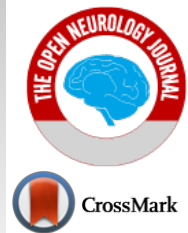




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REVIEW ARTICLE

Historical Sources on Epilepsy Surgery: From Antiquity Through the End 20th Century

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Abstract:

The history of epilepsy is an associate of humanity, and the reports date back to antiquity. Almost all ancient cultures, including the Babylonians, Egyptians, Greeks, Indians in pre-Buddhist period, Iranians, Chinese, and Byzantine epoch, bear witness to epilepsy. Therefore, the earliest beginnings of surgical treatment and epilepsy surgery can be traced back to antiquity. Trepanation as an attempt to treat the disease has often been found in prehistorical tombs (*Neolithicum*). In antiquity, fasting, a healthy diet, regulation of excretions, medical gymnastics and a decent lifestyle were used as treatment for epilepsy as a non-surgical solution. In the Middle Ages, the basis for treatment fell into three main categories: Conventional (diet and botanical remedies), magical (phases of the moon, trephining of the skull) and religious beliefs (fasting, prayer, exorcisms, and social marginalization).

The first neurosurgical operations on epileptic patients with focal semiology were performed during the early 19th century, and began with Godlee, Sommer, Macewen and later Horsley. From that time on, discoveries on epilepsy surgery progressed at a faster pace that started in a historical journey from ancient times until the end of the 20th century.

Keywords: Historical sources, Epilepsy surgery, Methods of surgery, Microsurgery, Disease, Antiquity.

Article History

Received: April 18, 2021

Revised: June 23, 2021

Accepted: July 12, 2021

1. INTRODUCTION

Historical archives of epilepsy have existed since 2,500 years B.C., and described accurately all clinical characteristics that are well-known today. Numerous documents about epilepsy can be found in multiple cultures, including the ancient Babylonians, Mesopotamians, Egyptians and Greeks [1 - 3]. References can also be seen in more modern medicine, including Indian (Ayurveda) [3, 4], Iranian (Avicenna) [5], and Chinese [6].

The basis for epilepsy therapy was put forth by *Hippocrates* (460-377 B.C.). Hippocrates questioned the natural opinion that epilepsy was a disease: 1) is not divine, 2) is not a sacred disease, 3) has the same origin as other illnesses, and 4) prognosis is worse in children than in adults. He even went as far as to propose a neurosurgical procedure as a treatment and that a craniotomy should be performed on the opposite side of the brain for seizure control in order to spare the patients from the phlegma that was causing the disease [7, 8]. In Greek Mythology, epilepsy was a mystical phenomenon called a miasma. Since then, various methods were used for the

treatment of epilepsy, which were founded on therapies during the Middle Ages. The Greek born physician Aretaeus of Cappadocia (2nd century A.D.) recommended solutions for the treatment of epilepsy, *e.g.*, emesis, diet, medical herbs and trepanation. Many centuries later, epilepsy therapy was introduced, as well as other treatments, such as the ketogenic diet (known since antiquity and documented in Biblical times) and vagus nerve stimulation in pharmaco-resistant epilepsy [9] in cases where neurosurgical intervention is not possible. The first neurosurgical pioneers during the second half of the 19th century were Macewen, Horsley, Krause, and the leaders of the second generation were Cushing, Dandy, Elsberg and Frazier.

The aim of this article is to provide a brief, yet concise overview of the most important milestones in the history of epilepsy surgery and other treatments for epilepsy. In comparison to the many books written on this topic, this document references a significant number of ancient texts up to the end of the 20th century.

2. THE ANCIENT EPOCH

The earliest beginnings of epilepsy surgery can be traced back to antiquity. Cranial trepanation, or trephination, is one of the most fascinating and ancient practices in the history of

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medicine. The word, trephination is a French variant (described drilling, incision or scraping into the skull). Trepanation is from the Greek word “τροπή” (to burrow/scrape), as an attempt to treat the disease was often found in prehistorical tombs in the neolithic era (*Neolithicum*), for example, in the Inca culture in Peru, in Egyptian mummies, in Australia, and North and East Africa. Peru (in the region of the highland and coastal Indians) has been recognized as a major source of ancient trepanned skulls, many of which date back 2,300 years [10 - 12]. Skulls from the National Archaeology Museum in Lima have been studied, and several of these showed multiple oval or circular trepanations, with diameters varying from 1 to 3 cm, and occasionally 4 cm. Most were located in the parietal and frontal regions, and seldom in the occipital bone. North Africa medicine men practiced trephination and some continue to do so today [9]. Trepanation is the oldest known surgical technique [12,13]. Skull trepanation (sometimes called cauterization) was performed in all of the continents and during all of the times, using various techniques, as it was a popular means of medical and spiritual therapy (mystical) in those days. By opening the skull, the intent was to let the evil spirits escape and thus rescue the patient from demons.

Table 1. Some important chronological milestones in epilepsy surgery.

Year	Pioneer
2,300 B.C.	Neolithic Epoch
1564	Amboise Paré
1831	Peter Heyman
1860	Josepf Lister
1861	Paul Broca
1879	William Macewen
1884	John Godlee
1886	David Ferrier
1886	Victor Alexander Horsley
1904	Charles Elsberg
1934	Wilder Penfield
1939	Hugo Krayenbuehl
1940	William van Wagenen
1947	Georg Dawson
1951	Arthur Earl Walker
1968	Murray Alexander Falconer
1982	Heinz Gregor Wieser
1985	Denis D. Spencer and Susan S. Spencer
1985	Gazi Yasargil

Ambroise Paré (1510-1590), who was one of the fathers of surgery, a pioneer in modern forensic pathology and surgical techniques, modified the skull trepan instruments [12]. In his thorough study, Paul Broca (1824-1880), a pioneer in cranial surgery, neuroscience and anthropology depicted three different groups of trepaninations/ trepanations: 1. trepanations of deceased persons (the most frequently performed ones) that were likely performed for magical reasons; 2. trepanations of living people who did not survive the trauma; and 3. trepanations of living people who survived the procedure and were relieved from evil spirits, epilepsy, headache or hysteria (Table 1) [14]. The Edwin Smith Papyrus an ancient Egyptian

medical text, dating from the seventeenth century B.C., named after the dealer who bought it in 1862, describes trephine of the skull of terminally ill, comatose Pharaohs [15].

Depending on the respective era, different trephination techniques were used until the time of Hippocrates. Later, it was utilized only sporadically towards the Middle Ages [12]. Hippocrates (460-377 B.C.) diligently described a surgical instrument and interventions in epileptic patients in his chapter of the Hippocratic Corpus: On the Sacred Disease. According to Hippocrates, cranial trepanation should be performed contralateral to the paralyzed side of the body to rescue the patient from *phlegma*, which was thought to be the cause of epilepsy, cranial fracture, and blindness [7, 12]. Depending on the respective epoch, different techniques of trephination were in use until the time of Hippocrates. Celsus (39 B.C. about 50 A.D.) supplemented his trephine drills with a chisel and a hammer. Aretaeus of Cappadocia (2nd century B.C) was the first to recommend trepanation for the treatment of epilepsy to emesis, medical herbs and trepanation.

3. EPOCH OF THE BYZANTINE YEARS

For most of the Middle Ages, scientific research in epilepsy experienced a deep setback, interest remained low and non-medical methods were being used as therapy. The predominating views of epilepsy involved symbolism, demonology, hyperbolic religiousness and distorted medical opinions from the Greek and Roman period. Mysticism and dogmatism prevailed among physicians practicing ancient methods from the Babylonian era, under the notion that epilepsy was a contagious or hysteric disease. Patients were considered as “*possessed*” or labeled as witches or warlocks.

The early *Byzantine*, late Antiquity epoch, in the beginning adhered to the views of *Hippocrates*, *Galen* of Pergamon, *Alexander* of Tralles, *Oribasius* of Pergamon, *Paulus* of Aegina (625-690 A.D.) and *Aetius* of Amida (6th-7th century A.D.) and mainly the Hellenistic and Roman traditions influenced Islamic and European medicine. During the Hellenistic period also the term hydrocephalus was coined [3, 8].

Overall, Byzantine doctors (324 - 1453 A.D.) recapitulated the theories of Ancient Greek physicians and further systematised the nosology of the disease by reporting interesting cases of epileptic patients. *Alexander* of Tralles (525-605 A.D.), who was one of the most eminent representatives of Byzantine medicine, distinguished in his Books on Medicine (twelve books in total) three kinds of epilepsy and reproduced Galen’s views on epilepsy (founder of experimental physiology).

Alexander provided in his Therapeutics, dietetic advice and other natural remedies, concentrating on epilepsy in infancy and the special dietary requirements, such as good quality milk. Oribasius of Pergamon (320-400 A.D) believed that phlegma provoked epileptic convulsions. He considered the influence of various external factors, such as the moon and the climate on the brain’s functions. Oribasius mentioned the mental effects of epilepsy which he could not distinguish for example, from apoplexy [3, 8].

Paulus of Aegina (625-690 A.D.) practiced medicine at Alexandria and Aetius of Amida (6th-7th century A.D.) and mainly the Hellenistic and Roman traditions influenced Islamic and European medicine [16]. Aetius analytically described many surgical diseases of the womb. The work of Paul of Aegina, an encyclopaedist, especially his contribution to the treatment of neurosurgical disorders and trauma was well-known. Paul was born on the island of Aegina, performed trepanation for head injuries in the tradition of the Egyptian and the Greek schools of medicine. He was an innovator concerning the treatment of several spine injuries, in his choice to perform laminectomies. Paulus' compendium of Medicine consisted of 7 books in which he described the medical and surgical knowledge of his time. The work was translated into various languages, such as English in 1843 and French in 1855. Paulus of Aegina made valuable contributions to surgical techniques and described diverse methods for trepanations and laminectomies [17, 18]. In the middle ages, the basis for treatment fell into three main categories: conventional (diet, botanical remedies, and take off blood), magical (phases of the moon, trepanation of the skull) and religious, such as prayer, religious exorcisms and social marginalization. Mysticism and dogmatism prevailed among physicians practicing ancient methods from the Babylonian era.

In medieval medicine, many mosaics, xylography, icons, miniatures, other artistic and painting techniques depict the exorcism of a particular disease or devil by a particular saint. In the Middle Ages, around the 13-16th century, diverse illustrations were identified, such as the epileptic around 1516 from Raffael, known as Raphael (Raffaello Sanzio, 1483-1520) in the Vatican Museum "The Healing of the Lame". Raphael was one of three great masters of High Renaissance art along with Michelangelo and Leonardo da Vinci. The Heller Altar piece in Frankfurt by Matthias Grünewald (1470-1528) depicts "Saint Cyriacus / Heilige Cyriakus" exorcizing the daughter of Emperor Diocletian. Epileptic can be found in xylography, in museums and in many icons in the monasteries of Mount Athos/Greece. In the German Museum in Kork for "epilepsy and history of epilepsy" more icons can be found with holies and epileptic patients, e.g., Jesus healing a man in chains who suffers from epilepsy.

A number of tools for trephining were described in the 16th and 17th centuries [17]. Benjamin Winslow Dudley (1785-1870), in the pre-antiseptic era, was the first to publish a series of reports of trephination for post-traumatic epilepsy (six patients) between 1819 and 1832 [19]. In 1860, John Shaw Billings, a student from the Medical College of Ohio described in his dissertation the therapeutic methods and technics from trephination to surgery. Trephining was the most important surgical procedure employed at the time in the treatment of epilepsy. The 72 cases reviewed by Billings were not evaluated according to etiologic factors. All cases in the series being operative interventions [17, 20].

4. THE 19th CENTURY

The next important surgical procedures on epileptic patients were performed during the 19th century. In 1831, Dr. Johann Peter Heyman (1787-1832), surgeon and

Medicinalrath-Assessor in Coblenz/Germany reported "Observations and remarks about the operative treatment of the head injuries" and "Late and dangerous aftermaths following a light head trauma by trepanation". He was the first to perform surgery on an 11-year-old girl with cerebral abscess and focal epileptic seizures [21]. Surgical excision was performed in 1884, by Rickman John Godlee (1849-1925) in an adolescent patient from Scotland with focal seizures, where a brain tumor was excised from the right precentral gyrus (fissura Rolandi) at the National Hospital of London [22]. In 1886, Ferrier (1843-1928) described his experiments on brain stimulation in his colorfully illustrated book "The functions of the brain" [23]. Ferrier, Jackson and Bennett produced fundamental data for diagnosing epilepsy in patients with brain tumors. Jackson, called the "father of epileptology" clarified that the mechanism underlying focal and generalized epileptic seizures was similar. Sommer (1852-1900) described in 1880 the typical sclerosis of Ammon's horn [24]. In the second half of the 19th century, modern neurosurgery in Great Britain was developed by William Macewen (1848-1924), professor in Glasgow [25]. In 1879, Macewen succeeded in developing a technology that made craniotomy possible, with the patient under anesthesia with endotracheal intubation, antisepsis, and cortical localization, and in 1887 operated a brain abscess (Table 1). He has pioneered in other fields such as asepsis, osteotomy, tracheal intubation, pneumonectomy, and surgical suturing and drainage. Another surgeon, Joseph Lister (1827-1912), professor of surgery at Glasgow, a pioneer in the field of antiseptic, used carbolic acid to sterilise surgical instruments and clean wounds during the 1860s [24]. In this period, anaesthetic agents were available, principally chloroform, and ether (to a lesser extent).

Among the pioneers in epileptic surgery, Emil Theodor Kocher (1841-1917) was an important figure, a Swiss surgeon from Bern, awarded the 1909 Nobel Prize in physiology and medicine. Together with Harvey Cushing (1869-1939), he is regarded as the founder of modern neurosurgery, neurosurgical techniques, and much more. Kocher investigated posttraumatic epilepsies, particularly in combination with increased intracranial pressure [26, 27]. In 1928, Bovie (1882-1958), an eccentric inventor with a doctorate in plant physiology, developed an innovative electrosurgical unit in which Cushing was introduced to clinical practice [28]. In his career, Cushing performed surgeries on more than two thousand brain tumors and he succeeded in significantly reducing the high mortality rate.

In Europe, epilepsy surgery started in 1886, when Viktor Alexander Horsley (1857-1916) from the National Hospital of London, a student of Gowers (1845-1915), and first Englishman of modern neurosurgery, succeeded in removing epileptogenic posttraumatic scar tissue from the motor cortex under general anesthesia [29]. Horsley, combining the analysis of clinical characteristics with cortical stimulation, performed a series of craniotomies and completed nine successful epilepsy surgeries, establishing the efficacy of the procedure. Horsley first used electrical stimulation diagnostically in 1884 and slightly later (1886) to define epileptic foci. Between 1889 and 1906, he operated on patients with pituitary tumors. Postsurgical outcomes, however, were not encouraging as the

mortality rates of 5 to 7% were relatively high.

Otto Binswanger (1852-1929), a professor of neurology and psychiatry at the University of Jena (Germany), proposed a longer postoperative follow-up and discussed the possible role of scarring for epileptogenesis. In his opinion, surgical intervention should be limited to patients with an impaired quality of life only [30], but he was not optimistic about the curative value of surgery for seizures. This led to limiting the excision of the epileptogenic scar tissue in order to reduce damage to the adjacent eloquent brain structures. Further development in the 1920's was driven by Fedor Krause (1857-1937) and Otfried Foerster (1873-1941), two prominent neurosurgeons in Germany as well as *Wilder Penfield* in America [31 - 33]. They were able to localize the responsible brain area (seizure focus) in epileptic patients by electrically stimulating the cerebral cortex before extirpation.

5. THE 20th CENTURY

Krause introduced faradic stimulation to map the brain during the operation, and Foerster (next to neurologist and later neurosurgeons) and Penfield developed a more detailed mapping of the human cortex. *Krause* operated on over 400 epilepsy patients under local anesthesia and published with Schum in a book on epilepsy titled "Die spezielle Chirurgie der Gehirnkrankheiten" in 1931 in German [31, 33, 34]. In 1904, *Charles Elsberg* (1871-1948) was recognized for successful operations in the cerebellopontine angle and later for surgery of the spinal cord [34, 35]. At the same time, Charles Harrison Frazier (1870-1936), a pioneer in neurology and surgery in Berlin who later worked as a neurosurgeon in the USA, became known for surgery of pituitary tumors [35]. Later, the Canadians Herbert Jasper (1906-1999), an epileptologist/electrocorticographer, and Theodore Rasmussen (1910-2002), a neurosurgeon, made further efforts to make Electro Encephalo Gram (EEG) possible in patients with epilepsy [36, 37]. In his first English textbook on neurosurgery (1911), *Krause* enthusiastically recommended epilepsy surgery for all forms of epilepsy.

The *Society of Neurological Surgeons* was founded in 1920 in the USA, and in 1944 the first issue of the *Journal of Neurosurgery* was published. The American neurosurgeon Walter Dandy (1886-1946) described pneumoventriculography and pneumoencephalography in 1918 and 1919 [38], and in 1930 *Rogers* published the history of craniotomy [17]. *Rogers* assumed that the operation was performed as early as the Carnac Epoch of the Neolithic period (new stone epoch).

In autumn 1919, the American College of Surgeons declared neurological surgery as a separate specialty in surgery. In 1920, five months after the meeting, the American College of Surgeons accepted the formal genesis of the neurosurgical specialty in the United States. In 1931, the Harvey Cushing Society, in 1938, the American Academy of Neurological Surgeons and in 1948 the Neurosurgical Society of America were established. In 1951, the Neurosurgical Society of America organized a Congress of Neurological Surgeons.

William P. van Wagenen (1897-1961) studied the effects of callosotomy in patients with epilepsy in the 1940 - two

decades before Sperry [39]. He also collaborated with Andrew J. Akelaitis in describing some of the features of "split-brain patients". William P. van Wagenen and RY Herren performed and perfected the procedure of callosotomy and published their results in a series of 10 patients operated upon in 1939 [39]. Roger W Sperry (1913-1994),

a neuropsychologist and neurobiologist who, together with *David Hunter Hubel* (1926-2013), a Canadian-American neurophysiologist and Torsten Nils Wiesel (born 1924), a Swedish neurophysiologist, won the 1981 Nobel Prize in Physiology or Medicine for their work on "The functional specialization of the cerebral hemispheres". The price was shared with Hubel and Wiesel for their discoveries concerning "The visual cortex" [40]. The "Montreal Neurological Institute" or MNI, was founded in 1934 by neurosurgeon Wilder Penfield. Jasper and Rasmussen joined Penfield later (1936 for Jasper), where they housed an EEG laboratory for the neurosurgical treatment of epilepsy. Penfield (1891-1976) established and perfected his surgical procedures as the treatment of choice for intractable epilepsy, especially of neocortical origin [34].

Corpus callosotomy is a well-known neurosurgical procedure first described by Dandy. In severe cases of epilepsy, hemispherectomy was performed by Dandy in 1923, by McKenzie in 1938 and by Rowland Krynauw in 1950 [41 - 43]. At the same time, the German American psychologist Heinrich Klüver (1897-1979), and the American neuropathologist Paul Bucy (1904-1992) worked in separate procedures on the field of psychomotor epilepsy in monkeys [44]. The eponym Klüver Bucy syndrome describes the polysymptomatic behavioural sequelae of bilateral temporal lobectomy, both members of the famous Chicago Neurology Club. Some years later, in 1941, Jasper and Kortmann described temporal lobe seizures (most common intractable epilepsy) in which specific patterns of electrical discharge from the brain, recorded through the unopened skull and found different forms of clinical seizures [36].

In 1939, Hugo Krayenbühl (1902-1985) opened the first neurosurgical unit in Switzerland, and about 10 years later (1948), the first neurosurgical hospital in Europe was founded [11, 45]. In 1935, Percival Sylvester Bailey *et al.* (1892-1973), a neuropathologist and neurosurgeon, and assistant to *Harvey Cushing*, and in 1951 *Bailey* and *Gibbs* improved electrophysiological and surgical techniques. He conducted a series of anterior temporal lobectomies; he would leave the mesial limbic structures intact, achieving better postoperative results [46, 47]. In 1947, somatosensory evoked potentials were introduced as a new diagnostic tool by *George Dawson* [48]. In 1951, the world-famous neurosurgeon *Arthur Earl Walker* (1907 -1995) published the first thorough book of neurosurgery from the prehistoric period to the current era "A History of neurological surgery", Baltimore: Williams and Wilkins company. The book includes *e.g.* diagnostic techniques, cranial, and intracranial surgery [49]. Some decades later in 1997, Samuel H Greenblatt (editor), born in 1939, a neurosurgeon, *T Forcht Dagi* and *Mel H Epstein* (contributing editors) published the next book on the "A History of neurosurgery - In its Scientific and Professional

Contexts” [50].

In the early 1950's, neurosurgery became a modern specialty, with the increased usage of intracranial pressure monitoring in patients with brain injuries. From 1953 onwards, neurosurgical centers, often involving surgeons and/or scientists who had studied at the Montreal Neurological Institute, used the procedure of temporal lobe (mesial region) resection for the treatment of seizures.

In 1957, the French psychiatrist/neurosurgeons Jean Tailarach (1911-2007) called *Daemon Tailarach* (Department of neurosurgery in St. Anne's Hospital/Paris), together with his team Pierre Toumoux and Gábor Szikla published his stereotactic atlas, a work that changed the future of epilepsy surgery for the years to come. In 1968, Tailarach and Toumoux published the second edition of this atlas, an art of brain cartography [51]. This fact led to a revolution of epilepsy surgery that completed the pre-surgical and therapeutic surgical phases of treatment. During the 1960's, *Bogen* and *Vogel* reintroduced the callosotomy procedure as a palliative treatment for certain cases of pharmacoresistant epilepsy with severe atonic-akinetic seizures [52]. In 1961, *White* published a comprehensive review on the surgical procedure of hemispherectomy, summarizing the results of 269 published cases in the treatment of infantile-type hemiplegia and seizures [53]. In the same year, *French* and *Darling* described detailed history of epilepsy surgery in 1861 [54].

Some years later, in 1968, the neurosurgeon *Murray Alexander Falconer* (1910-1977) and *Taylor* succeeded in performing the first epilepsy surgery in a patient with hippocampal sclerosis and temporal lobe epilepsy (Ammon's horn sclerosis), and neuropathological condition with severe neuronal cell loss and gliosis [55]. *Morrell* and *Hanbery*, in 1969, proposed performing “multiple subpial transections” in patients with non-resectable epileptic foci in circumstances of intractable focal epilepsy in eloquent cortical areas [56]. *Spencer* and *Spencer*, in 1985 and 1989, described diverse procedures for surgical control of seizures, such as hemispherectomy, corpus callosum section, and stereotaxy in patients with intractable epilepsy [57, 58]. In the subsequent years, epilepsy surgery became less popular because of all of the new anticonvulsant medication that appeared in the market.

The International Bureau for Epilepsy (IBE) was established in 1961, as an international organisation representing the national epilepsy Bureau's interest in the medical and non-medical aspects of epilepsy. In 1969, *Ralf W Gerard* (1900-1974), an American neurophysiologist, founded the Society for Neuroscience (SfN) and was an honorary president. SfN is the largest neuroscience society in the World and their research is focused on the study of the brain and nervous system.

After some encouraging results in epilepsy surgery, surgical therapy for the treatment of epilepsy became a preferred treatment in many centers in Europe and America for many types of epilepsy. A new era of epilepsy surgery arose with the development of pre- and perioperative diagnostic interventions, important technical innovations (microneurosurgery, neuronavigation, stereotaxy), and starting

in 1971, neuroimaging (CT) was a fundamental advancement in diagnosis of the brain, histology was also crucial for hippocampal sclerosis, Magnetic Resonance Imaging (MRI) a decade later in 1980, advances of modern diagnostic methods, and new techniques in the following years, such as Positron Emission Tomography (PET), Single Photon Emission Tomography (SPECT), [31] P- and [1] H-MR spectroscopy, and magnetoencephalography (MEG). The usage of brain CT and MRI contributed to important structural diagnostic findings in epilepsy, such as cryptogenic epilepsy and Ammon-horn's epilepsy. The microsurgery application (method) led to selective operations having fewer complications; such procedures included ‘*selective amygdalo-hippocampectomy*’ [59, 60]. *Yasargil et al.*, in the last publication, described exactly the anatomical archicortex area (hippocampus and parahippocampus area, cornu ammonis) and the surgical techniques of selective amygdalo-hippocampectomy (AHE) by patients with temporal epilepsy [60]. In the years before 1969, principal temporal lobe epilepsies were treated by a two-thirds standard anterior temporal lobectomy combined with amygdalo-hippocampectomy. According to *Wieser et al.* AHE is the surgery of the first choice in epileptic syndromes [61].

Nowadays, epilepsy surgery is recommended for only some forms of epilepsy after the application of strict selection criteria, whereas every case being individualized and presented in a multidisciplinary forum such as Epilepsy Rounds [62]. In the last twenty years, technical advances have provided precise diagnostic methods, especially for localizing the areas of seizure origin in the brain cortex [56, 59, 62]. There is continued refinement of surgical methods, microsurgical selective operations, advances in the intracranial localizing of epileptogenic zones in patients with refractory partial epilepsy, recommendations for patient selection, and the stereo-electroencephalography recording of patients with refractory epilepsies. In general, the interest in such interventions has improved along with the development and organization of Neurosurgery Epilepsy Centres worldwide [63].

CONCLUSION

Epilepsy was first mentioned in Assyrian and Babylonian documents dating back to almost 2500 B.C. Hippocrates was the first to describe epilepsy as a disorder of health, doubting the divine origin of the disease. Hippocrates also diligently described a surgical instrument and interventions in epileptic patients in his chapter of the Hippocratic Corpus: On the Sacred Disease. The earliest beginnings of epilepsy surgery can be traced back to antiquity and Trepanations have often been found in prehistorical tombs (Neolithicum). In the Byzantine years, all doctors recapitulated the theories of Ancient Greek physicians and further systematised the nosology of the disease by reporting interesting cases of epileptic patients. The first neurosurgical pioneers during the second half of the 19th century were Macewen, Horsley, Krause, and the leaders of the second generation were Cushing, Danty, Elsberg and Frazier. This communication is to provide a brief, yet concise overview of the most important milestones in the history on epilepsy surgery from antiquity through the end 20th century.

CONSENT FOR PUBLICATION

Not applicable.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

The author would like to thank Dr. Michael Vassilyadi, Dr. Christian Hagel, Dr. Erich Rutz and PhD student Georgios Sofianidis for their contribution in editing and proofreading the manuscript.

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