Turkish Journal of Neurology

Turk J Neurol 2026;32(2):113-124
https://doi.org/10.55697/tnd.2026.753

INVITED REVIEW

Is there localization in the brain or not? A 150-year-long scientific debate

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ABSTRACT

This historical review addresses the development of debates on the cellular unit of the nervous system and functional localization in the brain from the 19th century to the present. The first section summarizes the disagreements between the reticular theory and the neuron doctrine, based on the contributions of Remak, Gerlach, Deiters, Golgi, His, Forel, Nansen, Cajal, Waldeyer, and Sherrington. The second section evaluates discussions on phrenology, holistic cortical approaches, and cortical localization through the work of Gall, Flourens, Broca, Wernicke, Jackson, Hitzig, Fritsch, Ferrier, and Goltz. The final section emphasizes the transition of modern neuroscience from a strictly centralized localization concept to distributed, connectional network models. Historical evidence suggests that brain functions cannot be reduced to single centers nor fully explained within a homogeneous cortical area. The current approach accepts that specific functions emerge through anatomically distinguishable but strongly interconnected networks.

Keywords: Aphasia, cortical localization, history of neuroscience, neuron doctrine, reticular theory.

CELLULAR-LEVEL DEBATES

The question of whether brain functions are localized to specific anatomical regions or whether the brain operates as an integrated whole is one of the oldest and most enduring debates in modern neuroscience. This discussion is not limited to the clinical localization of cortical functions but is also closely related to the question of the fundamental structural unit of the nervous system; namely, whether neurons should be regarded as independent cellular units or as components of a continuous network. In this review, the contrast between the reticular theory and the neuron doctrine at the cellular level is first examined, followed by the historical tension between cortical localization and holistic conceptions of brain function at the clinical level. The final section summarizes how contemporary neuroscience has moved beyond this historical dichotomy toward a distributed, connectional, and network-based understanding of localization.

The idea that the cell is the basic unit of life in an organism has become generally accepted. For many anatomists, however, this view did not appear to apply to the nervous system. In the nervous system, cells exhibited a different morphology: they possessed long axons and spine-like cellular processes. These features gave rise to an alternative interpretation, according to which all nerve cells functioned together through their interconnections. Even the most powerful microscopes of that period could not clearly distinguish whether the cells were separate or fused. Consequently, two different views emerged. According to the view proposed by Robert Remak, the nerve cell and its fiber constituted a single entity. This concept was later incorporated into cell theory and subsequently into the neuron doctrine.

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Received: June 05, 2026 **Accepted:** June 06, 2026 **Published online:** June 11, 2026
Cite this article as: Süzen Ekinci A, Ertekin C. Is there localization in the brain or not? A 150-year-long scientific debate. Turk J Neurol 2026;32(2):113-124. https://doi.org/10.55697/tnd.2026.753.

According to Valentin, a student of Purkinje, the nerve cell and the nerve fiber were considered separate and distinct entities. This view should not be confused with the later reticular theory, which proposed a continuous neural network; rather, the idea of distinct cellular elements contributed more closely to the conceptual background from which the neuron doctrine would emerge. According to the reticular theory, even if the nerve cells and their fibers (axons and dendrites) were interconnected, they were thought to extend to other nerve cells, and communication was believed to operate collectively throughout the entire brain. However, if nerve fibers fused with other nerve fibers, could these nerve cells truly be considered cells in the functional sense? This question became the central focus of discussion.[1]

The debates that began in the 1840s continued into the 1860s. At that time, the German professor Joseph von Gerlach (1820-1896) of the University of Erlangen entered the discussion and became one of the proponents of the reticular theory. He used a solution containing a very small amount of carmine dye in sections of the cerebellum, clearly demonstrating the nerve cell and its processes. He reached the following conclusion: the nervous system is a network composed of extremely fine and highly complex nerve fibers. This applied to both the brain and the spinal cord. He published his findings in 1872. Many other neuroanatomists also accepted his view that anastomotic connections existed between nerve cells.[1,2] By the end of the 19th century, however, the reticular theory had receded, and the neuron doctrine had become dominant. It is useful to briefly mention other important investigators associated with these two views. Among the proponents of the reticular theory were Golgi, Kölliker, and Deiters.

The anatomist Albert von Kölliker (1817-1905), who defended the reticular theory, obtained data that contributed to the cell theory while studying somatic cells. Kölliker, who was born and educated in Zürich and later spent the major part of his academic career in Würzburg, made substantial contributions to microscopic anatomy and histology. In the illustrations of nerve cells in his books, the nerve cell and the nerve fiber were shown as a single unit. He was even credited with being the first to describe the independent nerve cell, although Remak had in fact made this observation earlier. Kölliker published Handbuch der Gewebelehre des Menschen (Handbook of Human Histology) in 1852, followed by the three-volume Mikroskopische Anatomie (Microscopic Anatomy) in 1854.[1] He later advanced his work on this subject, observed the myelin sheath surrounding nerves, and suggested that it was produced by other types of cells. However, he could not determine whether the endings of nerve fibers fused with other nerve cells or remained separate from them. In the twentieth century, his views shifted toward the neuron doctrine in response to the discoveries of Ramón y Cajal.[1,3]

The German neuroanatomist Otto Friedrich Karl Deiters (1834-1863) was born in Bonn and carried out his work at the University of Bonn. He stained nerve fibers emerging from the anterior horn cells of the bovine spinal cord and succeeded in isolating an individual nerve unit with the aid of a fine needle. This microscopic analysis was the first demonstration that individual nerve cells could be isolated. More importantly, it made it possible to observe the nerve cell and its processes in detail. Deiters observed that the nerve cell had many processes, which he called protoplasmic extensions. Today, these processes are known as dendrites. Deiters is regarded as the first neuroanatomist to distinguish dendrites from the axon. Using the same methods, he also visualized cells that are now called astrocytes. In fact, astrocytes had first been identified as glial cells (supporting cells) by Rudolf Virchow in 1858. According to Deiters, the brain was composed of different types of cells. He examined the anatomical structure of the medulla oblongata and found it to be more complex than the spinal cord. He also described structures in the brain, contributing to the identification of the reticular formation and the lateral vestibular nucleus. In later generations, the lateral vestibular nucleus came to be known as Deiters' nucleus. Deiters' drawings of single neurons supported the concept of an independent nerve cell favored by Kölliker and his group. Nevertheless, Deiters was still regarded as a proponent of the reticular theory and did not oppose the idea that neuronal processes formed a network. In his view, these neural networks formed connections in which groups of nerve cells in a particular region influenced specific parts of the body. However, Deiters could not technically demonstrate the connections among the nerve fiber endings. This issue would remain an important problem for neuroanatomists for many years. Deiters died of typhus at 29 years of age. It is unfortunate that he was unable to publish his work as a book; what remained were incomplete reports of his investigations. Fortunately, his colleague Max Schultze published a book containing his findings in 1865.[1,2,4]

Almost contemporaneously with these reticular theorists, the neuroanatomist and physiologist Robert Remak (1815-1865), who lived in Germany, was among the proponents of the cell theory. Remak had a difficult life. He was, in fact, one of the leading microscopists of the 19th century. As a Polish Jew, he encountered obstacles both in university life and later in his career. Antisemitism prevailed in Germany during that period. Although this racism had not yet reached the dangerous dimensions it would assume in the 20th century, Jewish individuals nevertheless faced various social barriers. Remak was allowed to conduct research at the university without being appointed to a paid position and without receiving a salary or official status. As a physician, he attempted to earn his living through private practice. He lived in Berlin. He first obtained a high-quality microscope and pursued his doctoral studies. He conducted studies on neural growth and embryogenesis in rabbits and on peripheral nerves. He observed that some nerve fibers were surrounded by a colored sheath, whereas this sheath was absent in other fibers.

In summary, Remak distinguished myelinated from unmyelinated nerve fibers. During this work, he also noticed that the myelin sheath was interrupted at certain points, but he regarded these interruptions as artifacts. In this respect, he was mistaken. These interrupted and depressed regions are now known as the nodes of Ranvier. The French histopathologist Louis Antoine Ranvier (1835-1922) identified and examined them in 1871. Shortly afterward, Remak made another important discovery. In the spinal cord, he observed that organic fibers emerged from the cell body, which he referred to as a globule. In other words, contrary to previous claims, he showed that the cell body and the nerve fiber formed a single unit. This work was clearly important: (1) a fiber emerges from a nerve cell, indicating the presence of a cell and its axon; (2) a nerve fiber leaves the nervous system from the spinal cord and reaches the muscle, which it innervates; and (3) the cell and the fiber constitute a single functional unit. Remak later discovered that one cell divides into two cells by division. He made this discovery in the red blood cells of chick embryos. This was his most important contribution to cell theory and brought him considerable recognition. However, cell division was not widely accepted for 15 years until Rudolf Virchow stated in 1855, while presenting his theory, that it was correct. Although Remak had reported cell division before Virchow, the discovery was attributed to Virchow, and Remak's earlier contribution was forgotten. In 1859, Remak's academic situation improved, and he was granted a salaried academic position. He died six years later.[1,3]

The last and most famous of the reticular theorists was the Italian Bartolomeo Camillo Emilio Golgi (1843-1926). As a young physician, he worked in 1872 at a chronic psychiatric hospital near Milan. He managed to establish a small histology laboratory in the kitchen of this hospital. There, in 1873, he discovered the tissue stain that would bring him great fortune. The method he developed, later known as the Golgi method or "black reaction" *(reazione nera)*, was based on tissue hardening with potassium dichromate followed by silver nitrate impregnation, producing a silver chromate precipitate that made selected neurons sharply visible. When he used this stain, the nerve cells and fibers in the preparation became highly distinct and sharply visible. In 1873, Golgi described the cells of the cerebral cortex using this new silver nitrate staining technique in an Italian medical journal. However, the article did not attract widespread attention. Using this technique, he also clearly demonstrated neurons in the cerebellum (1874), olfactory bulb (1875), and hippocampus (1883). In 1881, he studied spinal cord cells. During this work, he showed for the first time that axons were not always single fibers and could sometimes give rise to small branches. He divided axons into types 1 and 2. The type 1 axon was myelinated, whereas the type 2 axon lacked a myelin sheath. Each gave rise to collateral branches along its course. Dendrites also gave off a number of branches. Golgi interpreted these observations as follows: axons fused with other axons. More specifically, branches of a type 1 axon or nerve fiber formed anastomoses with branches of a type 2 nerve. According to Golgi, the gray matter of the brain and spinal cord formed a diffuse nervous network, which he called the rete nervosa diffusa. In this interlocking neural arborization, axons fused. He stated that the ends of these branches were free; in other words, he believed that nerve-cell processes connected to one another to create a neural network.[1,3-6] In 1876, Golgi was appointed professor of histology at the University of Pavia. In 1881, he became chair of general pathology. Later, he collected all his studies in a book. Within roughly two years, Golgi's staining technique became known abroad. Nevertheless, his theory concerning the network structure of the brain began to attract criticism. The first criticism came from Wilhelm His (1831-1904), a Swiss scientist at the University of Leipzig. Wilhelm His was a student of Remak. In 1886, His rejected the reticular theory and stated that nerve cells were like the other cells of the body: "The cells of the nervous system are independent units that maintain their own existence throughout life." In 1889, His gave the name "dendrite" to protoplasmic processes, deriving it from the Greek word "dendron," meaning "tree."[4]

Similarly, the Swiss scientist Auguste Forel (1848-1931) opposed the reticular theory on the basis of his studies. Forel was a professor at the University of Zurich. He attempted to examine the origins of the cranial nerves emerging from the brainstem, using the technique of Wallerian degeneration. This technique reveals the anatomical structure of a nerve in full detail. For example, when the nerve of the tongue is cut, the retrograde degeneration can be traced within the brainstem. To his surprise, in all cranial nerve lesions, the cranial degeneration was observed only in a small, somatotopically restricted region of the brainstem. At first, Forel could not explain these findings. Later, however, he reasoned that when a nerve was cut, the remaining portion of the cell (the proximal, cranial, or cephalad portion) invariably underwent neuronal degeneration.[7-10] In other words, this finding also led Forel to reject the reticular theory and accept the cell theory.[1-3]

Another line of evidence against the reticular theory came from the Norwegian explorer and scientist Fridtjof Nansen. He was the curator of the Bergen Zoological Museum. He began to examine the cells of crustaceans and mollusks with Golgi staining. The nervous systems of these marine animals are very simple, and their neurons are relatively large. In these animal studies, he found no evidence supporting the reticular theory. Neurons appeared to extend individually and independently. There was no axonal or dendritic connection or fusion. After submitting his thesis, he left for the 1888 Greenland expedition. The crossing itself lasted several weeks, and because no ship was available for the return journey, he and his party spent the winter of 1888-1889 in Greenland before returning to Norway. By the time he returned, his studies had likely been forgotten. He himself never returned to anatomical research. In 1922, however, he received the Nobel Peace Prize for his assistance and contributions to refugees fleeing war.[1,4]

This scientific, and at times personal, confrontation at the end of the 19th century carried the field toward the modern neuroscience of the 20th century. The Spanish scientist Santiago Ramón y Cajal (1852-1934) completely rejected the reticulum, or reticular theory, and replaced it with the neuron doctrine, establishing neurons and their connections as foundational scientific knowledge. When he began working in Barcelona, he was impressed and intrigued by Golgi's silver staining technique developed in 1873. He attempted to learn this new technique and, despite difficulties, succeeded in applying it. Golgi's method was inadequate for demonstrating myelinated axons. To overcome this limitation, Cajal used immature nervous tissue and examined nerves before they became myelinated. In this way, it became easier to study neural connections. While examining the development of young animals of different ages, he observed how the nerve cell structured the nervous system. Once Cajal had mastered the method, he began his true investigations. He translated the microscopic images into drawings with his skilled and artistic hands. He sent copies of six richly illustrated articles to the most famous and important anatomists in Europe. In the drawings he sent, there was nothing suggestive of a reticular structure. He also noted important histological differences between the cerebral cortex and cerebellar gray matter, a finding that contradicted the reticular theory. He observed that the axons of small granular cells in the cerebellum always terminated on the dendrites of Purkinje cells. He found that such organization existed throughout the brain. He understood that this offered a new way to understand how information is transmitted by the nerve cell. Golgi, however, had overlooked the role of dendrites and had assigned them only a nutritive function; indeed, he had claimed that nerve signals were carried from the cell body. Cajal reached a different conclusion. If the axon extended toward dendrites, then conduction could proceed to dendrites in this way. Thus, he concluded that first the cell body, or soma, received information and then transmitted it to its axon. This scientific insight was revolutionary. These observations indicated that dendrites were the receptive part of the nerve cell, serving, in a sense, as its antennae. By contrast, the axon was the apparatus that emitted and distributed signals. Cajal thus introduced a new theory of dendritic-somatic-axonal conduction, which he called the principle of dynamic polarization.[1,2,6]

Cajal's new discoveries did not immediately attract the attention of other scientists. In 1889, he went to a congress in Berlin. Many distinguished European anatomists were present. Cajal did not speak German. In broken French, he invited delegates to look through his microscope and examine the images he had obtained. Among the participants was Albert von Kölliker, the most respected and senior anatomist at the meeting and formerly a proponent of the reticular theory. Kölliker examined all of Cajal's images and preparations. After seeing the structure of brain cells under the microscope, his views changed. Kölliker was deeply impressed. He invited Cajal to the luxury hotel where he was staying; they talked over dinner, and Kölliker supported the dissemination of Cajal's technique among other microscopists. Within a year, summaries of Cajal's studies appeared in two prestigious German journals. Kölliker had been convinced and now believed in the validity of the cell, or neuron, doctrine. Cajal began to influence the scientific world through his pioneering investigations. His work was later confirmed by other researchers. Cajal's findings were exceptionally clear, accurate, and demonstrated considerable scientific insight.[4,9]

The German anatomist Wilhelm Waldeyer consolidated the concept of the nerve cell in 1891 by writing a six-part review. Waldeyer's review was written with great skill; it presented the nerve cell as the structural, embryological, and functional unit of the nervous system. Waldeyer made an important contribution: he gave the nerve cell the name "neuron." Thus, the new theory entered science as the neuron doctrine. Only Kölliker preferred the term "neurondendron." Although proponents of the reticular theory raised various criticisms of the neuron doctrine, these criticisms did not gain widespread acceptance in the 20th century. Cajal continued his work and identified neurons with two processes in certain regions of the brain; these are now called bipolar cells. This discovery also led him to revise his law of dynamic polarization. "The cell body (soma) is not directly involved in the transmission of impulses," he said. "In some cases, the impulse, or nerve current, passes directly from the dendrite to the axon." He called this new concept axipetal polarization and presented it at the Valencia Medical Congress in 1891. Later, he described the intracellular neurofibrils that we still recognize today. These are thin, band-like structures that allow impulses to pass from dendrite to axon. After making continuous anatomical discoveries, Cajal began to reflect on a new problem: "If there is no reticular structure in the nervous system, how does one axon activate another neuron?" By the 1890s, this question was receiving increasing attention. The most promising site in which to seek an answer was the neuromuscular junction. More precisely, how do spinal motor neurons connect to muscle, or how do they transmit the impulse? The German anatomist Wilhelm Kühne (1837-1900) showed microscopically that a cleft existed between the motor nerve fiber and the muscle at the neuromuscular junction. He reported that the nerve ending released a fluid-like substance, which crossed the narrow cleft to reach the muscle. Naturally, this raised the question of whether a similar mechanism might also exist in the central nervous system. Cajal investigated this in embryonic stem cells but could not reach a definitive conclusion. The matter would be resolved by the English physiologist Sherrington, who would also become a friend of Cajal. He gave this gap, or connection, the name "synapse." The term synapse thus emerged. Sherrington proposed that transmission of the nerve impulse occurred at the synapse. Accordingly, proponents of the neuron doctrine began to use this new and almost magical word for the connection between muscle and nerve cells. Nevertheless, definitive proof of the synapse became possible only in the 1950s, with newly developed microscopes.[1,2,4,11]

DEBATES AT THE CLINICAL LEVEL

Neurology, and particularly a deeper understanding of the brain, did not develop easily. Although the 18th century and even the first half of the 19th century were marked by scientific disputes and often by restrictive interventions from religious and political institutions, knowledge in science and medicine increased gradually. Studies of the brain and the controversies surrounding them generally did not attract much attention from the public. However, in the final years of the 18th century and the early 19th century, the German physician Franz Joseph Gall (1758-1828) and his theory of craniology began to attract substantial public attention. This movement, later called phrenology, influenced all of Europe and extended as far as the United States, gradually shifting from a scientific framework toward popular appeal. Gall defined 27 paired cerebral organs or functions within the cerebral cortex. He carried the idea of brain localization very far and, in 1796, began to present his theory and findings, which he called "craniology," through public lectures. He later renamed this theory organology, but the system eventually became known as phrenology. Albrecht von Haller (1708-1777), who lived in the 18th century, was also interested in the cerebral cortex. According to Haller, the cerebral cortex functioned as a whole, and there were no differences among brain regions in terms of their cortical functions. This view was the opposite of Gall's doctrine, which held that the mind and the brain were not a single functional unit but rather a collection of distinct parts.[1] The most significant scientific challenge and opposition to Gall and phrenology came from the French scientist Marie Jean Pierre Flourens (1794-1867). On the basis of animal experiments, Flourens stated that each part of the nervous system had specific functions; however, he also argued that the brain operated as an indivisible whole.

The philosopher Georg Wilhelm Friedrich Hegel (1770-1831), who lived during the same period as Gall, was aware of Gall's ideas. His views of Gall, however, were unfavorable. According to Hegel, "The skull has no significance in itself. Moreover, there is nothing in the skull that can be seen or discovered beyond the skull itself."[2] From a historical perspective, Gall moved beyond earlier speculative philosophical theories and recognized that mental functions or phenomena had a biological basis. This was his first and most important contribution at that time. His second contribution was that he rejected the idea of the brain as a single functional organ and proposed a model composed of parts with different characteristics, leaving this model to subsequent generations. Considering that these theories were advanced 200 years ago, it is important that, despite academic objections, rejection, contempt, and punishments in his time, he persistently defended and attempted to modernize his ideas about the brain.

The first serious clinical observations in favor of cortical localization were the recognition of speech disturbances in patients with right hemiplegia. In a book published in 1829, the Scottish physician John Abercrombie (1780-1844) described a 56-year-old man who suddenly developed an inability to speak together with right hemiplegia. The patient remained comatose for a time; when consciousness returned, difficulty in word finding was noted. At autopsy, a cyst was found in the left hemisphere. In the historical record, this was the first patient in whom attention was drawn to a speech disturbance associated with a left hemispheric lesion. Shortly afterward, the French physician Bouillaud described a similar patient. This physician was Jean Baptiste Bouillaud (1796-1881), the impoverished physician who had earlier appeared as a character in Balzac's famous novel Père Goriot. Bouillaud worked in Paris as a pupil of Magendie. While studying the relationship between heart disease and rheumatism, he became one of the first to use digitalis in patients with heart disease and hypertension. He later became a professor in 1831. From his youth, he had also observed loss of speech in individuals with frontal lobe lesions. He subsequently devoted more attention to this issue. In a short monograph published in 1825, he wrote that fluent speech was impaired in frontal lobe damage, while intelligence and comprehension were preserved to an adequate degree. He also emphasized that the speech disturbance in these patients was not accompanied by lingual paresis or dysphagia; the problem lay in the production of words. Based on these observations, he concluded that the frontal lobes could be responsible for language production. This view was debated in academic circles, but Bouillaud's interpretation was largely rejected. He was initially criticized for being influenced by Gall and phrenology. Bouillaud did not give up, however, and 10 years later presented his patients, together with autopsy reports, to the medical community but again failed to convince others.[1] His son-in-law, Ernest Aubertin, was a physician who supported him both materially and intellectually. While working in Paris, Aubertin concentrated on patients with aphasia.[12] One day he encountered an interesting patient: a man who had shot himself in the forehead in a suicide attempt. His left frontal lobe had been destroyed, yet his speech and intelligence were preserved. During the operation, when pressure was applied with a spatula to the left frontal lobe, the patient, who had been speaking at that moment, suddenly stopped speaking. When the pressure was removed, his speech immediately returned. Aubertin presented this observation to the Anthropological Society and argued that the speech center was normally located in the frontal lobes. Most participants did not find this conclusion convincing. Among the listeners was Paul Broca, the founding president of the society.

At that time, Broca was well known and highly respected in France. He did not participate in the discussion. However, with his first published case of aphasia, the views of many would soon shift rapidly in favor of cortical localization.[1,12,13]

Paul Broca (1824-1880) was recognized as a reliable and respected brain researcher of the 19th century. He was both a physician and an anthropologist. As an anthropologist, he described the Cro-Magnon people. As a physician, besides producing original work in other branches of medicine, he was also the first to report the existence of the limbic cortex and to propose that this structure was related to emotions. Shortly after Aubertin's lecture, again in 1861, Broca reported his first aphasic patient at Bicêtre Hospital. At autopsy, he found an egg-sized cyst in the second or third convolution of the left frontal cortex. Although Bouillaud and Aubertin had long argued that damage to these regions produced speech disturbance, from that time the region became known as Broca's area. While Broca continued working at Bicêtre Hospital, he examined a second patient, later known as Lelong, who had suffered a stroke and was severely limited in spontaneous speech. Unlike Leborgne, who was famous for repeatedly uttering the syllable "tan," Lelong could produce only a few words, including "oui," "non," "trois," "toujours," and a distorted form of his own name. Nevertheless, he understood questions and responded appropriately with gestures. According to Broca, this patient was not unable to speak in the general sense; rather, he had lost the ability to articulate words. After the patient's death, Broca performed an autopsy and found a lesion in approximately the same left lateral frontal region as in his first case. Thus, rather than weakening Broca's localizationist argument, the second case provided further support for the association between articulated speech and the left inferior frontal region. Broca termed this condition aphemia.[1,2] In this way, the terms aphemia and aphasia entered the literature of the cerebral cortex. As a result of his studies, Trousseau reported 135 patients who had lost the ability to speak despite having no demonstrable lesion in the frontal cerebral lobe. The ratio of 2 to 135, in fact, accelerated the debate over Broca's localization theory. Indeed, scientific debates regarding the functional organization of the cerebral cortex had not ended, and the view represented by Flourens and Goltz that the cerebral cortex could not be divided into functionally discrete parts began to gain increasing support.[2,3]

The term aphasia was first used by the internist Armand Trousseau (1801-1867), and it gradually replaced Broca's term in the medical literature. Trousseau's contribution further broadened the discussion of speech disorders and stimulated debate on whether language disturbances could be explained by a simple and rigid localization model. Although Broca's findings strongly supported cortical localization, scientific debates regarding the functional organization of the cerebral cortex had not ended. The view represented by Flourens and Goltz, according to which the cerebral cortex could not be divided into strictly discrete functional parts, continued to influence the discussion.[2,3] Despite these objections, Broca soon reported eight additional patients with aphasia associated with damage to the same region of the left frontal lobe, and his views received support from two sources.[1] First, support came from two French colleagues, Louis Pierre Gratiolet (1815-1865) and Francois Leuret (1797-1851), who were studying developmental changes in the human brain during fetal life. They observed that the left hemisphere was larger than the right during fetal development and that this asymmetry appeared in the early months of gestation. The second source of support came from England, from the renowned neurologist John Hughlings Jackson (1835-1911). According to Jackson, the left hemisphere learned, or was trained, earlier than the right hemisphere. Consequently, language capacity also developed earlier on the basis of the left hemisphere.[1]

Broca also offered further insights in this area. In right-handed individuals, the left hemisphere was dominant and provided superior motor control of the hand. If the left hemisphere was dominant over the right, this could account for right-handedness. In left-handed individuals, the right hemisphere would be dominant. According to Broca, the predominance of right-handedness in the population resulted from the superior development of the left hemisphere. Nevertheless, Broca had also encountered individuals in whom language was not localized to the left hemisphere. He explained this apparent contradiction as follows: "In certain situations, the right hemisphere may be responsible for speech, and when there is damage to the left hemisphere, the person may become left-handed." However, Broca was aware that some individuals were left-handed despite having no lesion in the left hemisphere, and he was unable to explain this phenomenon within the scientific framework of his time.

Broca then encountered another challenge. The speech center in the left frontal lobe had come to be known as Broca's area. However, a little-known French physician, Gustave Dax, challenged Broca's claim of priority. His father, the provincial physician Marc Dax, had described three aphasic patients with left hemispheric lesions at a medical conference in Montpellier in 1836, 25 years before Broca's report. These observations were subsequently published in two short articles. In 1865, the French Academy of Sciences issued a statement on the matter. Priority was awarded to Broca because he was likely unaware of Marc Dax and his publications. Furthermore, Broca had been able to provide detailed anatomical localization of the lesion to the third frontal gyrus of the left hemisphere.[1,2,14]

Around the same time, John Hughlings Jackson (1835-1911), one of the pioneers of neurology at the newly established and renowned National Hospital and Institute of Neurology in London, investigated the effects of brain lesions as well as epilepsy. He observed that speech disorders frequently occurred together with right hemiplegia and, in 1864, published observations on speech disorders in patients with left hemispheric lesions. In 1866, he partially revised his views and reported that speech disturbances could occasionally occur in patients with right hemispheric lesions, suggesting that the right hemisphere also possessed certain language functions. He regarded the left hemisphere as being responsible for intellectual speech, whereas the right hemisphere mediated involuntary and emotional aspects of speech. In other words, both hemispheres contributed to language, but each was involved in different aspects of speech processing. Accordingly, unlike Broca, Jackson referred to the hemispheres as the major and minor hemispheres. He also observed that some patients with left hemispheric lesions could recognize objects but were unable to name them. As he continued to study such cases, his views evolved, leading him to remark: "It is one thing to localize the lesion that disturbs speech; it is another thing to localize speech." Based on his observations of patients with epilepsy, Jackson described somatotopic organization (a body schema) within the motor cortex and demonstrated that neuronal discharges produced topographically ordered epileptic muscular contractions involving the contralateral side of the body. He further proposed the existence of three evolutionary levels within the sensorimotor system.[15]

While debates on aphasia were ongoing, the young German physician Karl Wernicke (1848-1905) identified a different type of aphasia arising from a distinct brain localization in 1874. After graduating from Breslau Medical School, he spent six months in Vienna working with Theodor Meynert (1833-1892). Meynert was both a physician and a neuroanatomist. Before Wernicke joined him, Meynert had treated a female patient whose speech was strange and incomprehensible. At autopsy, a large lesion was found in the superior portion of the left temporal lobe, where the auditory pathways were believed to terminate. Meynert therefore proposed that the temporal lobe contained an auditory area responsible for the recognition of speech. Wernicke was greatly influenced by Meynert's ideas. Upon returning to Germany in 1874, he published a paper on the different forms of aphasia and included the aphasia observed in Meynert's patient. This case attracted considerable attention. The patient's speech was incomprehensible and contained inappropriate expressions, yet individual words could still be recognized. Wernicke argued that this represented a new type of aphasia and that it resulted from damage to the left temporal lobe. This region was anatomically distant from the frontal lobe. For a young physician only 26 years of age, publishing such a paper on sensory aphasia represented a remarkable achievement. Wernicke's contribution lies in bringing a new approach to sensory aphasia and to aphasias in general. The disorder in this type of aphasia reflects an impairment of perception and comprehension. More specifically, auditory information reaching the temporal lobe was processed within an auditory language area, which was believed to contain memory representations of previously learned and recognized words. The information processed in the temporal lobe was then transmitted to the frontal cortex, where it could be compared with verbal motor patterns generated by the speech apparatus, including the larynx, thereby enabling fluent speech. Wernicke termed the speech disorder resulting from lesions in the temporal lobe as sensory aphasia. He also referred to aphasia originating from the frontal lobe as motor aphasia. Thus, the neuroanatomical organization of speech, along with brain structure, was elucidated. According to Wernicke's model, nerve fibers connecting the temporal and frontal lobes had to exist, although they had not yet been identified at the time, and Wernicke was naturally unaware of them. He further proposed that a lesion interrupting the connection between the two centers could result in motor aphasia, as the temporal auditory center remained intact. In such cases, since the disorder lay in the pathway between the two centers, patients were unable to repeat words fluently. The impairment became particularly evident during the repetition of abstract words, and patients were often aware of this deficit. This type of aphasia is now known as conduction aphasia.[1,2,16] Although Wernicke based his work on a patient he had not personally examined, in the booklet he wrote on this subject, he developed a theory that, consistent with modern understanding, grounded sensory and motor aphasia in an underlying pathophysiology. This theory had a major impact in Europe at the time and provided a model for understanding speech disorders. Patients with sensory aphasia do not die rapidly and may improve over long periods. Therefore, Wernicke himself may also have encountered other clinically distinct cases of sensory aphasia; however, as such patients could survive for long periods, opportunities for autopsy were limited.

Before moving to the localizationist approach, it is useful to briefly introduce the anti-localizationist approach, which viewed the brain functionally as a whole.

An understanding of the experiments and views of Marie Jean Pierre Flourens (1794-1867), a leading proponent of anti-localizationism, helps clarify the concept of cortical holism. Flourens was a Parisian French physician and surgeon. In his early years, he showed interest in phrenology, but in the 1820s, he became a critic of Gall, aligning his views more closely with Cartesian dualism, which was widely accepted in French academic circles at the time. From the 1820s onward, Flourens used ablation studies to investigate brain functions. Through this method, he sought to examine brain function in experimental animals, particularly its role in behavior. By producing lesions in specific brain regions, he conducted postoperative behavioral observations after the effects of anesthesia had worn off. This approach was considered an important and relatively reliable method for studying the relationship between brain and behavior. When he produced small cortical lesions, he observed no detectable change in the animals. Even when he ablated larger areas, he did not observe any clear or consistent deficits. After removing one cerebral hemisphere in a pigeon, he noted loss of vision in the eye contralateral to the lesion. When he decerebrated a pigeon, the animal was unable to localize sound and lost the tendency to feed; however, when food was placed in its beak, it swallowed it. Similarly, the bird remained largely immobile, entered a sleep-like state, and was difficult to arouse. Nonetheless, when the pigeon was thrown into the air, it was still able to fly without difficulty. On the basis of these findings, he proposed that the cerebral hemispheres as a whole were responsible for mental functions such as perception, memory, volition, and judgment. He also argued that the cerebral cortex was not divided into discrete functional units or faculties. This view was the direct opposite of the system proposed by the phrenologists of the time. It should also be noted that proponents of phrenology represented the speculative and empirically unsupported form of localizationism of their era. According to Flourens, perception and voluntary movement were represented throughout the cerebral cortex, and all functions were integrated: "All sensations, all perceptions, and all voluntary movements occupy the same place in the brain. Brain function is so evenly distributed across all parts that, even if a large portion of the brain is removed, the remaining part is sufficient to subserve all organic and psychic functions," he stated. In other words, no cortical area was more important than another. All regions of the cerebral cortex were considered to play equivalent roles in thought and behavior.[1,17,18]

Flourens stated that "the cerebral cortex and its connections perform higher functions of perception and recognition, as well as sensory functions." He referred to this final part as the encephalon. Intelligence and the general functions of the body are regulated in the encephalon and operate in a certain harmony. Gall was aware of Flourens' holistic conception of the cortex and was the only one who criticized his experiments. On the other hand, Flourens' ideas and findings were generally accepted. He became very well-known and was admitted to the French Academy of Sciences, where he eventually rose to the position of secretary. Thus, for a very long period, no one challenged Flourens' views. As a result, for a considerable period, his views were largely unchallenged, becoming a kind of dogma.

Clinical neurological findings and experiments involving electrical stimulation of the cerebral cortex later provided evidence against this earlier holistic view, yielding stronger support for localization. The role of the English neurologist David Ferrier (1843-1928) was particularly important in this regard. By the late 19th century, despite the accumulation of substantial evidence for cortical localization, another strong anti-localizationist approach emerged. This view was proposed by the German scientist Friedrich Goltz (1834-1902), who conducted decortication and decapitation experiments in frogs and dogs. According to him, these experiments produced results that contradicted the idea of cortical localization. Although he accepted that lesions in specific cortical areas could lead to certain deficits, he argued that no cortical region is responsible for a specific function. In Goltz's view, these deficits could be explained by a general impairment of attention resulting from damage to any cortical area, and the cerebral cortex as a whole was responsible in a global and holistic manner.[1] The German Goltz and the English localizationist neurologist Ferrier eventually confronted each other at the World Medical Congress held in London in 1881, effectively concluding this debate. However, earlier, two German researchers, Eduard Hitzig (1838-1907) and Gustav Theodor Fritsch (1838-1927), had experimentally demonstrated cortical localization in dogs using electrical stimulation with anodal electrodes and published their results in 1870. These results confirmed the concept of cortical localization and opened a new field in neurophysiology. However, the work also received some criticism. The fact that the paralysis induced in dogs was not complete suggested that other cortical areas might also be involved, implying that additional intact cortical regions must exist. Viewed from any perspective, their results refuted the holistic conception of the brain. The final word on this issue was left to David Ferrier (1843-1928), who, through cortical stimulation and ablation studies, particularly in monkeys, obtained convincing results in favor of localization.[1,3,19] Ferrier also considered the superior temporal region as the area responsible for processing sounds received from the ear. In 1881, Ferrier encountered the anti-localizationist German physiologist Goltz at the International Medical Congress in London, which was attended by more than 3,000 delegates from over 70 countries. One of the sessions was devoted to cortical localization, and it was in this session that the debate between Goltz and Ferrier took place and was long remembered. Ultimately, the victory belonged to Ferrier and the localizationists.

CURRENT UNDERSTANDING OF LOCALIZATION

After decades have passed, when we turn to the current understanding of localization, we can say that there is no single, definitive center for social behavior, intelligence, or reasoning. Moreover, vision and language are considered to have a highly distributed form of localization. There are systems composed of several interconnected brain units. These units are not functional; however, in an anatomical sense, they are still not fundamentally different from the classical localizationist view. These systems form the basis of mental functions and perform relatively separable roles. From the perspective of intelligence, it emerges from the activities of different components that constitute it and from the combined functioning of multiple systems formed by the integration of these parts.[20]

This holistic view was later referred to as the "aggregate field" theory. However, this theory was based solely on Flourens' experimental work. Moreover, the idea of explaining the human mind with a localizationist biological perspective was not acceptable in terms of the traditional concept of the soul. The first neurologist to oppose the aggregate field theory was Hughlings Jackson, who, while observing patients with focal cortical epilepsy, suggested that different parts of the cerebral cortex might have different motor and sensory functions.[15] The work of later physiologists and anatomists also supported the validity of the localizationist view.

The localizationist view was developed through the clinical study of aphasia by Broca and, in particular, Wernicke. In later years, the localizationist view was even called the theory of cellular connectionism.[21] At this point, it is worth making a special note of Wernicke. His view, which opposed that of the aggregate field theorists, was as follows: "Basic mental functions, such as simple perception and motor functions, are localized to distinct and specific areas. More complex cognitive functions arise through interconnections among multiple functional units." Thus, Wernicke showed that a single behavior is the result of processes involving different brain regions, and he was among the first to articulate the idea of distributed processing in the brain. This is a central mechanism in brain function. It should also be recalled that, in the early 20th century, the anatomist Korbinian Brodmann distinguished 52 different anatomical and functional areas in the cerebral cortex using the cytoarchitectonic method. Despite these advances, the aggregate field theory re-emerged during the first half of the 20th century, and this experimental perspective came to dominate clinical practice. The new advocates of this view included the English neurologist Henry Head, the German neuropsychiatrist Kurt Goldstein, Ivan Pavlov, and, above all, the American psychologist Karl Lashley (1890-1958).[22] Among this group, Lashley was the most influential. He was skeptical of the claim that the cortex could be divided into distinct functional regions on the basis of cytoarchitectonic methods. He argued that the cytoarchitectonic map was almost entirely invalid. As a result of Lashley's skepticism, the anti-localizationist view of Flourens from the 19th century re-emerged and gained strength.

According to Lashley, "the learning defect is not related to damage to a specific brain region; rather, it depends on the extent of the lesion." Psychologists who followed him also maintained the view that there was no specific focus for learning or other mental functions. Lashley used the term "law of mass action" for brain functions. Clinical scientists such as the English neurologist Henry Head (1861-1940) and the German psychiatrist Kurt Goldstein (1878-1965) also continued to be both localizationists and proponents of a holistic approach. For example, in their studies of aphasia and speech disorders, they argued that speech disorders could result from damage to almost any area of the brain. In other words, they suggested that cortical damage, regardless of its localization, could transform a patient's rich abstract language into the impoverished form of expression characteristic of aphasia.[1,17,21] Lashley's rat-maze experiments were later criticized by other scientists. It was subsequently demonstrated that these experiments did not provide sufficient evidence to reject the principle of localization.

The contributions of the American-Canadian neurosurgeon Wilder Penfield (1891-1976) and, later, the American neurosurgeon George Ojemann (1935-present) have been particularly important in studies of brain localization. These researchers stimulated the cerebral cortex with small electrodes in patients undergoing epilepsy surgery while the patients remained awake. The surgical procedure was performed under local anesthesia. Their investigations focused on cortical areas involved in language. Patients were first asked to name objects, after which microstimulation was applied to various cortical regions. If a particular cortical area was involved in language processing, electrical stimulation disrupted the patients' ability to name objects. Through these studies, they confirmed that language functions are localized in cortical regions corresponding to Broca's and Wernicke's areas.[23,24] In addition, Ojemann identified supplementary language-related areas. His work demonstrated that the cortical network involved in speech and language is more extensive than previously believed.[21]

In the second half of the 20th century, with the introduction of advanced techniques such as positron emission tomography and functional magnetic resonance imaging into medical practice, the cortical localization of speech in normal humans was demonstrated objectively. The holistic approach, which opposed the localizationist view, albeit with some reservations, thus returned to its historical position.

In conclusion, the outcome of approximately 150 years of debate demonstrates that brain functions can be reduced neither to rigidly centralized single areas nor to a homogeneous distribution across the entire cortex. The neuron doctrine has clarified the cellular organization of the nervous system, while clinical neurology, electrophysiological stimulation, and modern neuroimaging techniques have shown that specific functions are carried out through anatomically identifiable but widely integrated networks. Therefore, the current understanding of localization is based not on the search for a single center but on the dynamic interaction of interconnected functional systems.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: A.S.E., C.E.: Concept and design, literature review, final approval of the manuscript; A.S.E.: Drafting of the manuscript; C.E.: Critical revision for intellectual content.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

AI Disclosure: The authors declare that artificial intelligence (AI) tools were not used, or were used solely for language editing, and had no role in data analysis, interpretation, or the formulation of conclusions. All scientific content, data interpretation, and conclusions are the sole responsibility of the authors. The authors further confirm that AI tools were not used to generate, fabricate, or 'hallucinate' references, and that all references have been carefully verified for accuracy.

REFERENCES

1. Wickens AP. History of the Brain: From Stone Age Surgery to Modern Neuroscience. New York: Psychology Press, Taylor & Francis Group; 2015.
2. Eckoldt M. Beynin ve Zihnin Kısa Tarihi: Duygular ve Düşünceler Nasıl Oluşur? Mehmet Ali Erbak, çevirmen. İstanbul: Say Yayınları; 2018.
3. Haymaker W, Baer KA. The Founders of Neurology. Springfield, IL: Charles C Thomas; 1949.
4. Finger S. Origins of Neuroscience: A history of explorations into brain function. London: Oxford University Press; 1994.
5. Mazzarello P. Camillo Golgi (1843-1926). J Neurol Neurosurg Psychiatry 1998;64:212. doi: 10.1136/jnnp.64.2.212.
6. Glickstein M. Neuroscience: A historical introduction. Cambridge, MA: The MIT Press; 2017.
7. Lampert PW, Cressman MR. Fine-structural changes of myelin sheaths after axonal degeneration in the spinal cord of rats. Am J Pathol 1966;49:1139-55.
8. Truex RC, Carpenter MB. Human neuroanatomy. Baltimore, MD: Williams & Wilkins; 1969.
9. Ertekin C. Nörobilimin evrimi. İstanbul: Nova Kitap; 2025.
10. Ertekin C, Sarica Y, Uçkardeşler L. Somatosensory cerebral potentials evoked by stimulation of the lumbo-sacral spinal cord in normal subjects and in patients with conus medullaris and cauda equina lesions. Electroencephalogr Clin Neurophysiol 1984;59:57-66. doi: 10.1016/0168-5597(84)90020-0.
11. Sherrington C. The Integrative action of the nervous system. New Haven: Yale University Press; 1947.
12. Stookey B. Jean-Baptiste Bouillaud and Ernest Auburtin. Early studies on cerebral localization and the speech center. JAMA 1963;184:1024-9. doi: 10.1001/jama.1963.73700260007011.
13. Meyer A. Karl Friedrich Burdach and his place in the history of neuroanatomy. J Neurol Neurosurg Psychiatry 1970;33:553-61. doi: 10.1136/jnnp.33.5.553.
14. Öncel C. Nörobilimin öncüleri: Antikçağdan 20. yüzyıla. İstanbul: Nobel Tıp Kitapları; 2018. s. 140-2.
15. Viets HR. The history of neurology in the last 100 years. Bull N Y Acad Med 1948;24:772-83.
16. Greenfield S. İnsan beyni. 2. Baskı. İstanbul: Varlık/Bilim; 2006.
17. Thorwald J. Cerrahların Yüzyılı: Cerrahların dünyası. Ankara: Ankara Üniversitesi Basımevi; 2005.
18. Yildirim FB, Sarikcioglu L. Marie Jean Pierre Flourens (1794 1867): An extraordinary scientist of his time. J Neurol Neurosurg Psychiatry 2007;78:852. doi: 10.1136/jnnp.2007.118380.
19. Ertekin C. EMG'nin tarihsel gelişimi (1890-1960). Klinik Nörofizyoloji EEG-EMG Derneği Yayınları, No. 11. İstanbul: Kitap Vitrini; 2014.
20. Damasio AR. Descartes'ın yanılgısı. 2. Baskı. İstanbul: Varlık Yayınları; 1999.
21. Kandel ER, Schwartz JH, Jessell TM. Principles of neural science. 4th ed. New York: McGraw-Hill; 20000.
22. Todes D. Ivan Pavlov: Hayvan makinasını araştırırken. Ankara: TÜBİTAK; 2003.
23. Penfield W, Jasper HH. Epilepsy and the functional anatomy of the human brain. Boston: Little, Brown; 1954.
24. Ojemann G, Ojemann J, Lettich E, Berger M. Cortical language localization in left, dominant hemisphere. An electrical stimulation mapping investigation in 117 patients. J Neurosurg 1989;71:316-26.