



Review Article

The anatomy of the brain – learned over the centuries

Luiz Severo Bem Junior^{1,2}, Nilson Batista Lemos¹, Luís Felipe Gonçalves de Lima¹, Artêmio José Araruna Dias¹, Otávio da Cunha Ferreira Neto¹, Carlos Cezar Sousa de Lira³, Andrey Maia Silva Diniz⁴, Nicollas Nunes Rabelo⁵, Luciana Karla Viana Barroso¹, Marcelo Moraes Valença², Hildo Rocha Cirne de Azevedo Filho²

¹College of Medical Sciences, Unifacisa University Center, Campina Grande, Paraíba, ²Neuroscience Post-Graduate Program, Federal University of Pernambuco, Recife, Pernambuco, ³Department of Neurology, Psychology and Psychiatry, State University of São Paulo, São Paulo, ⁴College of Medical Sciences, Federal University of Paraíba, João Pessoa, Paraíba, ⁵Department of Neurosurgery, São Paulo State University, São Paulo.

E-mail: *Luiz Severo Bem Junior - luizseverobemjunior@gmail.com; Nilson Batista Lemos - nilsonlemos18@gmail.com; Luís Felipe Gonçalves de Lima - luizfelipeglima1@gmail.com; Artêmio José Araruna Dias - ararunadias@gmail.com; Otávio da Cunha Ferreira Neto - otaviocferreiraneto@gmail.com; Carlos Cezar Sousa de Lira - oneuroensina@gmail.com; Andrey Maia Silva Diniz - andreymaiasd@gmail.com; Nicollas Nunes Rabelo - neurobrazil2020@gmail.com; Luciana Karla Viana Barroso - lkarlab@yahoo.com.br; Marcelo Moraes Valença - marcelo.valenca@ufpe.br; Hildo Rocha Cirne de Azevedo Filho - azevedoh@uol.com.br



***Corresponding author:**

Luiz Severo Bem Junior,
Neuroscience Post-Graduate
Program, Federal University
of Pernambuco, Recife,
Pernambuco, Brazil.

luizseverobemjunior@gmail.com

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ABSTRACT

This article reports the evolution and consolidation of the knowledge of neuroanatomy through the analysis of its history. Thus, we propose to describe in a historical review to summarize the main theories and concepts that emerged throughout brain anatomy history and understand how the socio-historical context can reflect on the nature of scientific knowledge. Therefore, among the diverse scientists, anatomists, doctors, and philosophers who were part of this history, there was a strong influence of the studies of Claudius Galen (AD 129–210), Leonardo da Vinci (1452–1519), Andreas Vesalius (1514–1564), Franciscus Sylvius (1614–1672), Luigi Rolando (1773–1831), Pierre Paul Broca (1824–1880), Carl Wernicke (1848–1905), Korbinian Brodmann (1868–1918), Wilder Penfield (1891–1976), Mahmut Gazi Yasargil (1925), and Albert Loren Rhoton Jr. (1932–2016) on the fundamentals of neuroanatomy.

Keywords: Anatomy, Brain, History of medicine, Neuroanatomy, Neurosurgery

At present, it is known that the brain has an anatomical and functional distribution due to the complexity of the organization of the cells. This division due to the cortex organization of highly compacted neurons that cover outermost part and make up the gray matter. In addition, according to recent studies, the cerebral cortex is divided into seven lobes: frontal, central, parietal, occipital, insular, temporal, and limbic.^[22] This distribution in lobes is given, mainly, by the presentation of its alternating protuberances with deep fissures denominated, respectively, as gyrus and sulcus. The reason why the brain presents a tortuous conformation results from its adaptation to the drastic cell growth acquired during evolution. The various convolutions allowed the large brains to adapt to the relatively small cranial vaults that needed to take up little volume to accommodate the birth process.

However, before we understand the current brain anatomical division, it is important to know the nature of scientific knowledge and how it was recorded in a socio-historical context. In antiquity, the search for knowledge of the brain anatomy was marked by several protagonists who, over the centuries, produced proposals to justify the clinical findings of the period and define the functioning of the organ. The purpose of this article is to report, through temporal

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progress, who are the main characters who guided the path to obtain knowledge of neuroanatomy and what are their theories [Figure 1].

ANCIENT EGYPT: THE OLDEST WRITTEN RECORDS OF NEUROSCIENCE FOUND ON PAPYRUS

The construction of these hypotheses, initially, was based on the observation of nature and suffered a lot of influence from the religion and beliefs of each civilization. This behavior in the elaboration of knowledge about the brain was first found in Egyptian medical papyri. In addition, through its famous mummification technique and its records, several scholars came to recognize the mastery of part of human anatomy by this ancient society.

In the 17th century BC, the Egyptians, through the treatment of individuals affected by head injuries, started to correlate the pattern of fractures of the skull bones with brain injuries.^[12] Through the study of these traumas, they were able to develop the first surgical treatments and anatomical records of this organ, as reported in Edwin Smith's Papyrus.^[12,30] In addition, this ancient civilization was able to describe relevant structures for neuroanatomy, such as the dura mater, nervous tissue convolutions, and brain fluids, and to obtain significant advances in trepanation technique.^[12] These results reinforce the importance of observation to propose an interpretation of the anatomical components of the human body. However, although we currently understand a large part of the distribution of the cortical gyri of the brain and the value as an essential organ for life, it is worth noting that the Egyptians described these convolutions as structures similar to molten copper that had pulsations and were

devoted to cardiocentric theory, which presented the heart as a fundamental structure for the organism.^[12]

CLASSICAL ANTIQUITY: ENCEPHALOCENTRIC THEORIES AND THE STUDY OF VENTRICLES

The brain's intriguing machinery is something that fascinates many scholars worldwide. Its role in the control of the central and peripheral nervous system, despite having achieved great advances, begins to be discussed still in Classical Antiquity, since the Greeks gave greater importance to this organ, unlike the Egyptians. In ancient Greece, Alcmaeon of Croton (sixth-fifth century BC) recognizes the brain as a central organ responsible for higher activities such as intelligence, memory, and thought.^[24] This encephalocentric theory, in turn, came to coordinate the thinking of Hippocrates and most of the presocratic philosophers.^[5] During the Hellenistic period, the Alexandria School presented Herophilus of Chalcedon (325–280 BC) and Erasistratus of Chios (310–259 BC) as the main exponents of the systematic study of brain anatomy and responsible for the identification of the ventricles.^[33] These cavities, however, started to gain more importance through Galen formulations.

The ventricles, in the center of the brain itself, are filled with cerebrospinal fluid, a fluid produced, in large part, by ependymal cells present in its walls, whose primary function is to provide mechanical protection to nervous tissue. Today, we know that the lateral ventricles contribute with a greater cerebrospinal fluid volume, which passes to the III ventricle through the interventricular foramina and from this to the IV ventricle through the midbrain aqueduct. Claudius Galen, through his extensive studies of the anatomy of the brain, formulated the hypothesis that the ventricles were the place of

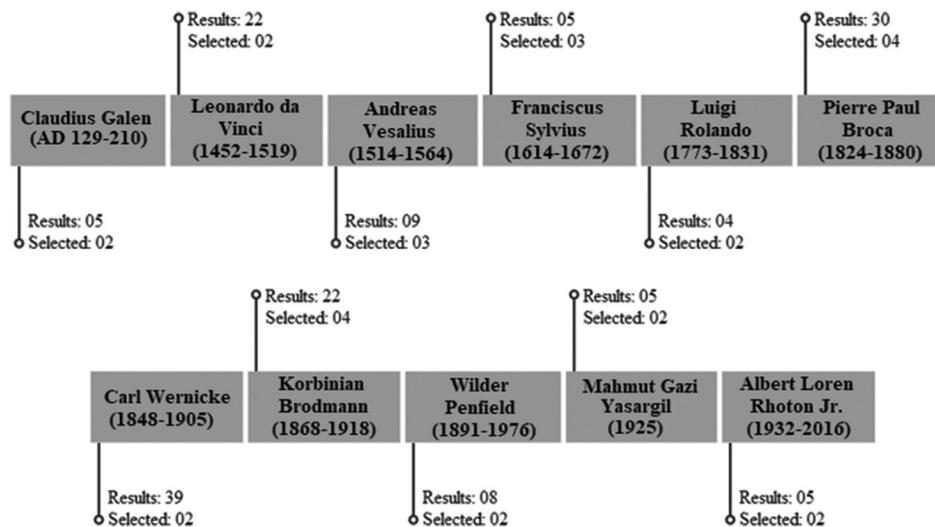


Figure 1: Distribution of articles according to the main scholars who contributed to the understanding of neuroanatomy.

the intellect and the cornerstone of the human physiological system.^[31] For the philosopher, the nervous system should behave in the same way that the heart operates through its ventricles. To justify this hypothesis, Galen proposes that from the air present in the lungs, a spirit-like substance reaches the left ventricle of the heart, and through the action of vital heat, is transformed into a vital spirit.^[23,31] This vital substance, through the circulatory system, would have access to all parts of the body and reach the brain through the carotid rete mirabile and the choroid plexus. However, it is in the latter where the vital spirit is transformed into a psychic and can flow through the nerves to the effector organs of the body.^[23] Although the philosopher does not understand exactly the activity performed by the brain's own substance, he also states that this substance is similar to nerves since it has a large amount of psychic spirit and can act as a conductor or protective layer of this entity.^[23]

During his dissections, Galen observed that exposure of the brain does not result in loss of sensation or movement.^[23] These complications, on the other hand, were obtained through the incision of the ventricles and the increase in intraventricular pressure. By studying these injuries, he could conclude that the incision of the posterior ventricle resulted in greater loss of consciousness than the incision of the middle and anterior ventricles, respectively.^[23] Today, it is known that the reason for this loss of consciousness is linked to the fact that the IV ventricle is part of the brainstem floor, a structure that contains the reticular activating system (RAS) responsible for the ascending activating system of the brain. In addition to all this, it was through these experiences that Galen could distinguish the vital spirit of the individuals' soul because, otherwise, those who had their ventricular cavity pierced would not be able to return to consciousness.^[23] Although Galen ventricular system is contrary to the current functioning of the central nervous system, it is important to note that his anatomical reports contributed significantly to the identification of brain ventricles.

About 2 centuries after Galen's death, Western culture came to live in the Dark Ages. During this period, the practice of dissecting human corpses was prohibited, leaving only access to the vestiges of the cultural collection of the Greeks and Arabs. The church, through its institutional and moral power, consolidated the influence of medieval patristic and scholastic philosophy on understanding the functioning of the brain and rekindled the search for the location of the soul.

MODERN AGE: LEONARDO DA VINCI AND ANDREAS VESALIUS – THE RENAISSANCE AND THE ARTISTIC REPRESENTATION OF THE BRAIN

In 1493, Leonardo da Vinci (1452–1519), trying to interpret the “Senso Comune,” was surprised to notice that a toad's

spinal cord injury was capable of causing instant death in the animal.^[6,21] This fact made the artist conclude that the soul should be present in the brain since it is essential to life. However, Da Vinci still felt the need to accurately find the anatomical location of the soul. Thus, he judged that the soul should reside in the judgment seat, where all the senses come together, which corresponds to the middle ventricle and current III ventricle.^[6,21] In addition, he also attributed to the anterior and posterior ventricles, respectively, the exercise of intellect and memory. Although he was not a doctor, it is worth emphasizing the importance of his studies on brain anatomy for the development of neuroscience because through the use of wax in the ventricular cavities of cattle and his description of the layers of the scalp to the cerebral cortex,^[21] it was possible to represent these structures through precise drawings and contribute to the integration of art and science.

The great increase in the quality of painting and the artistic description of the brain reflects how robust his understanding was in the 16th century. The relentless search to characterize this organ has led artists, philosophers, and scientists to dedicate a large part of their works to illustrative representation and to the written account of its anatomy. Among the most influential books published in this period, we can highlight the *De Humani Corporis Fabrica* by Vesalius. The rich detail of his images made by using the woodcut technique and the use of the best artists in their elaboration demonstrates how far the brain illustrations have evolved. Andreas Vesalius (1514–1564), challenging the ventricle-centered model, decides to portray the anatomy of the brain only by observing its physical form since historical knowledge about anatomy had been affected by theological thinking.^[15] Under the influence of cultural renaissance and through the anatomical observation of his own dissections, Vesalius paved the way for the elaboration of high-quality brain illustrations.^[4,15,18] The Belgian doctor, on the topography of the brain, describes that the turns were covered by the cortex but does not specify the organization of these gyri or the sulci.^[15] In addition, he also maintains that he did not observe the empty cavity of the nerves described by the texts of his predecessors, but that each nerve had three layers,^[15] being that of the brain's constituent medium and the two extremes derived from the dura mater. Although Vesalius was not exempt from making mistakes, his effort to interpret the nature of man in the light of reason and empiricism must be recognized, as it was through his dissection works that the field of neuroanatomy had some great advances.

FROM THE MODERN AGE TO THE CONTEMPORARY AGE: THE BRAIN GYRI AND SULCI

The gyri and sulci of the brain are fascinating structures. Upon knowing that its formation results from the progressive

increase of cortical tissue in a limited bone cavity show how important the development of these structures is for the elevation of the human encephalization coefficient, which holds the apex of the evolution of the nervous system and which presents about 86 billion neurons in the brain.^[11] Among the deepest and most significant sulci, we can highlight the Sylvian fissure. In the 17th century, Thomas Bartholin (1616–1680), a famous physician who contributed to the discovery of the limbic system, recorded the Sylvian fissure in the new edition of the anatomical book written by his father as a way to honor his professor Franciscus Sylvius (1614–1672).^[29] This famous anatomical structure, although previously described by Erasistratus of Chios, was initially illustrated by Girolamo Fabrizio (1533–1619) in his publication of *Tabulae Pictae*.^[12]

Franciscus Sylvius, after gaining prominence in the teaching of anatomy in Dutch universities, came to exercise the position of rector of the University of Leiden and to be recognized as responsible for the elaboration of the iatrochemical theory of the body.^[2,28,29] As a teacher, he trained brilliant students and was remembered, in an honorable way, for the rich detail of the anatomical description of relevant brain structures, especially the lateral sulcus.

In 1860, contradicting the idea that the arrangement of the cerebral cortex had no defined orientation, Luigi Rolando (1773–1831) detects, for the 1st time, the existence of a pattern in the convolutions of the brain.^[3,25] Through his extensive anatomical and histological studies on nerve tissue, he proposed the idea that brain functions were divided into different areas of the brain and that the hemispheres were responsible for higher activities such as thinking. This theory, in addition, challenging the prevailing thought that the brain was a tissue mass that had a uniform functional expression,^[3] contributed significantly to the development of the current cortical division of this vital organ. Among its most important anatomical discoveries, we can highlight the central gyri and the central sulcus, structures that profoundly marked the history of cerebral cortex neuroanatomy.^[3,25]

With the advances in neurophysiology and its efforts to try to understand the brain's network of connections, several hypotheses and questions about its arrangement, function, and area of action arose in the 19th century. Many of these doubts are still frequent today, such as the classic dichotomy between the areas associated with language discovered by Broca and Wernicke. This persistent questioning originates for the understanding of the complex connections among themselves, through the arched fascicle, and among other areas of the brain. To understand part of the elaboration of this current knowledge and what were the paths taken by the study of the functional division of the cortex, it is necessary to go back to how it all came about. The belief that the cerebral cortex was composed of functional units responsible for different psychic activities contributed to the

rise of Franz Joseph Gall's phrenology (1758–1828).^[7,9] While trying to study the distribution of these mental faculties present reading the narrative history of neuroanatomy, we come across the detailed task of the physician Pierre Paul Broca (1824–1880) on the cortical location of the speech articulation.^[20] Although the relationship between the current inferior frontal gyrus and the integrity of speech was reported by Broca's predecessors, it is through his publications that brain-behavioral relationships are highlighted in the 19th century.^[19] Paul Broca, through the clinical description of two patients with lesions in the same area of the left frontal lobe, comes to the conclusion that the integrity of the third left frontal convolution seems indispensable to the exercise of the articulated language faculty.^[7,9,19,20] This proves that efforts by Johann Gaspar Spurzheim (1776–1832), Jean Baptiste Bouillaud (1796–1881), and Achille Louis Foville (1799–1878) for phrenology were fundamental to conceptualize motor aphasia. Furthermore, it should be noted that the continuous study of neuroanatomy in this same century was able to define that Broca's area, in addition to not being the only "site of spoken language," is not restricted to this function.

In 1874, the German physician, Carl Wernicke (1848–1905), described, for the 1st time, the existence of the sensory center of speech.^[10,13] This discovery, unlike Broca's findings, resulted from the analysis of Theodor Hermann Meynert's publications (1833–1892) on the motor task of the frontal and sensitive lobe of the temporal lobe. Through this statement, Wernicke was able to recognize that Broca's area was not the only center of speech and to distinguish motor aphasia from sensory aphasia.^[13] In addition, he pointed to the possibility of the existence of conduction aphasia since he came to understand the arrangement of the brain's extrinsic and intrinsic connections. As his publications point out, he defined that the sensory information reached its corresponding area in the cerebral cortex through projection fibers. From there, this information, following the association system, would be distributed to different regions of the cortex, integrating sensory processing.^[10,13] This understanding of neural flow, in addition to allowing the German physician to correlate psychopathological symptoms with brain damage, contributed to defining consciousness as the sum of sensory impressions, making him an important figure for the consolidation of neuropsychiatry.^[13]

Although Carl Wernicke's developed in the 19th century his publications, it is worth noting how similar his theories are to the contemporary view of neuroanatomy, such as the organization of the white medullary center in projection and association fibers. Following the analysis of the history of the study of neuroanatomy, we find the founder of anatomical mapping of the brain, Korbinian Brodmann (1868–1918). Born in the small city of Hohenfels in Germany, Brodmann went a long way until the publication, in 1909, of his first studies on the cytoarchitecture of the cortex.^[27,37] Considering

the evolutionary principles of biologist Charles Darwin, he found a certain degree of homology between the disposition and distribution of the six-cell layers of the human cortex with the cerebral cytoarchitecture of other mammals.^[14,27,36,37] In addition, it was through understanding the cellular composition of the brain and the new Nissl staining methods that Korbinian elaborated the mapping and subdivision of the cortex in areas of similar histological structure, resulting in the identification of 52 parts of the brain topography.^[14] Taking as an example the comparison between the precentral and postcentral gyrus, the German physician observed that the first had a thicker pyramidal layer than the second and this, on the other hand, had a more robust granular layer.^[27] Therefore, it was possible to assume the importance of these layers for the motor and sensory activities of the body. Although some areas of Brodmann's do not have a defined frontier due to the technical conditions available in the 20th century, it is worth noting the significance of his work which still integrates the literature of current medical education. The evidence of this fact is based on the constant use of his map by many neuroscientists in the study of neurological images.

In the first half of the twentieth century, by observing the electrical stimulation of the brain, Wilder Penfield (1891–1976) managed to represent the somatosensory area of different parts of the body in the central lobe cortex.^[26] The extent and comparative order of the functional distribution of these regions were represented schematically by the mnemonic figures of the motor and sensory homunculus. In addition, his studies have also enabled the development of new surgical options for epilepsy and modern electrophysiological instruments.^[26] Although Penfield has expanded his knowledge of the cortical location, several current studies point out the limitations of these maps, the methodological problems of his study, and the use of ambiguous terms that hinder their interpretation.^[17] These criticisms, in turn, are based on the idea that the patients studied may have undergone neuroplastic induction after surgery and that different sensory modalities were classified as the same sensation.^[17]

CONTEMPORARY AGE: THE MICROSCOPIC VIEW OF NEUROANATOMY BY YASARGIL AND RHOTON

To emphasize the importance of neuroanatomy for neurosurgical practice and the on-demand to overcome its macroscopic barrier might highlight how valuable the creation of the microscope was in the history of medicine.^[32] From the results obtained by studies based on the observation of structures that were not previously seen without it, such as the stratification of cortical neurons and the identification of brain nuclei, it was possible to think about its use for the handling of delicate and difficult to access structures present

in the brain. Thus, to combine the findings of neuroanatomy with clinical and surgical practice, we must highlight the legacy left by Mahmut Gazi Yasargil (1925) for the development of microsurgical techniques in neurosurgery, for the manufacture of sophisticated instruments, such as retractors, flow microscopes, and aneurysm clips and for the elaboration of studies that justify the current division of the brain into 07 lobes: frontal, central, parietal, occipital, insular, temporal, and limbic.^[1,22,35] His efforts to improve and follow the path of this new direction in the medical sciences were fundamental for the consolidation of techniques that would guarantee better surgical results for patients in the last decades. Moreover, it is also necessary to recognize the considerable work of the physician Albert Loren Rhoton Jr (1932–2016) in the elaboration of several microsurgical approaches. Their studies have changed the way neurosurgeons perform microsurgery significantly.^[1] Among those present in his task, Cranium – Anatomy and Surgical Accesses, we can mention the frontotemporosphenoidal craniotomy, usually called pterional. This access, in addition to being the most used today, offers a basal and wide exposure of the lateral fissure to perform neurovascular and neuro-oncological surgeries.^[8,16,34] In education, the scientist lights-up, together with 119 fellows, the Rhoton's Lab, a research institution that was responsible for enhancing and spreading his knowledge and dedication to neurosurgery to the world¹. Therefore, after highlight part of the origin of the scientific knowledge of neuroanatomy and the socio-historical context of its development, we come to understand the value of the contribution of each of these protagonists in the consolidation and development of this science.

The importance of this article is based on the study of the main characters that guided the path toward consolidating the knowledge of neuroanatomy and what were their respective contributions. Through the study of the origin of scientific knowledge about the brain, it is possible to conclude that much of the knowledge of neuroanatomy in Classical Antiquity until the Modern Age had little progress. Moreover, it is from the second half of the 19th century that the understanding of the cortex is a view at a microscopic level and achieves a greater resemblance to the current view of neuroanatomy, reflecting the considerable significance of the publications of its main protagonists and its influence on the interpretation of cortex topography. From these advances in macroscopic anatomy and the use of the microscope, the use of microsurgery in brain structures and the development of new accesses and more sophisticated techniques begin. As a result of all this work, there has been a significant evolution in the way that neurosurgeons perform microsurgery. It is clear, from this historical study, how important it is to know about the origin of scientific knowledge and how it was generated and its socio-historical context to understand the origins of the anatomical and functional layout of the brain.

Declaration of patient consent

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