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1971

In 1971, American psychobiologist John O'Keefe (b. 1939), joined by a Masters in Science (MSc) student named Jonathan Dostrovsky, published his influential study, "The Hippocampus as a Spatial Map: Preliminary Evidence from Unit Activity in the Freely-Moving Rat," in the journal *Brain Research*. The article described the discovery of cells in the CA1 field of the hippocampus coding for an animal's location, which would later be named "place cells." For this, O'Keefe was awarded the Nobel Prize for Physiology or Medicine in 2014, together with his coworkers Edvard Moser (b. 1962) and May-Britt Moser (b. 1963), both from Norway.

The first CT scanner was constructed by Sir Godfrey Hounsfield (1919–2004), who was an electrical engineer by training. He did early tests with a laboratory CT using a gamma ray source and a single detector. In 1971, high-resolution images were produced in cooperation with neuroradiologist James Ambrose at Atkinson Morley Hospital (London; 1st clinical scan, October 1, 1971: 41-year old woman with left frontal tumor).

Allan M Cormack formulated mathematics of reconstruction for simple attenuating objects with certain symmetry and applied a reconstruction technique (1957) with some success.

Hounsfield and Cormack were awarded the Nobel Prize for Physiology or Medicine in 1979.

1921

Wilhelm Heinrich Erb (1840–1921; Figure 1) was an influential German neurologist. In 1880, he was offered the Chair of Special Pathology at the University of Leipzig. In 1883, he succeeded Nikolaus Friedreich (1825–1882) at the University of Heidelberg, where he worked until his retirement in 1907. Psychiatrist Emil Kraepelin (1856–1926) and neurologists Ernst Julius Remak (1849–1911), Max Nonne (1861–1959), and Paul Julius Möbius (1853–1907) were among his better-known students and assistants. Until his death in 1921, Erb served as honorary president of the Gesellschaft Deutscher Nervenärzte. Among his numerous publications are several handbooks: *Zur Pathologie and Pathologische Anatomie Peripherischer Paralysen* [On the Pathology and Pathological Anatomy of Peripheral Paralyses] (1867/1868,) *Handbuch der Krankheiten der Peripheren Cerebrospinalen Nerven* [Textbook of Diseases of the Peripheral Cerebro-Spinal Nerves] (1874), *Handbuch der Krankheiten des Nervensystems* [Textbook of Diseases of the Nervous System] (two volumes; Leipzig, F. C. W. Vogel, 1876–1878), and *Handbuch der Elektrotherapie* [Textbook of Electrotherapy] (1882).

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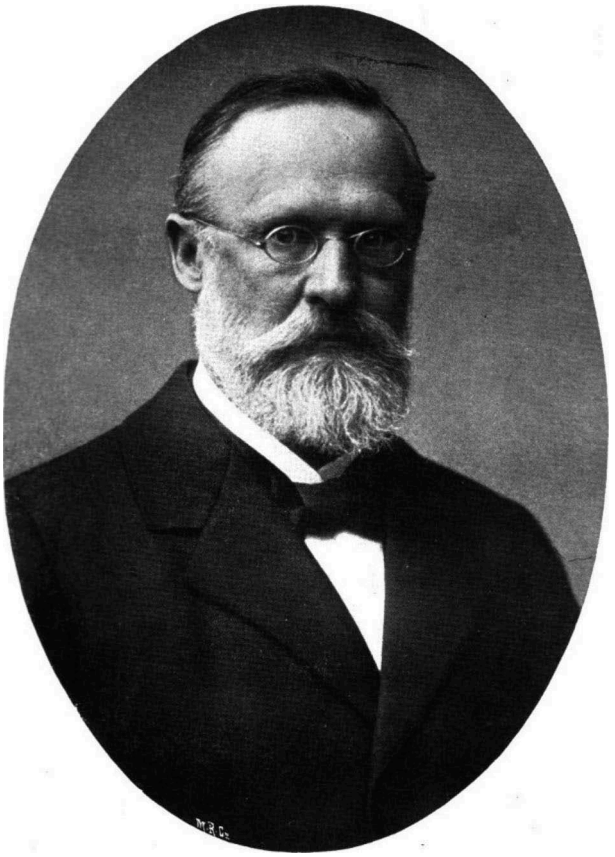

Figure 1. Wilhelm Heinrich Erb (1840–1921).

British physiologist Robert Henry Clarke (1850–1921) developed the first device for stereotaxic surgery in 1908, together with Sir Victor Horsley (1857–1916). To ensure that a lesion would be made at the correct site, Horsley and Clarke created atlases containing pictures of the brains of the animals on which they experimented.

Eugene Aserinski (1921–1998) was a graduate student in physiology at the University of Chicago in 1953, when he discovered rapid-eye movement (REM) sleep. He and his Ph.D. adviser, Nathaniel Kleitman (1895–1999), showed that REM was correlated with dreaming and a general increase in brain activity.

Heinrich Wilhelm Gottfried von Waldeyer-Hartz (1836–1921) was a German anatomist known for summarizing the neuron theory and introducing the term "neuron" in a series of article in the main medical German journal, *Deutsche Medizinische Wochenschrift*, in 1891. He synthesized discoveries by neuroanatomists and later Nobel Prize winners Camillo Golgi (1843–1926) and Santiago Ramón y Cajal (1852–1934). He is also known for naming the chromosome in 1888. And he is remembered by anatomical structures named after him: Waldeyer's tonsillar ring (the lymphoid tissue ring of the naso- and oropharynx) and Waldeyer's glands (of the eyelids).

Henri-Étienne Beaunis (1830–1921) obtained his medical doctoral degree in Montpellier in 1856. He held the chair of physiology in Nancy. He is known for his

works on anatomy, physiology, psychology, and hypnosis. He argued that hypnosis was a state similar to sleep produced by suggestion, and not of hysteria, as stated by Jean-Martin Charcot. In 1889, he founded at the Sorbonne the first French psychology laboratory. In 1894, he founded, with Alfred Binet (1857–1911), the scientific journal *L'Année Psychologique*.

In 1921, Austrian pharmacologist Otto Loewi (1873–1961) produced the final proof of chemical neurotransmission, when he stimulated an isolated frog heart by perfusing it with blood from a heart to which the vagus nerve had been stimulated. The first neurotransmitter he identified was acetylcholine. For this discovery, he was awarded the Nobel Prize in Physiology or Medicine in 1936, which he shared with Sir Henry Dale (1875–1968), who helped to inspire the neurotransmitter experiment.

Pio del Rio Hortega (1882–1945) was a Spanish neuroscientist and collaborator of Santiago Ramón y Cajal (1852–1934). Staining cells with silver carbonate, he discovered the oligodendroglia cells. The finding was reported in a seminal article in 1921 titled, "Studies on Neuroglia-Glia with Very Few Processes," in which he also suggested these cells were associated with myelination. He was able to distinguish microglial cells and oligodendrocystes from astrocytes, and since then we have known these three major types of glial cells in the central nervous system.

In 1920, German neurologist Hans Gerhard Creutzfeldt (1885–1964), then working in Munich, described a disorder in a 23-year-old woman with a peculiar nodule-forming neurological disorder that he called "pseudosclerosis." A few months later, in 1921, German neurologist Alfons Maria Jakob (1884–1931) published details of three cases of patients suffering from what he called "spastic pseudosclerosis," in an article titled, "Ueber Eigenartige Erkrankungen des Zentralnervensystems mit Bemerkenswerten anatomischen Befunden (Spastische Pseudosclerose-Encephalomyelopathie mit Disseminierten Degenerationsherden)" [On Special Diseases of the Central Nervous System with Remarkable Anatomical Findings: Spastic Pseudosclerotic Encephalomyelopathy with Disseminated Foci of Degeneration]. The eponym "Creutzfeldt-Jakob disease" was introduced by Walther Spielmeyer in 1922.

John Newport Langley (1852–1925) made seminal discoveries on the functional organization of the autonomic nervous system. He introduced the term "autonomic nervous system" in 1898. His own research was summarized in his most substantial scientific work, *The Autonomic Nervous System*, published in 1921.

1871

François Achille Longet (1811–1871) was a French anatomist and physiologist who was a native of Saint Germain-en-Laye, Yvelines. He was a student of François Magendie (1783–1855) and a pioneer in the field of experimental physiology. In 1853, he attained the chair of physiology of the Faculté de Médecine in Paris. Longet is remembered for his extensive research of the autonomic nervous system and physiological experiments of the anterior and posterior columns of the spinal cord in regard to sensory and motor functionality. He is also credited with providing a detailed comprehensive description of nerve innervation of the larynx. With Marie-Jean-Pierre Flourens (1794–1867), he performed pioneer experiments on the effects of ether and chloroform on the nervous system.

German anatomist and physiologist Eduard Friedrich Weber (1806–1871), born in Wittenberg, studied medicine at the University of Halle and served as prosector in the anatomical institute at the University of Leipzig, where he became *privat-docent* in 1838 with a thesis involving physiological studies on the "galvano-magnetic phenomena" in humans. From 1847 to 1871 he was an associate professor at Leipzig. He assisted his older brother, Ernst, with experimentation involving the inhibitory power of the vagus nerve.

Alfred Bielschowsky (1871–1940) was born in 1871 in Namslau, Lower Silesia. In 1912, he became chair of the Ophthalmology Department at the University of Marburg. In 1923, he moved to Breslau, where he published his epoch-making work *Die Lähmungen der Augenmuskeln* [The Palsies of the Eye Muscles] in 1932. He is remembered in various eponyms, including Bielschowsky's disease (early juvenile type of cerebral sphingolipidosis), Bielschowsky's head tilt test (used for examining the trochlear nerve), and Bielschowsky's squint (upward movement and inward rotation of the squinting eye as a sign of trochlear nerve neuropathy).

Walter Bradford Cannon (1871–1945) was an American physiologist, professor, and chairman of the Department of Physiology at Harvard Medical School until 1942. In 1915, he coined the term "fight or flight" in his 1915 book *Bodily Changes in Pain, Hunger, Fear and Rage: An Account of Recent Researches into the Function of Emotional Excitement*. Cannon developed the Cannon–Bard theory with physiologist Philip Bard (1898–1977) to try to explain why people feel emotions first and then act on them. He discovered Sympathin E (the excitor factor) and Sympathin I (the inhibitor), now called epinephrine and norepinephrine, and he coined the word "homeostasis."

Adolf Aron Baginsky (1843–1918) was a German professor of diseases of children at Berlin University. Working in a hospital in Nordhausen in 1871, he described two patients with kidney problems and what he considered aphasia. He added to these cases an elaborate theory on language systems, akin but prior to Wernicke, and he prepared the first diagram in his article, "Aphasie in Folge Schwerer Nierenerkrankungen–Uraemie" (Aphasia Resulting from Severe Kidney Disease–Uremia) in the *Berliner Klinsche Wochenschriften.*

Silas Weir Mitchell (1829–1914) coined the term "phantom limb" in an 1871 article in *Lippincott's Magazine*, referring to a clinical condition that had been described by a number of authors, most notably sixteenth-century French surgeon Ambroise Paré (1510–1590).

1821

German physician and physicist Hermann Helmholtz (1821–1894) made significant contributions in several scientific fields. In physiology and psychology, he is known for his theories of vision, on space perception, color perception, and the sensation of tones. In physics, he is known for his theories on the conservation of energy and a mechanical foundation of thermodynamics, and for his work in electrodynamics and chemical thermodynamics. The sensory physiology of Helmholtz formed the basis of the work of his student Wilhelm Wundt (1832–1920), the founder of experimental psychology. His main publication was *Handbuch der Physiologischen Optik* [Handbook of Physiological Optics or Treatise on Physiological Optics], published in 1867 (English translation published in 1924–25). In 1849, while at Königsberg, Helmholtz determined the speed at which the signal is carried along a nerve fiber at 24.6 to 38.4 meters per second. In 1851,

Figure 2. Rudolf Ludwig Carl Virchow (1821–1902).

he invented the ophthalmoscope. In 1883, he was raised to nobility by the Emperor, meaning that he and his family were now called von Helmholtz.

Rudolf Ludwig Carl Virchow (1821–1902; see Figure 2) was a German physician, anthropologist, pathologist, prehistorian, biologist, writer, editor, and politician. Known as the father of modern pathology, he studied medicine at the Friedrich-Wilhelms Institute under Johannes Peter Müller (1801–1858) and worked at the Charité hospital under Robert Froriep (1804–1861), whom he succeeded as prosector. A prolific writer, his scientific writings alone exceeded 2000 publications. *Cellular Pathology* (1858), regarded as the root of modern pathology, introduced the third dictum in cell theory: *Omnis cellula e cellula* [All cells come from cells]. Virchow was the first to describe and name diseases such as leukemia, chordoma, ochronosis, embolism, and thrombosis. He coined biological terms such as chromatin, neuroglia, agenesis, parenchyma, osteoid, amyloid degeneration, and spina bifida; terms such as Virchow's node, Virchow–Robin spaces, Virchow–Seckel syndrome, and Virchow's triad are named after him.

The concept of neuroglia was introduced by Rudolf Virchow in 1856. Virchow conceived neuroglia as a kind of connective tissue and found that this tissue also contained cellular elements. However, the first glial cell was described even before Virchow drafted his neuroglia concept. Robert Remak (1815–1865) had described nerve fibers and their

surrounding sheaths, later on called Schwann cells, in his thesis, published in 1838. Heinrich Müller (1820–1864) described cells—which were named after him, the Müller cells—and published the first drawings of these radial glial cells in Würzburg in 1851. We owe the first drawings of a star-shaped glial cell to Otto Deiters (1834–1863), who died at a young age and whose work was published posthumously in 1865. Some years later, Jacob Henle (1809–1885) and Friedrich Merkel (1845–1919) produced drawings of glial networks in the gray matter.

In 1821, Sir Charles Bell (1774–1842) described the anatomy of the facial nerve and its association with the unilateral facial palsy that bears his name.

1771

Giovanni Battista Morgagni (1682–1771) was an Italian anatomist, generally regarded as the father of modern anatomical pathology. He was professor of anatomy at the University of Padua for 56 years, teaching thousands of medical students from many countries. His magnum opus was *De Sedibus, et Causis Morborum per Anatomen Indagatis Libri Quinque* [On the Seats and Causes of Disease], in which he argued that most diseases are not dispersed throughout the body but originate in specific organs.

Marie François Xavier Bichat (1771–1802) was a French anatomist and pathologist, considered the father of modern histology. Although he worked without a microscope, Bichat distinguished 21 types of elementary tissues from which the organs of the human body are composed. In his 1800 book, *Recherches Physiologiques sur la Vie et la Mort* [Physiological Researches on Life and Death], he argued that animals exhibited vital properties that could not be explained by physics or chemistry. He distinguished between the organic and the animal life. The organic life was the life of the heart, intestines, and other organs. Bichat theorized that this life was regulated through the ganglionic nervous system, a collection of small independent "brains" in the chest cavity. In contrast, the animal life involved harmonious, symmetrical organs such as the eyes, ears, and limbs. It included habit and memory and was ruled by the wit and the intellect. This was the function of the brain itself, although it could not exist without the heart—the center of the organic life.

In 1771, German physician Johann August Unzer (1727–1799) wrote his *Erste Gründe einer Physiologie der Eigentlichen Thierischen Natur Thierischer Korper* [Principles of a Physiology of the Proper Animal Nature of Animal Bodies]. He argued that reflex action, as described by Thomas Willis (1621–1675), was the functional principle of the nervous system, and that many separate pathways could be followed by careful preparation of brains.

1671 and earlier

The original description of the septum pellucidum is attributed to Franciscus de Le Boe Sylvius (1614–1672) in 1671.

Thomas Willis (1621–1675) established neurology as a distinct discipline and made numerous significant original contributions to many related fields, including anatomy, pathology, cardiology, endocrinology, and gastroenterology. He was a founding member of the Royal Society. His anatomy of the brain and nerves is described in his *Cerebri*

Anatome of 1664, and in this book he coined the term "neurology." In 1667, Willis published, *Pathologicae Cerebri, et Nervosi Generis Specimen* [An Essay of the Pathology of the Brain and Nervous Stock), primarily dealing with pathology and neurophysiology of the brain. In it he developed a new theory of the cause of epilepsy and other convulsive diseases, and contributed to the development of psychiatry. In 1672, he published the earliest English work on medical psychology, *Two Discourses Concerning the Soul of Brutes, Which Is That of the Vital and Sensitive of Man*. Willis was the first to number the cranial nerves in the order in which they are now usually enumerated by anatomists (six of which are still classified in the same way today). He described the corpora striata and optic thalami; the four orbicular eminences, with the bridge, which he first named annular protuberance; and the white mammillary eminences, behind the infundibulum. He described in the cerebellum the arborescent arrangement of the white and gray matter and gave a good account of the internal carotids and the connection with the branches of the basilar artery. He deduced that the ventricles contained cerebrospinal fluid that collected waste products. He regarded the cortex as the substrate of cognition, and he claimed that the gyrification was related to a progressive increase in the complexity of cognition. He coined the term "mellitus" in diabetes mellitus, also called Willis's disease in the past. He was also first to describe myasthenia gravis, in 1671.

The Anatomy of Melancholy, What It Is: With All the Kinds, Causes, Symptomes, Prognostickes, and Several Cures of It. In Three Maine Partitions with Their Several Sections, Members, and Subsections. Philosophically, Medicinally, Historically, Opened and Cut Up was written by Robert Burton (1577–1640) and first published in 1621. In this nearly 1300-page book Burton described his own melancholy. The book catalogs the symptoms, causes, and cures of melancholy while also suggesting possible treatment of the illness. Robert Burton was born in Lindley, Leicestershire, and studied in Oxford, where he became vicar of St. Thomas the Martyr. Burton died shortly after the sixth edition of his book appeared.

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