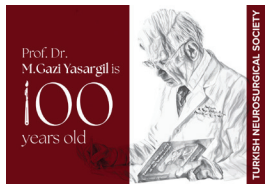
Turk Neurosurg 35(6):963-973, 2025
DOI: 10.5137/1019-5149.JTN.48377-24.1

Historical Article

Received: 31.12.2024
Accepted: 18.03.2025
Published Online: 30.10.2025



The Contributions of Four Pioneers in the Incunabula Period of Modern Neurosurgery

Uygur ER[1], Sait NADERİ[2], Mehmet Nur ALTINORS[3]

[1]Acibadem Ankara Hospital, Neurosurgery Clinic, Ankara, Türkiye
[2]Umraniye Training and Research Hospital, Neurosurgery Clinic, Istanbul, Türkiye
[3]Lokman Hekim Hospital, Neurosurgery Clinic, Ankara, Türkiye

Corresponding author: Uygur ER ✉ uygurer@gmail.com

ABSTRACT

AIM: To highlight the contributions of four surgeons who practiced neurosurgery in the late nineteenth century by examining their works and assessing their impact on the field.

MATERIAL and METHODS: The study focuses on the works of four pioneering neurosurgeons—Fedor Krause, Victor Horsley, Harvey Cushing, and Walter Dandy—who were ahead of their time due to their groundbreaking ideas and meticulous research. Their contributions directly related to neurosurgery are analyzed.

RESULTS: The formative years of modern neurosurgery, spanning from 1879 to 1919, were marked by significant challenges that were addressed through the dedication and efforts of numerous surgeons and basic scientists. While many played a role in this progress, four surgeons stand out for their substantial contributions to shaping the discipline.

CONCLUSION: These surgeons solidified their surgical techniques, scientific advancements, and systematic approaches through their publications and books. As a result of these developments, neurosurgery transitioned from its early stages to an established modern discipline.

KEYWORDS: History of neurosurgery, Fedor Krause, Victor Horsley, Harvey Cushing, Walter Dandy

ABBREVIATIONS: CSF: Serebrospinal fluid, **DES:** Direct electrical stimulation

INTRODUCTION

The 1900s are widely regarded as the era of enlightenment in neurosurgery. This period is considered pivotal in the establishment of modern neurosurgical practices (13). Three major medical advancements in the nineteenth century transformed surgical procedures and laid the foundation for modern techniques. The introduction of general anesthesia enabled pain-free operations and prevented patient movement during surgery. The adoption of antiseptic techniques allowed for aseptic surgical conditions, significantly reducing infections. Additionally, continuous improvements in postoperative care further enhanced surgical outcomes.

On April 25, 1884, Rickman Godlee (1849–1925) successfully removed a brain tumor that had been diagnosed and localized by Alexander Hughes Bennett (1848–1901) (13,31). Three years later, Victor Horsley (1857–1916) excised a spinal cord tumor identified by William Gowers (1845–1915) (13,16). A key but less recognized advancement leading to modern neurosurgery was the development of the cerebral localization concept. Built upon anatomical knowledge from the previous century, this was one of the most significant breakthroughs in neurosurgery, distinguishing it from other surgical specialties (12). During this period, several notable surgeons specialized in cranial and spinal procedures, leading to the development of techniques for treating intracranial pathologies.

Uygur ER : 0000-0002-6641-0075 Sait NADERI : 0000-0002-6784-4270 Mehmet Nur ALTINORS : 0000-0003-1346-0041

Among them, four surgeons made particularly significant contributions to the advancement of neurosurgery in the late nineteenth century. This article aims to examine their contributions by analyzing the works they left behind.

MATERIAL and METHODS

The works of four neurosurgeons who were considered ahead of their time due to their groundbreaking ideas and meticulous research were examined. These surgeons were Fedor Krause (1857–1937), Victor Horsley (1857–1916), Harvey Cushing (1869–1936), and Walter Dandy (1886–1946). The study focuses on their contributions specifically related to neurosurgery. However, these four surgeons were highly prolific authors who also produced significant works in other areas of surgery and medicine.

Works examined:

i. Fedor Krause
   a. *Chirurgie des Gehirns und Rückenmarks* (*Surgery of the Brain and Spinal Cord*)
   b. *Chirurgische Operationslehre des Kopfes* (*Surgical Operation Lessons of the Head*)
   c. *Die allgemeine Chirurgie der Gehirnkrankheiten* (*The General Surgery of Brain Diseases*)

ii. Victor Alexander Haden Horsley
   a. *Experiments on the Functions of the Cerebral Cortex*
   b. *The Structure and Functions of the Brain and Spinal Cord*
   c. *Functions of the Marginal Convolutions*

iii. Harvey Williams Cushing
   a. *The Pituitary Body and Its Disorders*
   b. *Tumors of the Nervus Acusticus and the Syndrome of the Cerebellopontine Angle*
   c. *Meningiomas: Their Classification, Regional Behavior, Life History, and Surgical End Results*
   d. *A Classification of the Tumors of the Glioma Group on a Histogenetic Basis with a Correlated Study of Prognosis*

iv. Walter Edward Dandy
   a. *Intracranial Arterial Aneurysms*
   b. *Orbital Tumors: Results Following a Transcranial Operative Attack*
   c. *Benign, Encapsulated Tumors in the Lateral Ventricles of the Brain: Diagnosis and Treatment*
   d. *Benign Tumors in the Third Ventricle of the Brain: Diagnosis and Treatment*

The listed works, along with selected articles by these four pioneering surgeons, were analyzed to highlight their groundbreaking ideas and concepts, which were considered revolutionary for their time.

RESULTS

Fedor Krause

Fedor Krause is regarded by some as the father of German neurosurgery and by others as one of the pioneers of modern neurosurgery. He was born on March 10, 1857, in Friedland, Niederschlesien (now Mieroszów, Poland) (2). After completing his surgical training at the University of Halle, he presented a thesis on peripheral nerve tumors titled "Über malign Neurome Und das Vorkommen von Nervenfasern in denselben" (On Malignant Neuromas and the Presence of Nerve Fibers in Them). At this institution, he initially performed temporal craniotomies for the extradural Gasserian ganglion approach on cadavers before applying the technique to patients (5,25). Krause continued to refine surgical approaches while working at the municipal hospital in Hamburg. In 1898, he performed a suboccipital craniotomy to transect the eighth cranial nerve in a patient suffering from tinnitus. In 1900, he used a frontal osteoplastic craniotomy to extract a missile lodged in the clinoid process. Through his observation of the optic chiasm and pituitary stalk, he later proposed a technique for surgically treating pituitary tumors (1). Before 1907, Krause successfully removed a cerebral angioma, and in 1908, he likely became the first surgeon to remove a herniated lumbar disc via laminectomy. He documented this case under the title "Über Einklemmung bzw. Strangulation der cauda equinae" (On the Entrapment or Strangulation of the Cauda Equina). Krause resected a cerebellar tumor in 1911 and was likely the first surgeon to examine the interior of the fourth ventricle in a patient. In 1913, he removed a pineal tumor using an infratentorial supracerebellar approach. He documented his surgical experiences in "Die Chirurgie des Gehirns und Rückenmarks nach eigenen Erfahrungen" (Surgery of the Brain and Spinal Cord Based on Personal Experience), with the first volume published in 1908 and the second in 1911. In this neurosurgical book, Krause advocated for the use of suction for glioma removal, proposed performing surgery over two separate days, and described cortical stimulation using faradic current. In 1932, while in Breslau, he edited a textbook on surgery for brain disorders.

Krause was a pioneer in functional and stereotactic neurosurgery and a strong advocate of electrostimulation. He was among the first to perform direct electrical stimulation (DES) in humans, following the work of Robert Bartholow (1831–1904) and Victor Horsley (1857–1916) in 1890 (2). On July 14, 1898, he described the use of intraoperative nerve monitoring during a cochlear nerve section (22). Krause was also a leading figure in epilepsy surgery, having performed over 400 epilepsy procedures alongside Foerster. In 1909, he published an article titled "Die operative Behandlung der Epilepsie" (The Surgical Treatment of Seizures) (34). He passed away in 1937 in Bad Gastein, Salzburg, Austria.

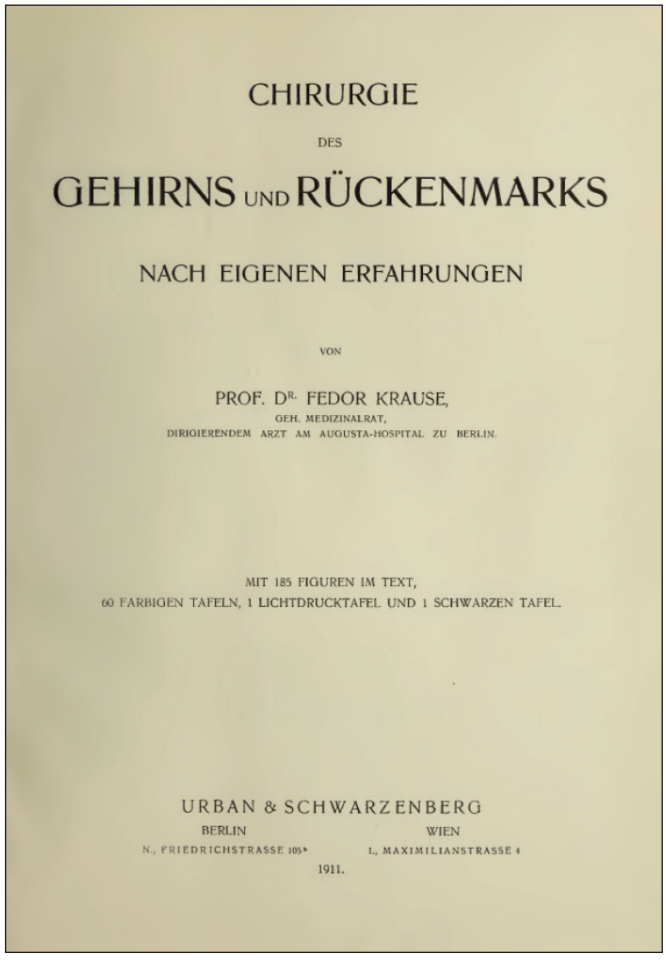
Chirurgie des Gehirns und Rückenmarks (Figure 1) includes 185 sketched illustrations, some of which are colored. These

figures primarily depict the removal of pathologies or the topographic approach to accessing them (Figure 2). The book provides extensive coverage of trepanation, followed by a section dedicated to general technical considerations for brain surgeries. Subsequent sections discuss interventions involving brain tissue and the skull base. Craniocerebral trauma treatment is addressed in detail, covering topics such as surgical preparations, wound dressing, healing time, complications in the wound healing process, pressure-relieving trepanation, and closure of large skull defects. Each subject is examined with precise attention to topographic anatomy and tissue details. The inclusion of a dedicated chapter on topography highlights the significance placed on this aspect of surgical planning. Additional techniques such as brain, ventricular, and lumbar puncture, as well as X-ray procedures, are discussed in separate sections. The chapters on epilepsy and its surgical management are among the most comprehensive in the book. Brain structures are analyzed according to lobar divisions, with a separate chapter devoted to metastatic processes. Furthermore, the book provides an in-depth discussion of laminectomy for spinal canal access, spinal cord tumors, and meningitis.

In 1914, Krause's two-volume work "Die allgemeine Chirurgie der Gehirnkrankheiten" was published by Enke in Stuttgart. Moreover, his book *Chirurgische Operationslehre des Kopfes* was released in two volumes in 1912 and 1914 in Berlin.

Victor Alexander Haden Horsley

Victor Alexander Haden Horsley was born in Kensington, London, on April 14, 1857. He studied medicine in London and Berlin and introduced significant advancements in surgery, particularly in neurosurgery. In 1887, he became the first physician to remove a spinal tumor via laminectomy. Among his key innovations were the use of hemostatic bone wax, carotid artery ligation for the treatment of cerebral aneurysms (35), the transcranial approach to the pituitary gland (23), and the intradural division of the trigeminal nerve root for surgical management of trigeminal neuralgia. Between 1884 and 1886, Horsley was the first surgeon to utilize intraoperative electrical stimulation of the cerebral cortex for localizing epileptic foci in humans, predating the work of Fedor Krause and Wilder Penfield. He was also a pioneer in studying thyroid gland function. His most notable contribution was the development


CHIRURGIE

DES

GEHIRNS UND RÜCKENMARKS

NACH EIGENEN ERFAHRUNGEN

VON

PROF. DR. FEDOR KRAUSE,

GEH. MEDIZINALRAT,

DIRIGIERENDEM ARZT AM AUGUSTA-HOSPITAL ZU BERLIN.

MIT 185 FIGUREN IM TEXT,

60 FARBIGEN TAFELN, 1 LICHTDRUCKTAFEL UND 1 SCHWARZEN TAFEL.

URBAN & SCHWARZENBERG

BERLIN N., FRIEDRICHSTRASSE 105b

WIEN I., MAXIMILIANSTRASSE 4

1911.

Figure 1: The title page of "Chirurgie des Gehirns und Rückenmarks". It was published in 1911, in Berlin by Urban&Schwarzenberg.

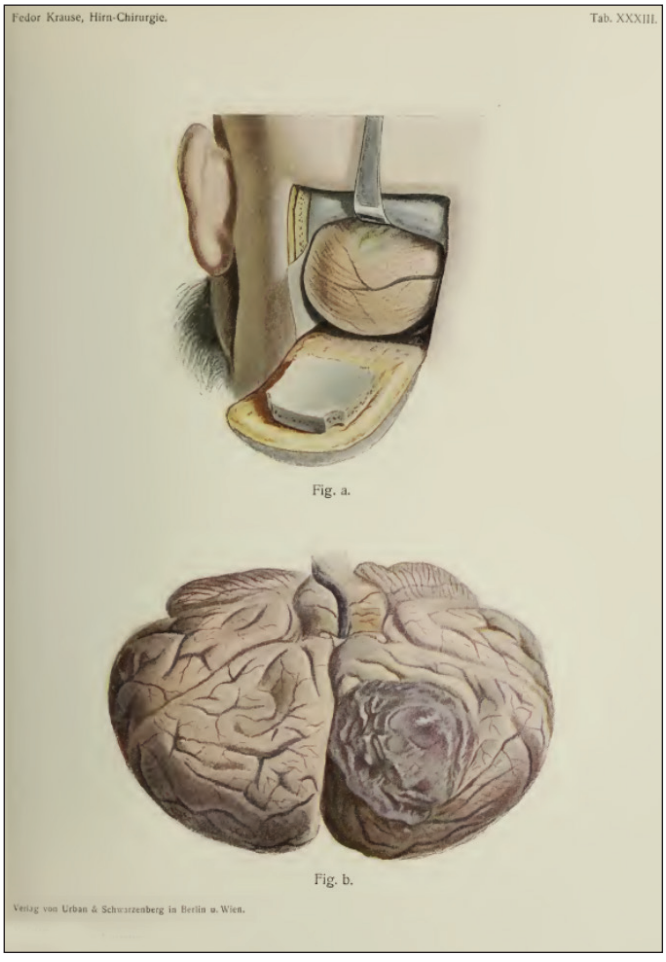


Figure 2: Picture showing the opening of the dura and the removal of the tentorium on page 350 of the "Chirurgie des Gehirns und Rückenmarks".

of the Horsley–Clarke apparatus in 1908, in collaboration with Robert H. Clarke, which became instrumental in performing stereotactic surgery.

Horsley authored several significant works, including *Functions of the Marginal Convolutions* (1884), *Experiments upon the Functions of the Cerebral Cortex* (1888) in collaboration with Edward Albert Sharpey-Schafer (Figure 4), *Alcohol and the Human Body* (1902), and *The Structure and Functions of the Brain and Spinal Cord* (1892).

His 1982 publication, *The Structure and Functions of the Brain and Spinal Cord* (Figure 3), stands out from similar works in several ways. It begins with a historical overview, followed by an analysis of the nervous systems of Protozoa, Coelenterata, and medusae. The book then examines the nervous systems of arthropods and echinoderms before progressing to vertebrates. Horsley studied the vertebrate nervous system by region, focusing on nerve fibers and conduction pathways. The book includes detailed cross-sectional illustrations of the nervous system. Among his numerous articles, some of the most notable include "Cerebellum" (21), "Epileptiform Neuralgia of the Fifth Nerve" (19), "The Morality of Vivisection" (20), and a collaboration work with Robert H. Clarke titled "The Classic: On a Method of Investigating the Deep Ganglia and Tracts of the Central Nervous System (Cerebellum), published in the *British Medical Journal* in 1906 (6).

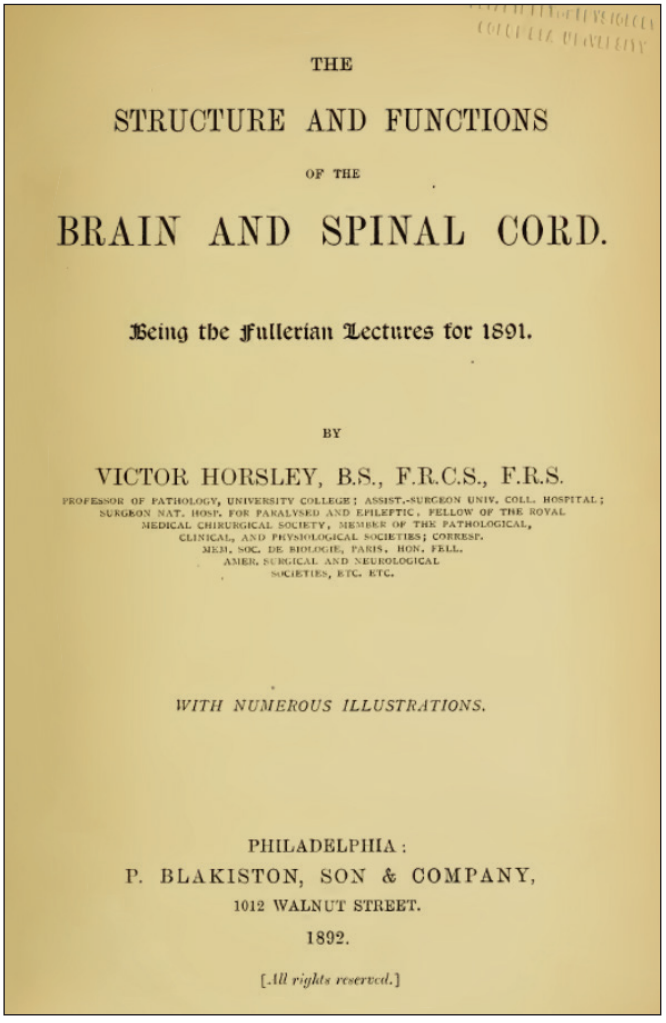
Horsley passed away unexpectedly on July 16, 1916, at the age of 59 due to heatstroke and severe hyperpyrexia during the siege of El-Amarah (now in Iraq), where he was serving as a volunteer surgeon with the British army.

Harvey Williams Cushing

Harvey Cushing was born in Cleveland, Ohio, on April 8, 1869, and is regarded by many medical historians as the first dedicated neurosurgeon. However, beyond neurosurgery, his contributions as a pathologist and draftsman are also significant. He studied medicine at Harvard Medical School, earning his medical degree in 1895. Following an internship at Massachusetts General Hospital, he completed surgical residency under William Stewart Halsted at the Johns Hopkins Hospital in Baltimore. He later received specialized neurosurgical training under Emil Theodor Kocher in Bern and Charles Scott Sherrington in Liverpool.

In the early twentieth century, Cushing pioneered many fundamental surgical techniques for brain operations. His contributions established neurosurgery as a distinct and widely recognized surgical specialty. During the first few decades of the twentieth century, he was regarded as the foremost educator of neurosurgeons worldwide. In recognition of his contributions to surgical science, he was awarded the Lister Medal in 1930. Additionally, Cushing was nominated for the Nobel Prize in Physiology or Medicine at least 38 times (18).

His landmark publication, *The Pituitary Body and Its Disorders*, featuring 319 illustrations, was released by JB Lippincott Company in 1912 (Figure 5). The book provides an extensive and detailed examination of the subject (8). It begins with sections on anatomy, physiology, pathology, and chemistry, cov-


THE

STRUCTURE AND FUNCTIONS

OF THE

BRAIN AND SPINAL CORD.

Being the Fullerian Lectures for 1891.

BY

VICTOR HORSLEY, B.S., F.R.C.S., F.R.S.

PROFESSOR OF PATHOLOGY, UNIVERSITY COLLEGE; ASSIST.-SURGEON UNIV. COLL. HOSPITAL; SURGEON NAT. HOSP. FOR PARALYSED AND EPILEPTIC. FELLOW OF THE ROYAL MEDICAL CHIRURGICAL SOCIETY, MEMBER OF THE PATHOLOGICAL, CLINICAL, AND PHYSIOLOGICAL SOCIETIES; CORRESP. MEM. SOC. DE BIOLOGIE, PARIS. HON. FELL. AMER. SURGICAL AND NEUROLOGICAL SOCIETIES, ETC. ETC.

WITH NUMEROUS ILLUSTRATIONS.

PHILADELPHIA:

P. BLAKISTON, SON & COMPANY,

1012 WALNUT STREET.

1892.

[*All rights reserved.*]

Figure 3: The title page of Horsley's "The Structure and Functions of the Brain and Spinal Cord". It was published in 1892, in Philadelphia by P. Blakiston, Son & Company,

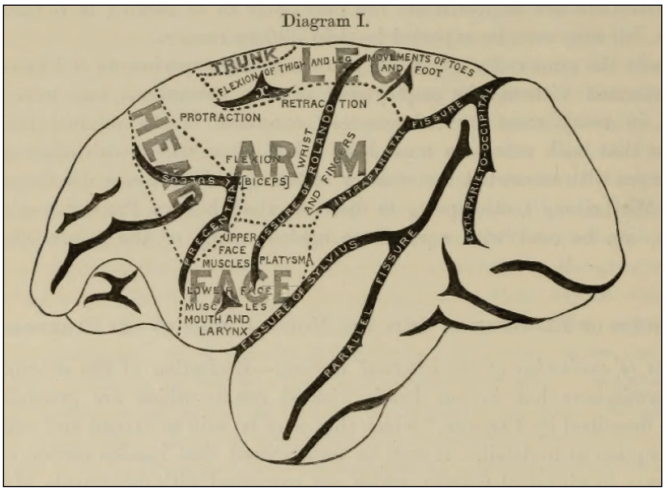


Figure 4: A diagram showing roughly the functions on the outer surface of the brain in Horsley's "Experiments upon the Functions of the Cerebral Cortex" (pp. 6).

ering these foundation areas in depth. Clinical manifestations are analyzed in categories and supported by case studies. The third chapter discusses the incidence, symptomatology, and treatment of pituitary disorders. The work includes both gross and microscopic images of pathological specimens, as well as images of pituitary tissues extracted from experimental animals (Figure 6). Cushing's book provides a detailed account of the neurological effects of pituitary diseases, even in dogs. It is evident from his work that X-rays were utilized for diagnostic purposes. Nearly every symptom is accompanied by an X-ray image along with the patient's physical appearance. He also conducted autopsies on patients who passed away during follow-up and included photographs of the autopsy specimens in his book (Figure 7A, B). In terms of methodology, content, detail, and innovation, the book is significantly more comprehensive and advanced than other works of its time.

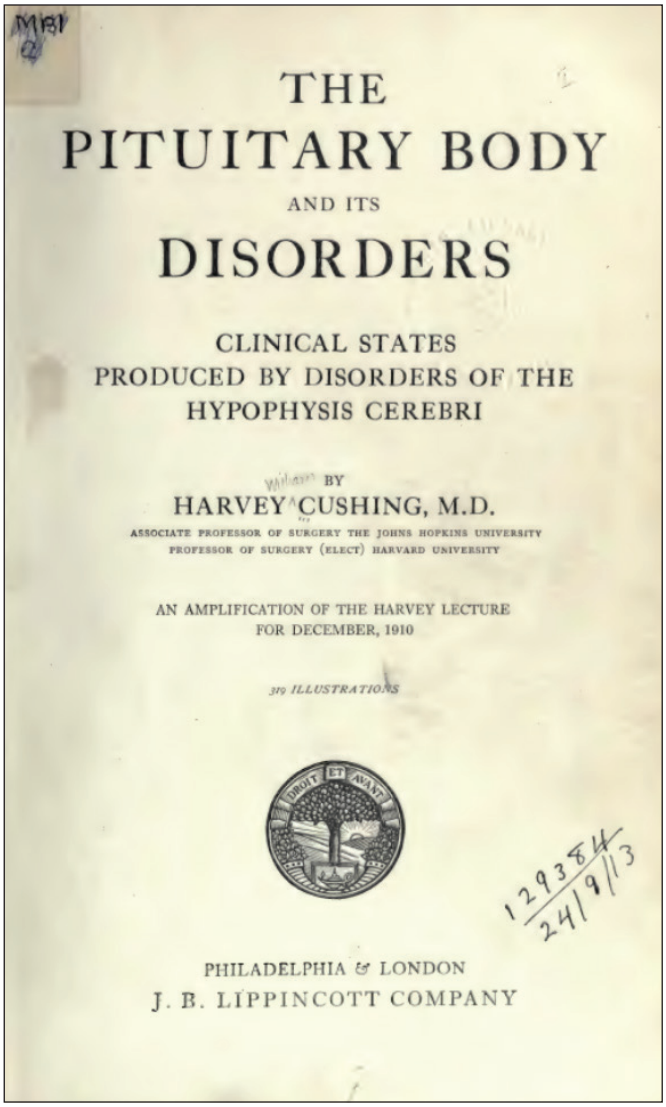

THE
PITUITARY BODY
AND ITS
DISORDERS
CLINICAL STATES
PRODUCED BY DISORDERS OF THE
HYPOPHYSIS CEREBRI
BY
HARVEY CUSHING, M.D.
ASSOCIATE PROFESSOR OF SURGERY THE JOHNS HOPKINS UNIVERSITY
PROFESSOR OF SURGERY (ELECT) HARVARD UNIVERSITY
AN AMPLIFICATION OF THE HARVEY LECTURE
FOR DECEMBER, 1910
370 ILLUSTRATIONS
PHILADELPHIA & LONDON
J. B. LIPPINCOTT COMPANY

Figure 5: The title page of Cushing's monumental work "The Pituitary Body and Its Disorders". The book was published in 1912.

Figure 6: A pathological specimen from the book at high magnification showing formation of colloid by cluster of pars intermedia cells, making temporary vesicles which discharge their contents into tissue spaces of pars nervosa as hyaline bodies **(H)** from "The Pituitary Body and Its Disorders".

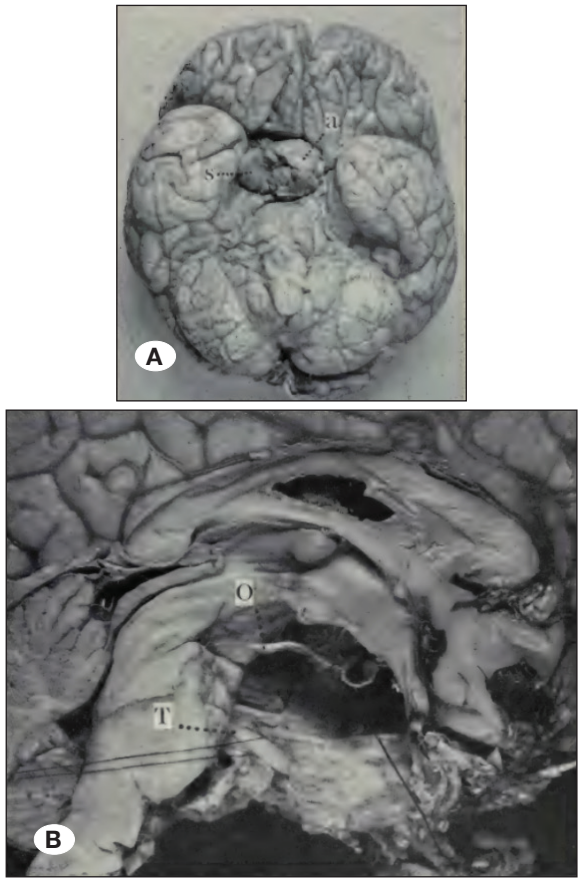
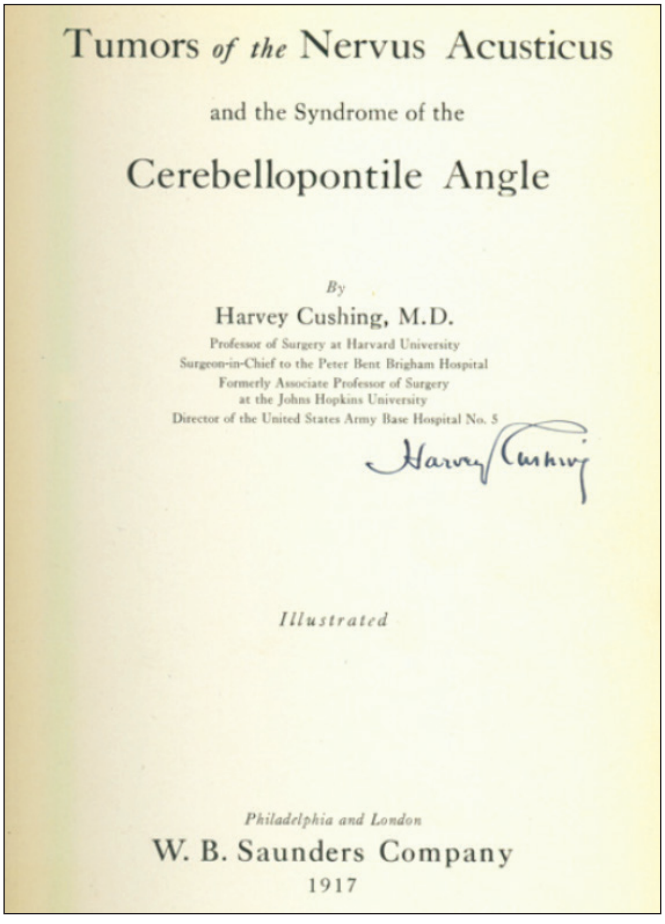


Figure 7: The patient, named Case XV in the book, had pituitary struma and aneurysm **(A)**; and the patient, named Case XVII, Mesial view of left hemisphere after enucleation of tumor mass. Note flattening of nerves, especially trigeminus (T) and oculomotorius (O), which have been held aside by threads **(B)** from "The Pituitary Body and Its Disorders".

His publication *Tumors of the Nervous Acusticus and the Syndrome of the Cerebellopontine Angle* was released by WB Saunders in 1917 (Figure 8). This work was compiled with the same level of precision. A historical overview is included at the beginning of the book, and it features preoperative images illustrating surgical incision sites on patients. Similar to his book on the pituitary, this work not only presents outcomes but also includes images of functional examinations, such as visual field tests and audiometry results.

Cushing co-authored *A Classification of the Tumors of the Glioma Group on a Histogenetic Basis with a Correlated Study of Prognosis* with Percival Bailey, which was published by JB Lippincott in 1926. He described the monograph as a significant contribution to neurology, as it was the first systematic attempt to classify gliomatous tumors of the central nervous system based on histological features while correlating them with the progression of each tumor type. This classification later served as the foundation for the most subsequent glioma classifications. The work was dedicated to the Spanish neurohistologist Santiago Ramón y Cajal. It categorizes tumors according to their histogenetic origin and considers the prognosis of different pathologies. The study also includes images of pathological specimens for each tumor examined.


Tumors *of the* Nervus Acusticus

and the Syndrome of the

Cerebellopontile Angle

By

Harvey Cushing, M.D.

Professor of Surgery at Harvard University
Surgeon-in-Chief to the Peter Bent Brigham Hospital
Formerly Associate Professor of Surgery
at the Johns Hopkins University
Director of the United States Army Base Hospital No. 5

Illustrated

Philadelphia and London

W. B. Saunders Company

1917

Figure 8: The title page of "Tumors of the Nervous Acusticus and the Syndrome of the Cerebellopontile Angle" by HW Cushing.

Meningiomas: Their Classification, Regional Behavior, Life History, and Surgical End Results was Cushing's final and most significant clinical text, co-authored with Louise Eisenhardt and published by Charles C Thomas in 1938. The book contains highly detailed surgical photographs, drawings, gross and microscopic pathological specimens, and postmortem study images (Figure 9A, B). True to his style, Cushing began the book with a historical overview, this time also incorporating a section on terminology. Additionally, the work includes a comprehensive demographic analysis and statistical data on the locations of meningiomas. Both the depth of its figures and textual content surpass not only contemporary works but also many later publications on the subject. This study had a profound impact on all subsequent books on meningiomas.

In 1902, Cushing published his experimental research on intracranial hypertension, now referred to as "Cushing's triad" (7). In 1912, he described an endocrinological disorder resulting from pituitary gland dysfunction, which he called "polyglandular syndrome." He later published his findings in 1932 under the title *The Basophil Adenomas of the Pituitary Body and Their Clinical Manifestations: Pituitary Basophilism* (8). In 1925, he co-authored a paper with Bailey titled *Medulloblastoma Cerebelli: A Common Type of Midcerebellar Glioma of Childhood* (3).

Beyond these works, Cushing authored numerous articles and books. However, since this article does not focus on his personnel life, additional experiments are not necessary.

Cushing passed away on October 7, 1939, in New Haven, Connecticut, due to complications from a myocardial infarction.

Walter Edward Dandy

Walter Edward Dandy was born in Sedalia, Missouri, on April 6, 1886, and was regarded as Harvey Cushing's most outstanding student. He made significant contributions to neurosurgery, including identifying cerebrospinal fluid (CSF) circulation, advancing surgical treatments for hydrocephalus, developing air ventriculography and pneumoencephalography, designing brain endoscopy, establishing the first intensive care unit, and performing the first surgical clipping of an intracranial aneurysm. Dandy authored 5 books and published over 160 articles. In 1913 and 1914, he collaborated with Kenneth D. Blackfan on two pivotal papers examining CSF production, circulation, and absorption, and the causes and potential treatments of hydrocephalus (15). In 1921, he documented a case of hydrocephalus resulting from CSF outflow obstruction in the fourth ventricle, in which he described what is now known as Dandy-Walker syndrome.

In 1918, Dandy described air ventriculography and pneumoencephalography (9). He detailed a surgical procedure for removing tumors in the pineal region in 1921, followed by the complete excision of cerebellopontine angle tumors in 1922. That same year, he introduced the use of endoscopy for treating hydrocephalus. In 1938, he pioneered the ligation or "clipping" of an intracranial aneurysm.

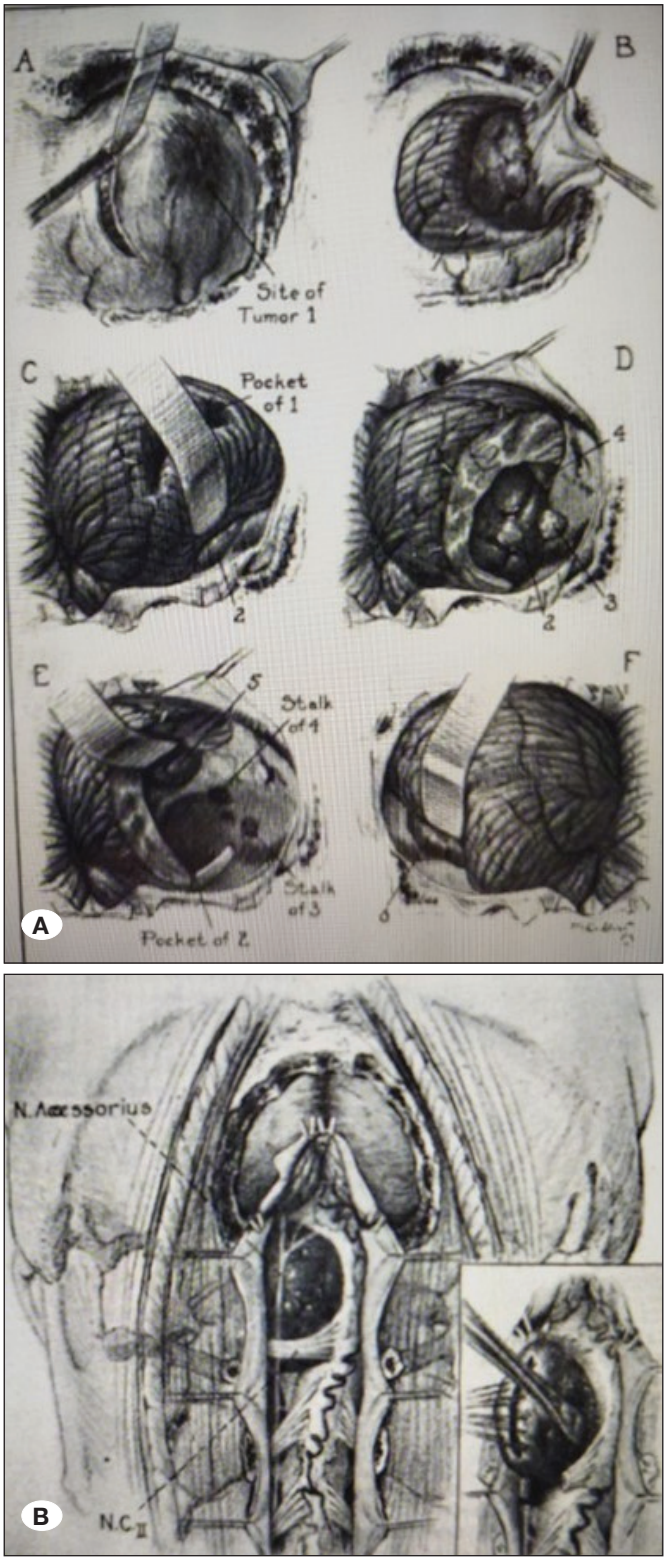


Figure 9: Drawings of the surgical steps of the patient, he named Case 2 **(A)**, and illustration of the removal of a spinal meningioma in a patient from the so-called Group 17 series **(B)** from "Meningiomas".

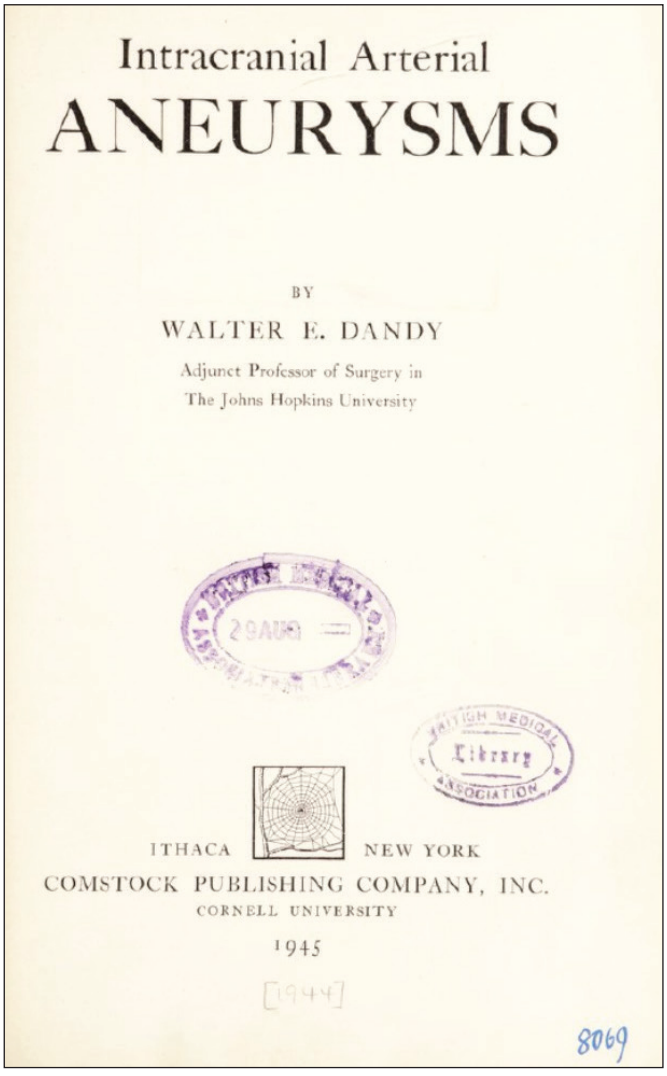


Figure 10: Title page of Dandy's "Intracranial Arterial Aneurysms".

His book *Intracranial Arterial Aneurysms* (Figure 10) was published in 1945 by the Comstock Publishing Company (34). The first chapter discusses the application of ventriculography and angiography in diagnosis, followed by a section on localization. The book also includes detailed explanations of preoperative and operative techniques (Figure 11).

Dandy's *Benign, Encapsulated Tumors in the Lateral Ventricles of the Brain* was published in 1934. This work categorizes tumors based on their location in the brain and includes numerous photomicrographs. Dandy presents many of his cases, along with operative technical drawings and postmortem study photographs.

Orbital Tumors: Results Following the Transcranial Operative Attack, published in 1942, is an extensive and detailed work showcasing numerous surgical techniques for the first time. The book includes highly detailed illustrations, as well as pathological studies of all cases.

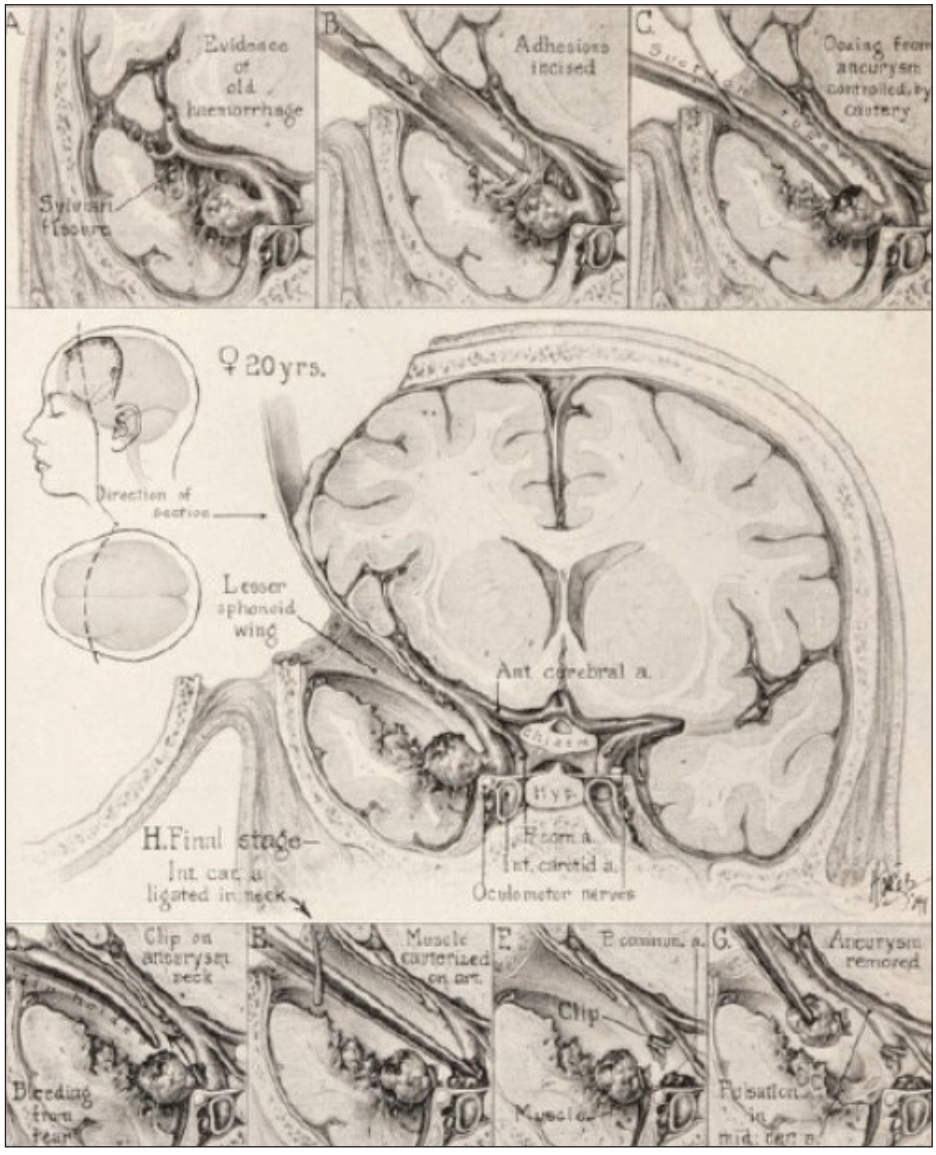


Figure 11: Drawing of operative techniques of an internal carotid aneurysm from the Dandy's book "Intracranial Arterial Aneurysms".

In 1933, *Benign Tumors in the Third Ventricle of the Brain: Diagnosis and Treatment* was published, detailing surgical approaches to the third ventricle and describing endoscopic interventions.

DISCUSSION

Since the traces of surgical procedures on hard tissues, such as bones, have been preserved over time, while soft tissues leave no such evidence, it is reasonable to assume that neurosurgery is the oldest branch of medicine based on the findings of cranial defects. Excavations at Aşıklı Höyük in Aksaray, Türkiye, suggest that neurosurgery dates back approximately 10,000–11,000 years (36). However, it has been just over a century since this ancient medical field shifted its focus from the skull to the brain itself. This transformative shift was made possible by three crucial medical advancements at the end of the nineteenth century: the introduction and application of asepsis and antisepsis in surgical procedures, advancements in anesthesia that allowed for painless and controlled operations, and the development of cerebral localization, a fundamental concept for neurosurgery.

The period of neurosurgery before the introduction of these three key advancements, up until around 1879, is referred to as "pre-modern" neurosurgery. The year 1879 marks a significant milestone when a frontal meningioma was removed solely based on clinical symptoms and signs. William Macewen (1848–1924) identified "irritation to the lower and middle portions of the ascending convolutions...in the left frontal lobe" in a young girl with focal epileptic symptoms. He performed surgery, successfully removing the tumor. When the patient passed away 8 years later, an autopsy confirmed the absence of tumor tissue (11,24). This groundbreaking procedure marked the beginning of modern neurosurgery.

From this operation in 1879 onward, the field evolved into "modern neurosurgery," characterized by the routine use of asepsis, antisepsis, anesthesia, and cerebral localization, along with advanced diagnostic techniques such as radiology. Medical historians often refer to the period after 1919, when these methods became standard, as the "post-Cushing neurosurgery" era.

The challenges faced during the formative years of modern neurosurgery, between 1879 and 1919—the period covered in this article—were overcome through the dedication and efforts of numerous surgeons and basic scientists. Each of these individuals made meaningful contributions. However, four surgeons stand out for the significant impact of their work: Fedor Krause, Victor Haden Horsley, Harvey William Cushing, and Walter Edward Dandy. Through their books, articles, and the research environments they established, these pioneers made groundbreaking advancements that propelled neurosurgery into a new era. Their work was far ahead of its time, and their innovative ideas played a crucial role in shaping the future of the field. For these reasons, they should be regarded as distinct from their contemporaries.

Fedor Krause introduced numerous innovations to neurosurgical practice. He utilized X-rays for diagnostic purposes less than a year after their discovery in 1895 (10,32). Through extensive cadaver studies conducted before surgery, he developed various surgical techniques and illustrated their topographic anatomy. His illustrated books facilitated learning for new surgeons and heightened interest in neurosurgery. Krause also designed specialized surgical instruments that simplified neurosurgical procedures. He pioneered two major surgical approaches: in 1898, he provided a detailed description of the cerebellopontine angle approach via a unilateral suboccipital osteoblastic flap, as well as the supraorbital frontal osteoplastic craniotomy for accessing the sella. These techniques significantly improved the removal of acoustic neuromas and pituitary tumors.

Krause was likely the first surgeon to perform a laminectomy for lumbar disc herniation, though he did not recognize the excised tissue as disc material and instead referred to it as an "enchondroma" (5). In his book *Die Chirurgie des Gehirns und Rückenmarks nach eigenen Erfahrungen*, he introduced the use of suction for glioma removal, a groundbreaking concept for excising glial tumors. Both in this work and in *Chirurgische Operationslehre des Kopfes,* he described numerous innovative surgical procedures, including accessing the pituitary gland using a frontal osteoplastic flap and approaching vermian tumors. He was among the first surgeons to apply direct electrical stimulation in humans, enabling him to map motor and sensory functions. Krause also detailed the use of intraoperative nerve monitoring. Alongside Foerster, Krause was a pioneer in epilepsy surgery, performing over 400 operations (14). He emphasized that resecting the ictal onset zone was crucial for achieving successful surgical outcomes. Additionally, he was the first to surgically remove a brain angioma. Krause made significant contributions to surgical techniques and instrument development across all subfields of neurosurgery.

Fedor Krause was a versatile surgeon with a strong dedication to neurosurgery and a highly innovative approach. Alongside his contemporary Horsley, he was considered one of the most significant surgeons in Europe and is recognized as a key figure in the early advancements of twentieth-century neurosurgery.

Similarly, Victor Alexander Haden Horsley was a pioneering surgeon responsible for several groundbreaking contributions to neurosurgery. He was the first to perform cranial decompression to prevent brain swelling, carotid ligation for subarachnoid hemorrhage, and the removal of spinal cord tumors. Along with Krause and a few other contemporaries, he was also among the early pioneers in pituitary tumor and epilepsy surgery. Horsley introduced a revolutionary approach to spinal cord tumor surgery by localizing tumors through neurological examination before surgical removal. He was a trailblazer in experimental neurosurgery, conducting significant research on the pituitary gland in cats, dogs, and monkeys. His experimental findings are documented in *Experiments upon the Functions of the Cerebral Cortex* (33). In 1908, Horsley and Clarke developed the stereotactic frame to study the deep connections of the cerebellum. His research led to the creation of a functional cortical map (35). Additionally, he conducted experiments on intracranial pressure, cerebral circulation, and systemic blood pressure. He discovered that increased intracranial pressure compromised cerebral capillary circulation, and that respiratory arrest inevitably resulted in cardiovascular failure (30), fundamentally altering medical understanding.

Horsley developed and published numerous modifications of the subtemporal approach. Over his career, he produced approximately 600 papers, books, and monographs covering various neurosurgical topics.

Harvey Williams Cushing fundamentally transformed neurosurgery not only through advancements in surgical techniques but also by shaping the field as a structured discipline through his writings, teaching, and the system he established. If one were to name a single individual as the founding father of modern neurosurgery, it would undoubtedly be Cushing.

His books, *The Pituitary Body and Its Disorders*, *Tumors of the Nervus Acusticus and the Syndrome of the Cerebellopontine Angle*, and *Meningiomas: Their Classification, Regional Behavior, Life History, and Surgical End Results*, were far ahead of their time. All three works are exceptionally detailed, comprehensive, and systematic. The books feature meticulous illustrations, case follow-ups, and postmortem images of deceased patients. Gross and microscopic pathology are consistently analyzed throughout. One of Cushing's meticulous approaches was documenting the history of diseases and procedures in his works. He also placed great emphasis on the classification of diseases and tumoral pathologies, which kept his books systematically relevant even a century later.

A key indicator of his commitment to classification and systematic knowledge organization is his book *A Classification of the Tumors of the Glioma Group on a Histogenetic Basis with a Correlated Study of Prognosis*. While little has been done to expand on its histopathological foundation, the book has

served as the basis for numerous subsequent classifications. His classification method considers prognosis, making it one of the first instances of such an approach in medical sciences. Cushing's system was derived from his own patients, with each tumor group accompanied by histopathological gross and microscopic specimens, as well as postmortem study figures. This approach was groundbreaking not only in neurosurgery but in medical science as a whole.

Harvey W. Cushing successfully operated on numerous brain tumors that were previously considered inoperable, documenting these cases in his books on the pituitary gland, acoustic neuroma, and meningioma (28). His surgical innovations extended even to the shape of incisions, and he provided a topographic representation of every step of the procedures. As evident from his books and writings, Cushing was among the first surgeons to recognize the significance of the newly discovered X-rays, incorporating them extensively into his routine clinical practice (4,17). He illustrated all these advancements through both drawings and photographs in his publications. While other physicians in neurosurgical history have had their complete works preserved, Cushing stands out as a rare example of a surgeon who meticulously documented every aspect of his practice.

Walter Edward Dandy was Cushing's most outstanding pupil and one of the most determined and hardworking surgeons in neurosurgical history. He made several groundbreaking discoveries, including elucidating cerebrospinal fluid (CSF) circulation, pioneering the surgical treatment of hydrocephalus, describing brain endoscopy, and performing the first intracranial aneurysm clipping. His revolutionary ideas led to the invention of air ventriculography and pneumoencephalography. In 1918 and 1919, he published milestone articles on these techniques, and in recognition of his contributions, he was nominated for the Nobel Prize in 1933 (9,27). His aneurysm treatment using surgical clipping, along with his detailed descriptions in *Intracranial Arterial Aneurysms*, played a foundational role in establishing the field of neurovascular neurosurgery. Many of Dandy's articles were pioneering contributions to neurosurgery. In 1910, he published a paper on fetal blood circulation and neural networks, followed by a study on pituitary arterial and venous circulation in 1913. Alongside Kenneth D. Blackfan, he authored two landmark papers on CSF production, circulation, and absorption, as well as the causes and potential treatments of hydrocephalus (26). Before Dandy, hydrocephalus was largely considered fatal and remained untreated. He classified it into two types: "obstructive" and "communicating," establishing a theoretical framework for its rational treatment. His significant contributions to hydrocephalus research, including the description of Dandy-Walker malformation, positioned him as a key figure in both pediatric and vascular neurosurgery.

Dandy's surgical innovations encompassed a wide range of procedures, including the complete removal of acoustic neuromas, excision of pineal tumors, orbital surgery, closure of carotid cavernous fistulas, and aneurysm clipping. His books on orbital tumors and intracranial arterial aneurysms provide a step-by-step explanation of these surgical techniques, emphasizing their topographic anatomy (29). Many of the operative techniques he introduced remain in use today with little modification.

CONCLUSION

The four pioneering surgeons discussed in this article played a crucial role in establishing neurosurgery on a systematic foundation, leading to significant advancements in education, clinical practice, and surgical techniques. Their contributions not only introduced numerous innovative procedures but also revolutionized the understanding of preoperative, intraoperative, and postoperative care. Additionally, they prioritized the training of future neurosurgeons and conducted groundbreaking scientific research, particularly in experimental studies. Most importantly, they ensured the longevity of their surgical advancements, scientific findings, and methodologies through their extensive publications. These collective efforts helped neurosurgery transition from its early incunabula phase into the modern discipline it is today.

ACKNOWLEDGEMENTS

Preparation for publication of this article is partly supported by Turkish Neurosurgical Society.

Declarations

Funding: The authors declare no competing financial interests and no sources of funding and support, including any for equipment and medications.

Availability of data and materials: The datasets generated and/or analyzed during the current study are available from the corresponding author by reasonable request.

Disclosure: The authors declare no competing interests.

AUTHORSHIP CONTRIBUTION

Study conception and design: UE, SN
Data collection: UE, SN, MNA
Analysis and interpretation of results: UE
Draft manuscript preparation: UE, SN, MNA
Critical revision of the article: UE, SN, MNA
All authors (UE, SN, MNA) reviewed the results and approved the final version of the manuscript.

REFERENCES

1. Albert-Niedler U, Arnold H: Gain and loss of the ability to compete: Some aspects of German neurosurgery up to 1939. Acta Neurochir (Wien) 126:4-10, 1994. https://doi.org/10.1007/BF01476487
2. Bacigaluppi S, Bragazzi NL, Martini M: Fedor Krause (1857–1937): The father of neurosurgery. Neurosurgical Review 43:1443-1449, 2020. https://doi.org/10.1007/s10143-019-01186-1
3. Bailey P, Cushing H: Medulloblastoma cerebelli a common type of midcerebellar glioma of childhood. Arch Neur Psych 14:192-224, 1925. https://doi.org/10.1001/archneurpsyc.1925.02200140055002

4. Bruce SS, Bruce JN: Harvey cushing, neurosurgical pioneer. Curr Surg 62:138-140, 2005. https://doi.org/10.1016/j.cursur.2004.03.011.
5. Buchfelder M: From trephination to tailored resection: Neurosurgery in Germany before World War II. Neurosurgery 56:605-613, 2005. https://doi.org/10.1227/01.neu.0000155336.06394.7f.
6. Clarke RH, Horsley V: The Classic: On a method of investigating the deep ganglia and tracts of the central nervous system (cerebellum). Br Med J 1906:1799-1800. Clin Orthop Relat Res 463:3-6, 2007. https://doi.org/10.1097/BLO.0b013e31814d4d99.
7. Cushing H: Some experimental and clinical observations concerning states of increased intracranial tension.1: The mutter lecture for 1901. Am J Med Sci (1827-1924) 124:375, 1902
8. Cushing, H: The basophil adenomas of the pituitary body and their clinical manifestations (pituitary basophilism). Bulletin of the Johns Hopkins Hospital 50:137-195, 1932. https://doi.org/10.1002/j.1550-8528.1994.tb00097.x.
9. Dandy WE: Ventriculography Following the injection of air into the cerebral ventricles. Ann Surg 68:5-11, 1918, https://doi.org/10.1097/00000658-191807000-00002.
10. Elhadi AM, Kalb S, Martirosyan NL, Agrawal A, Preul MC: Fedor Krause: The first systematic use of x-rays in neurosurgery. Neurosurg Focus 33:1-9, 2012. https://doi.org/10.3390/su13084389
11. Ellis H: Sir William Macewen and the first successful excision of an intracranial tumour. J Perioper Pract 30:283-284, 2020. https://doi.org/10.1177/1750458920915162.
12. Er U, Naderi S: Beyin ve sinir cerrahisinin tarihsel gelişimi. In: Avcı E (ed), Temel Nöroşirürji. Ankara:Türk Nöroşirürji Derneği Yayınları 29, 2023:3-19
13. Er U, Naderi S: Prominent neurosurgery books of the western world: How they defined the era of modern neurosurgery in the 19th century. Turk Neurosurg 34:535-541, 2024. https://doi.org/10.5137/1019-5149.JTN.44803-23.2
14. Feindel W, Leblanc R, de Almeida AN: Epilepsy surgery: Historical highlights 1909-2009. Epilepsia 50:131-151, 2009. https://doi.org/10.1111/j.1528-1167.2009.02043.x.
15. Fox WL: Dandy of Johns Hopkins. Baltimore: Williams & Wilkins, 1984
16. Gowers WR, Hosley V: A case of tumour of the spinal cord. Removal; recovery. Med Chir Trans 71:377-430, 1888. https://doi.org/10.1177/095952878807100125.
17. Gunderman RB, Seymour ZA: Harvey W. cushing. AJR Am J Roentgenol 194:296-298, 2010. https://doi.org/10.2214/AJR.09.3356.
18. Hansson N, Schlich T: "Highly qualified loser"? Harvey cushing and the nobel prize. J Neurosurg 122:976-979, 2015. https://doi.org/10.3171/2014.11.JNS14990
19. Horsley V: Epileptiform neuralgia of the fifth nerve. Am J Dent Sci 21:145-158, 1887
20. Horsley V: The Cerebellum. Hospital (Lond 1886) 46:410, 1909
21. Horsley V: The Morality of Vivisection. Hospital (Lond 1886) 13:92, 1892
22. Horwitz NH: Fedor Krause (1857-1937). Neurosurgery 38:844-848, 1996
23. Horwitz NH: Library: Historical perspective. Neurosurgery 36:428-430, 1995. https://doi.org/10.1097/00006123-199505000-00029
24. Horwitz NH: William Macewen (1848-1924). Neurosurgery 37:352-355, 1995. https://doi.org/10.1227/00006123-199508000-00029.
25. Krause F: Die Neuralgie des Trigeminus nebst der Anatomie und Physiologie des Nerven. Leipzig, F.C.W. Vogel, 1896
26. Lifshutz JI, Johnson WD: History of hydrocephalus and its treatments. Neurosurg Focus 11:1-5, 2001. https://doi.org/10.3171/foc.2001.11.2.2
27. Ligon BL: The mystery of angiography and the "unawarded" Nobel prize: Egas Moniz and Hans Christian Jacobaeus. Neurosurgery 43:602-611, 1998
28. Malekpoor M, Cohen-Gadol AA: Making the "inoperable" tumors "operable": Harvey Cushing's contributions to the surgery of posterior fossa tumors. Neurosurg Focus 36:1-6, 2014. https://doi.org/10.3171/2014.2.FOCUS13580.
29. Marmaduke ME: Walter Dandy: The Personal Side of a Premier Neurosurgeon. Lippincott Williams & Wilkins, 2002
30. Mott FW, Horsley VA: On the existence of bacteria, or their antecedents, in healthy tissues. J Physiol (Lond) 3:188-194, 1882. https://doi.org/10.1113/jphysiol.1882.sp000094.
31. Obituary: Alexander Hughes Bennet, MD, FRCP, Lond. Br Med J 2:1444, 1901. https://doi.org/10.1136/bmj.2.2132.1444-a
32. Piek J, Lidke G, Terberger T, von Smekal U, Gaab MR: Stone age surgery in Mecklenburg-Vorpommern: A systematic study. Neurosurgery 45:147-151, 1999. https://doi.org/10.1097/00006123-199907000-00033.
33. Powell MP: Sir Victor Horsley at the birth of neurosurgery. Brain 139:631-634, 2016. https://doi.org/10.1093/brain/awv345.
34. Schijns OE, Hoogland G, Kubben PL, Koehler PJ: The start and development of epilepsy surgery in Europe: A historical review. Neurosurg Rev 38:447-461, 2015. https://doi.org/10.1007/s10143-015-0641-3.
35. Tan TC, Black PMcL: Sir Victor Horsley (1857–1916): Pioneer of neurological surgery. Neurosurgery 50:607-612, 2002. https://doi.org/10.1097/00006123-200203000-00032.
36. Tugcu B: Anadolu'da, canlıda yapılan ilk trepanasyon örneği: Aşıklı Höyük insanı. Türk Nöroşir Derg 20:70-75, 2010