to draw attention to his work, but it was strange that his findings 'produced no single ripple in the pool of physiologists'. This, while it is nowadays accepted that the 'feeble currents of varying direction' he described forms the basis of what is now known as the electroencephalogram. This implies that Richard Caton must be seen as the discoverer of the electrical brain activity. At that time the main stream of neuroscientic physiologists was focused on cortical localization of functions, and not on such enigmatic novelty as the fluctuating brain waves. Even influential British physiologists were so involved in brain locations to sensory stimulations that they completely ignored the important work of their countryman.

Despite the relative unfamiliarity of his work, Caton found some recognition and satisfaction by his studies and this was strengthened by the fact that recognized electrophysiologists working in the field regarded him in 1891 as the discoverer of the electroencephalogram. Despite this honor, he turned away from physiology and resigned as Chair of Physiology of the University of Liverpool, which post he held from 1884 to 1891 [7]. A secret reason was that his family and close colleagues were unaware of his growing aversion against experiments with animals. He took deliberate steps to hide this, feeling ashamed that he had done this work so long. Caton's interests developed than to more public affairs; he hold several representative offices and became President of the Medical Institution and initially mayor of Liverpool in 1907. After his death in 1926 most people remembered Caton better as the gentleman who was the Lord Mayor of Liverpool, than as the scientist which deserved credits for the significant discovery of the electroencephalogram.

SECTION 3. ADOLF BECK, A FORGOTTEN PIONEER IN ELECTRICAL BRAIN ACTIVITY

Adolf Beck [8] (1863-1942) (Fig.3) a physiologist affiliated to the Jagiellonian University in Kraków (Poland) started with a study to electrical brain activity under the leadership of the eminent professor of electrophysiology and biochemistry Napoleon Cybulski (1854-1919). Beck started with a study to the spontaneous and evoked electrical activities of the brains of animals. He explored, in frogs as well as in dogs and rabbits, the parts of the cortex that reacted upon stimulation with electronegativity. He was able to localise the sensory modalities on the cerebral cortex by electrical and sensory stimulation together with electrical recordings. In doing this, Beck found not only the spontaneous fluctuations of the brain potentials but analysed simultaneously the evoked responses to sensory stimulation. In fact this was the first description of 'evoked potentials'.

Fig. 3. Adolf Beck, a Polish neurophysiologist who recorded evoked brain potentials to stimuli at the end of the 19th century.

He further showed that these fluctuating oscillations had to be regarded as genuine electrical brain activities in noting that this activity was not related to heart and breathing rhythms. Moreover, Beck brought up the decrease of the amplitude of these potentials upon afferent and electrical stimulation in observing a blocking in the fluctuations of the electrical waves. Hence, he described two essential new elements after afferent stimulation: the 'evoked potentials' and the 'desynchronisation' of the electrical waves after stimulation.

As all physiologists, Beck was not aware of Caton's work, but he explored the electrical brain activity much more extensively and detailedly than Caton did. Beck confirmed the localization of sensory modalities and the fluctuating character of the spontaneous brain oscillations and added two important features in the electrical brain actvity. He did this with clay electrodes and a Wiedemann mirror galvanometer with a low sample rate. The deflections of the galvanometer were amplified by a light beam falling on a tiny mirror fixed on the galvanometer wire, and the reflected beam was directed to a metric scale.on the wall and Beck noticed by hand the size of these deflections. In one of his reports he mentioned the deflections of the spontaneous brain activity followed by activity after a ligh flash and after a handclap. The fluctuating waves in the rest situation, the evoked response after a light flash, as well as the desynchronization after flash and after hand clap, can easily be observed. Beck had no problem to explain the evoked potentials, but had problems with the desynchronization. Indeed, a desynchronization is a counter-intuitive phenomenon: a decrease of electrical activity instead of an expected increase as the consequence of stimulation. With more sensitive instrumentation, it appears that the flat line is more apparent than real. Due to stimulation and arousal the amplitude of the waves decreases significantly, so that it looks a line without activity.

The paper he sent in 1890 to the leading European physiology magazine 'Centralblatt für Physiologie' under the title 'Die Bestimmung der Localisation der Gehirn- und Rückenmarksfunctionen vermittelst der elektrischen Erscheinungen' [9]. was a summary of his extensive thesis in Polish. The paper got a huge attention, because Beck indirectly claimed to be the discoverer of the electrical brain activity. Several claims for priority in finding the electrical brain activity followed. The first was from Ernst Fleischl von Marxow [10], a famous physiology professor at the University of Vienna. He wrote that he had already, seven years earlier, deposited a covert letter at the Imperial Academy of Sciences in Vienna, containing claims on the electrical brain activity. Indeed in that sealed letter indications of electrical brain activity were given, but Fleischl's observations missed crucial points. Also famous Englishman Francis Gotch [11] (refractary period of nerve impulse) and his brother in law Victor Horsly (stereotactic apparatus) responded, but they also overlooked essential elements. The discussion concerning the claim on the discovery of the electrical brain activity was abruptly ended by a letter of Richard Caton, who referred to a brief abstract he published in 1875, 15 years earlier than Beck. In his abstract, published in the British Medical Journal, Caton described the spontaneous waxing and waning of the electrical activity recorded from the brain of rabbits and monkeys. Caton's claim was convincing and indisputable. And nowadays, it is generally accepted that Caton's abstract in 1875 contains the first description of the electroencephalogram,

In 1895, at the age of 32, Adolf Beck accepted the offer to be appointed professor of physiology at the University in Lemberg (Lwów-Lviv). Beck started the extension the Department of Physiology, where he continued his electrophysiological research wih assistant Gustav Bikeles, locating the places on the cortex associated with pain, and with Cybulsky in his alma mater, in the question of cortical electronegativity versus electropositivity in cortical areas. At the outbreak of the First World War in 1914 when Lwów was occupied by the Russions, was Beck as the Rector of the University imprisoned in Kiev [8]. By the intervention of the famous Russian scientist Ivan Pavlov, a friend of Napoleon Cybulsky, was Beck released. During the Second World War, when the Nazi's had occupied Lemberg, life became extremely dangerous for the Jewish Beck. Beck was brought to a hiding place, but he was betrayed. His son Henryk could hand his father a cyanide capsule to save him from the gas chamber. In the chaos it is not known which day it was in August 1942. His death, just before his 80th birthday, after a dedicated and scientific life, was painfully tragic for this great man. The Second World War with all his consequences is probably also the main reason that Beck with his work is so unknown. The occupation of Poland, the tragedy for the Jewish community in the Nazi concentration camps in Poland, the separation of West and East by the iron curtain, and the complete chaos in Polen with migration of numerous people, seemed to be the reason that Beck became the forgotten pioneer in the history of electroencephalography.The entire family of Beck was killed, except a daughter with her son.

SECTION 4. RISE AND FALL OF ELECTRICAL BRAIN ACTIVITY IN EASTERN EUROPE

In the latter half of the nineteenth century, Russian neurophysiology saw a upswing inspired and influenced by Western concepts and views of the brain and behavior. It was common that Russian scientists visited Western Europe for training and experiences. Most important visitor was Ivan Sechenov [12] (1829-1905) a Russian psychologist and physiologist, which around 1850 received training under Emil du Bois-Reymond, Johannes Müller and von Helmholtz in Berlin, and later from 'the father of modern psychology' Wilhelm Wundt (1832-1920) in Leipzig. In 1860 Sechenov returned to St. Petersburg and with his rich bagage on ideas, views, demonstrations and even instrumentation for electrophysiology, he became the founder of a powerful school of eminent neurophysiologists. He got the title of 'Father of Russian physiology and scientific psychology'. Almost all leaders of electrophysiology study groups from Russia and Ukraine were trained by Sechenov. It was in the time that electroencephalography was in a dip in Western Europe.

Fig.4 Vasili Danilevsky in 1877 shortly after he finished his thesis which he forgot to publish.

Vasili Danilewsky [13] (1852-1939) (fig 4.), a Ukrainian-born Russian physiologist working at the University of Charkov in the Ukraine responded just as others to the paper of Beck. In his letter to the 'Centralblatt', Danilewsky mentioned his doctoral thesis 'Investigations into the physiology of the brain' from 1877, written in the Russian language on an age of 25 years. In his thesis, he reported about the research on the electrical activity of a dog's brain, with a comprehensive description of fluctuating brain potentials, evoked potentials and even a brief note about the desynchronisation process. In fact he was the first, 13 years before Beck, to describe all main features of the electrical brain activity. Unfortunately, Danilewsky, a classmate of Vladimir Ulyanov (Lenin), published a summary of his thesis in his interesting response-publication to Beck in the 'Centralblatt', but not earlier than 1891. His unpublished thesis was from 1877, one year after Caton's discovery in 1876, implying that he was earlier than Beck but later than Caton. The discussion concerning the claim on the discovery of the electrical brain activity, following the paper of Beck in 1890 was ended by a letter of Richard Caton. He referred to his brief abstract published in 1875, 15 years earlier than Beck, and one year earlier than Danilewsky. Caton's claim was convincing and indisputable. Nowadays, it is generally accepted that Caton's abstract in 1875 contains the first description of the electroencephalogram.

The first photographic registration of electrical brain activity was reported in 1913 by Vladimir Práwdicz-Neminski [14] (1879–1952) a Russian-Ukrainian from Kyiv. He used an Einthoven string galvanometer in conjunction with moving photographic paper, a technique introduced by the Dutch Willem Einthoven. Práwdicz-Neminski recorded electrical activity from the brain, the dura or the intact skull of a curarized dog and he reported the existence of two pattern rhythms which were distinguished for the first time. These were initially denoted as ''waves of the first and 'waves of the second order' and later called alpha and beta waves. He named the registration of the brain activity the 'electrocerebrogram'. Práwdicz-Neminski worked at the Kyiv University of St. Vladimir and later at the Ukrainian Academy of Sciences'. In Kyiv he worked together with Pavel Kaufman (1877-1951) and they expressed the view that an epileptic attack would have to be associated with abnormal electrical discharges.

Cybulski continued after the success of Beck and his leave to Lwów in 1895, with new enthusiasm electrophysiology. Often was Beck involved in common research with his old department in Kraków and already in 1896 published Cybulski together with Beck a paper on 'Further Investigations of the Electrical Processes in the Brain'. They established that the electrophysiological methodology delivered adequate information on the localization of functions on the cerebral cortex. Cybulski [15] worked on physiological changes in the cortex associated with (un)conscious states. In 1914 he published with his assistant Sabina Jeleńska-Macieszyna the first photograph of an epileptic seizure recorded in the cerebral cortex of a dog.

One of the most influential Russian neurologist at that time was Vladimir Bechterev (1857-1927), a disciple of du Bois-Reymond. He occupied the chair of psychiatry, including clinical neurology, in St. Petersburg. Neuroscientist Bechterew developed a theory of conditioned reflexes, the automatic responses to the environment, while the famous psycho-physiologist Ivan Pavlov (1849-1936) did the same independently from Bechterev. The two concepts were essential identical, but were called the 'association reflex' by Bechterew and the 'conditioned reflex' by Pavlov. Nevertheless between the medically oriented neuroscientist Bechterew and the (famous) psychologically oriented Pavlov arose increasing rivalry. In 1927 Bechterew took part in a medical congress in Moscow, where he received a telegram, to move urgently to the Kremlin. He examined Joseph Stalin and he diagnosed him as paranoid. The next day Bechterew died on a supposed food poisoning, while the name of Bechterew was under removal from all Soviet textbooks [16]. Obviously, the psychological Pavlovian concept was closer to the ideology of the Soviet regime than the physiological concept of Bechterew. The victory of the dogmatics, approved by Stalin, caused great damage to Russian physiology. As a consequence the Russian and Ukrainian leadership in electrophysiology in that time, decimated fast after 1926 and slowly disappeared.

SECTION 5. HANS BERGER, RECORDING OF THE HUMAN EEG

While electrophysiological studies flourished in Eastern European countries, they were in a dormant state in Western Europe. Physiologists followed in West Europe the experiments of neuroanatomists, the studies of the cerebral hemispheres and the controversies between network and neuron theories. This neuropsychology stood far away from the electrophysiology. After a near fatal incident a man named Hans Berger [17] (1873-1941) (Fig. 5), became interested in the functioning of telepathy, because his sister, being on a distant place, experienced telepathically his accident. Berger became interested in the phenomenon of 'psychic energy' behind telepathy, and tried to understand this mysterious phenomenon. This motivated him to record the supposed brain energy by electrodes over the brain. When he was appointed as professor of neuropsychiatry in Jena (Germany), he began with dogs trying to replicate the achievements of Caton and Práwdicz-Neminski, but often with disappointments. Berger was a hard working professor, who was absorbed in his work, and had a complex character, strict and authoritarian and not not easy in dealing with others. Berger did his work privately in a small and primitive laboratory in the cellar of the Psychiatrische Klinik in Jena.

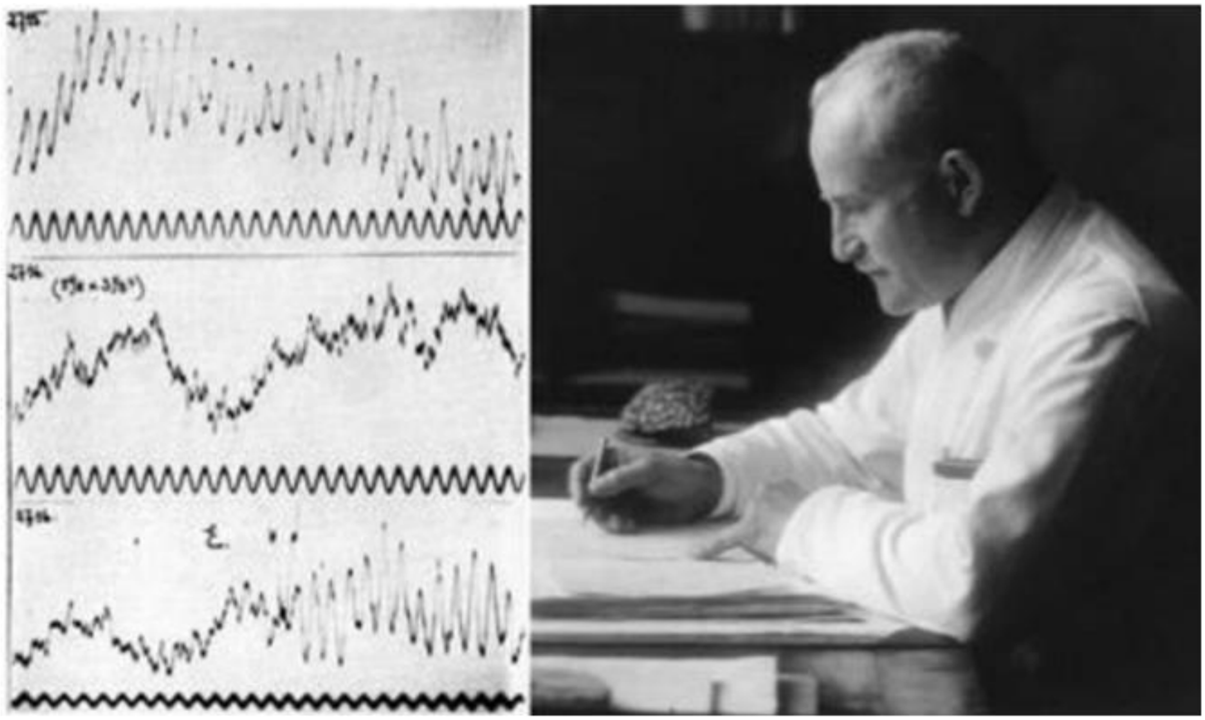

Fig. 5. Hans Berger with the EEG of daughter Ilse. Upper trace: Ilse in rest (alpha waves), middle trace: Ilse calculates a sum (beta waves), lower trace: Ilse gives the result of the sum (mixed waves).

In 1924 he switched to human studies, using non-polarising pad electrodes and a double coil galvanometer, which was more sensitive than the instruments of his predecessors. Apointments were made with several patients with large skull bone defects, easy to get after World War I. However, soon recognized Berger that skull defects were not necessarely advantegeous in obtaining good recordings. He went on with healthy persons and his children, son Klaus and daughter Ilse, were main, obedient, but often unwilling, subjects. On October 14th, 1927, Berger [18] exclaimed: 'Eureka! The waves of Klaus are identical to the intracerebral recorded waves. I am able to record the electroencephalogram of an intact human skull!'. Indeed, Berger was the first who recorded the electrical activity of the intact human brain, and promoted the technique as a non-invasive brain registration method for humans, with evident clinical perspectives. Moreover, it appeared from his publication of 1929 that Berger was aware of most studies published earlier. In an interesting historical introduction of his lengthy paper, he gave full credit to all researchers, even to Caton and Beck. In this introduction he already described the main phenomena, such as the spontaneous fluctuations, the blocking after sensory stimulation, as well as the existence of two pattern rhythms. These rhythms were first distinguished in dogs by Vladimir Práwdicz-Neminski [14] in 1913. The latter was also the researcher who coined the German term 'Elektrocerebrogramm', which for (strange) linguistic reasons, was changed by Berger into 'Elektrenkephalogram', generally translated to 'electroencephalogram', abbreviated to EEG. He described the conditions under which the two waves of the first and the second order, now termed by Berger alpha and beta waves, appeared in humans. These waves placed Berger with an analogous problem as Beck. He noticed that the small beta waves arose in higher mental states than the larger alpha waves, appearing under low-active brain states. Berger discussed this only in vague statements, since he was not focused on theory and had a pragmatic, attitude. He described changes in the electrical brain waves during sleep and narcosis, and recorded aberrant activities during epileptic attacks in humans, a major discovery in the clinical field. Berger came to the conclusion that the electroencephalogram was not only a major breakthrough in neurophysiology, but saw also that this technology was of outstanding importance as a diagnosticum. Berger founded also clinical electroencephalography!

Berger himself was not completely convinced concerning the validity of his observations, and it is also true that many scientists considered the strange and global brain activity from Berger, with his enigmatic ideas, as an artefact. They mostly ignored and neglected the (important) findings of Berger. Crucial for Berger was that recognized neurophysiologists of that time, who recorded action potentials from large squid nerves, became less sceptical. British electrophysiologist and 1932 Nobel prize winner Edgar Adrian [19] (1889-1935), together with colleague Bryan Matthews, of the University of Cambridge, started to replicate Berger's findings in 1934. Adrian had a beautiful alpha rhythm and was so fair to call this the Berger rhythm. After their positive results Berger was considered reliable and seriously, and he could now convince scientists of the value of the new method.and his international reputation was slowly growing. This brought the modest Berger to the International Congress in Psychology in Paris in 1938, where he was treated as a celebrity, and to Bologna for the birthday of Galvani in 1937. Back in Germany he found, however, only humiliation especially by the Nazi regime who distrusted his work. The Nazis did even not allow him to receive the Nobel price in Stockholm for which he was nominated, and forced him to become an emeritus and give up his Chair at the Psychiatric Clinic in 1938. That was a hard blow for Berger, 65 years old and still dreaming of future experiments. However, the few extra years mostly granted to highly qualified persons did not come, and he became seriously depressed. Perhaps external factors may have contributed to this. He felt challenged by a group of scientists working at the Department of Electrophysiology of the Kaiser-Wilhelm Institut in Berlin-Buch. This group was led by Alois Kornmüller, [20] and did outstanding localisation work by using multiple electrodes, on the advice of the prominent electronic engineer Jan Tönnies (1902-1970). The highly sensitive and often insecure Berger was afraid that the Berlin-Buch Institut, favoured by the regime, might use or misuse his discoveries. Berger's endogenous depression became more and more severe and on the 1st of June 1941 he took his life by hanging. Berger's wife Freiin Ursula von Bülow had a hard time also since son Klaus fell on the battlefield in Russia half a year later. Many similarities can be seen in life and work of the two great pioneers of electroencephalography: Adolf Beck and Hans Berger.

SECTION 6. ELECTROENCEPHALOGRAPHY IS A MATURE TECHNOLOGY

The collapse of three empires in Europe around 1914-1918, the German Empire the Austro-Hungarian (Habsburg) Empire, and the Russian Empire in 1917, caused finally World War I, lasting from 1914 until 1918. The repartition of countries by the new powers was the reason for World War 11 During these turbulent times for entire Europe, science had not a high priority. There were only a few electrophysiology groups with a great leader such as Lord Edgar Adrian in Cambridge, with the confimation of Berger's observations, William Grey Walter, pioneer of clinical electroencephalogram in England, and finally Frédéric Bremer in Brussels, using the electroencephalogram in brain studies, but the center of research shifted in these times from Europe to America.

American human EEG work started at Harvard in Boston with the electrophysiologist Hallowell Davis (1896-1992). When a graduate student of Davis brought Berger's paper of 1929 to his attention in 1933, Davis could not believe that regular alpha rhythms originated from the brain. All workers tried than in vain to demonstrate their alpha rhythms. Shouts of joy came up when Hallowell Davis himself found to have a good alpha rhythm! In particular the era of the 1930s with Frederic Gibbs [21] (1903-1992) and his wife Erna Gibbs (1904-1987) got in 1935 an international breakthrough in clinical electroencephalography, with their studies of epileptic patients. For the quality of electrophysiological tracings the Gibb's group had visited Hans Berger in Jena in 1934. Also due to Erna Gibbs, who had a German background, the group could have long talks with Berger, who hardly spoke English. Alfred Loomis started with sleep studies in New Jersey in 1935. The first study by Loomis was about the identification of EEG stages in human sleep. This resulted in an important publication but appeared some months later than the excellent sleep-stage report of Herbert Jasper (1906-1999) a Canadian psychophysiologist. Neverthelesss, the Loomis study is regarded as the first study based on the human electroencephalogram. Loomis stopped in 1939 with his sleep studies, and Herbert Jasper [22] went to the McGill University in Montral where he did most important research with the American-Canadian neurosurgeon Wilder Penfield (1891-1976). His EEG work of focal epilepsies in collaboration with the neurosurgical procedures of Penfield were worthful. The neurosurgical operations made the McGill University supreme as the place for the treatment of epilepsies.

William Grey Walter [23] (1910-1977) was an American professor in clinical neurophysiologist working at the Burden Neurological Institute in Bristol (UK). Grey Walter was in the 1930s, the first to determine the surface location of the strongest alpha waves within the occipital lobe and demonstrated the use of delta waves located over hemispheric brain tumors. This had opened in England and the USA the search for further relationships between brain lesions and focal EEG correlates.

When the 1930s ended America found itself in a leading position in the domain of the EEG. By contrast, progress made in Europe was quite limited. It is further striking that the EEG in this first period is primarely used for understanding better the features of the EEG, what precisely is measured and what is the interpretation of what is measured. Furthermore, the EEG is particularly applicable to study the function of sleep and to collect more information about epilepsy. It can also be effectively used in brain disorders. Around the 1950s electroencephalolography became a normal tool and almost every university and hospital had such instrument. It is not possible to give an overview of all researcg with the EEG and here it will suffice to mention a few representative investigations in which elctroencephalography played a main role.. The study of Kleitman and Aserinsky [24], with the discovery of the REM sleep in 1953 has had an great impact on the states of consciousness of the brain. Nathaniel Kleitman (1895-1999) born as a Russian in Moldava, immigrated on a young age to America. As a physiologist and sleep researcher he became professor at the University of Chicago. A graduate student of him, Eugene Aserinsky (1921-1998), noticed that sleepers went through periods in which their eyes dartled back and forth. Aserinsky thought that this type of sleep, showing an EEG of wakefulness, was a second type of sleep, highly associated with dreaming. Kleitman, as an adept of the passive sleep theory, was sceptical but when his daughter Esther also showed rapid eye movements, Kleitman and Aserinsky introduced the REM sleep to the world.

Giuseppe Moruzzi [25] (1910-1986) an Italian neurophysiologist of the University of Pisa went in 1948 to the laboratory of Horace Magoun (1907-1991), professor in anatomy at the Northwestern University. Moruzzi and Magoun identified in cats with electrical stimulation brainstem centers responsible for sleeping and waking determined by the EEG. They showed that stimulation of brain stem structures caused awakening of the animal, while a destruction made that the cat fall into a permanent coma-like sleep. In this way they established the active ('reticular') sleep theory in 1949.

Fig.7. Nathaniel Kleitman did in 1953 with Eugene Aserinsky a great discovery with electroenceplalography: the REM sleep

In the fifties the scientific EEG work was scarce in Europe. The war was ended in 1945, but it took much effort to overcome the post-war troubles. Richard Jung [26] (1911-1986) a German neurologist and neurophysiologist built on the remnants of the post-war department of neurology in Freiburg a new neurological clinic with basic research and attention for sleep medicine. Jung became one of the greatest electroneurophysiologists of his time. He introduced the microelectrode recording for activity of single units measurements and related them to the features of the EEG waves of the simultaneous recorded EEG. In this way he could understand how EEG waves were build up by action potentials of single units.

Jürgen Aschoff [27] (1913–1998) was a German physiologist and a co-founder of chronobiology. Aschoff studied in the 1960s with colleague Rütger Wever (1923-2010) humans circadian rhythms by placing them in an underground 'bunker' in constant condirions to isolate them from environmental cues. Aschoff and Wever concluded that humans have endogenous circadian oscillators. Free running periods in humans showed a free running period of 25 hrs and some participants showed a desynchronization of the body temperature with the sleep-wake period. Body temperature showed approximately a 25 hrs rhythm, while the sleep-wake rhythms fluctuated. This might mean that humans may have multiple circadian clocks.

Epilogue

Hans Berger is generally considered as the father of electroencephalography, probably since he applied the technology, which was developed for animals, to humans. Caton and Beck were nearly half-a century ahead with their views of this technology, but suffered from a lack of attention and recognition to their animal studies. While looking back, it seems best to attribute the discovery of electroencephalography to the trio Richard Caton (for the first description of brain waves), to Adolf Beck (for his extensive brain work in animals, identifying essential features in brain waves), and to Hans Berger (for making the technique applicable for humans and seeing its clinical value). It is, however, undisputed that since the time of Berger, the importance of electroencephalography and clinical electroencephalography blossomed up and the methodology soon was regarded as an indispensable tool in electroneurophysiology. In all, it seems fairly to regard Berger as the grandfather of electroencephalography.

The greatest value of electroencephalography must be viewed in the progress the functioning of brain has gone through this technique. Much more is known about the meaning and localisation of the several types of waves. The EEG recording in combination with the microelectrode technique delivered gates to new electrophysiological and biochemical processes. The different modes of neuronal firing provided information of the level of consciousness of the brain. It is particular in the field of the states of consciousness that important discoveries were done, not only about subconscious states but also about high active brain states, such as the REM sleep, with its positive association with dreaming. Moreover, the cooperation of the passive and active sleep theories were recognized, and the important restoration sleep theory was discovered due to the power of encephalography. The (clinical) electroencephalography appears to have a great value for diagnosis and therapy for sleep disturbances, such as sleep apnoe and rhythm disorders. Epilepsy is a brain disorder for which electroencephalography is a valued technology to recognize and identify the several types of attacks. More discoveries and treatments will follow in the future.

For recording and evaluation of brain activity is electroencephalography a non-invasive, safe and painless tecnnique, which is of great usefulness for brain diagnosis and therapy, and cannot longer be missed. It is impressive that in 300 years of research with so few scientists, a conception concerning animal electricity, is transformed into a usable technique. All scientists had ups and downs. Galvani discovered the animal electricity with a heavy dispute with Volta, Caton did the first electrical recording of the animal skull, and developed aversion to animal research, Beck was succesfull in work, but the Nazis came for him, Danilevsky did excellent work, but forgot to publish his thesis, and it was too late when Stalin ordered to stop electrophysiology, Berger saw the advantage of human recordings, but at the end the Nazi regime blocked him. The pathway from the conception of animal electricity to the non-invasive recording of this electricity, was a complex, strange and erratic advonture. But because the inventivity and the deep interest in their work in which they got stuck, electroencephalography became a great success, used all over the world. The scientifc and medical world wishes to express great appreciation and gratitude for the eminent work the electroencephalic researchers have performed under complex circumstances. Thanks to Galvani, Caton, Beck, Cybulski, Danilevsky, Práwdicz-Neminski and Berger and all their collaborators.

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