**Epilepsy Surgery: Historical Highlights 1909–2009**

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**SUMMARY**

This review focuses on some historical highlights of the surgery of epilepsy, beginning with the reports of Horsley, Krause, and Cushing to which appeared in 1909, the year that The International League Against Epilepsy (ILAE) was inaugurated. We then outline key contributions from Europe and North America, and examine particularly the evolution of our understanding of temporal lobe seizures, which have now become the most common form of epilepsy amenable to surgical cure.

**KEY WORDS:** Epilepsy surgery, Cortical mapping, Temporal lobe resection, Amygdala, Hippocampus, Mesial temporal sclerosis.

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**A Landmark Year for Epilepsy**

The year 1909 stands out as a landmark in the annals of the history of epilepsy and as a year of hope for the millions afflicted with epileptic seizures. In the late summer of that year, the inaugural meeting of the International League Against Epilepsy (ILAE) took place in Budapest, amid the elegant ambiance of the XVI International Medical Congress. The Congress was attended by a host of distinguished physicians in neurology and the emerging specialty of neurosurgery. Scientific talks were presented by the pioneer neurosurgeons Sir William Macewen (1848–1924) of Glasgow and Professor Fedor Krause (1857–1937) of Berlin; by Professor Emil Theodor Kocher (1841–1917), who received the Nobel Prize that same year (the first surgeon laureate) for his studies on the thyroid gland; and by Kocher’s former student, Dr. Harvey Cushing (1869–1939), from The Johns Hopkins Hospital, a rising star in the new field of pituitary surgery, who reported at The Congress his first case of partial hypophysectomy for acromegaly, with a successful outcome (Cushing, 1909a, 1909b). Cushing’s travel diary gives a lively account of these crowded days, with colorful descriptions of the titled Hungarian hosts and eminent dignitaries assembled from many nations (Fulton, 1946).

A few months before the founding of the ILAE, on May 6, Sir Victor Horsley (1857–1916) delivered the Linacre Lecture at Cambridge University on The Function of the So-called Motor Area of the Brain (Horsley, 1909). He cited his report of 1886 on his first three cases of focal Jacksonian epilepsy. He had operated upon these patients, urged and abetted by John Hughlings Jackson (1835–1911) and David Ferrier (1843–1928). Although Horsley did not stimulate the cortex in any of these three operations, he was informed by his brain-mapping experiments using electrical stimulation of the rolandic cortex on monkeys. In his Linacre Lecture, he also reported an operation on a boy who had developed uncontrollable, violent movements of his left arm. Horsley used a bipolar electrode to obtain responses from the cortex in front of the central fissure; these ranged from movements of the face at the inferior portion, then of fingers, elbow and shoulder, as he went upward on the precentral cortex (Fig. 1). After excision of the mapped “motor” cortex, the boy developed not only paresis of the arm but also demonstrable sensory loss in his face and arm, an observation that led Horsley to conclude that the pre-rolandic cortex served both as a motor and sensory center. This viewpoint was at odds with the contemporary findings of Sherrington and others, and one still under debate today (Uematsu et al., 1992; Boling et al., 2002).

Also in 1909, Fedor Krause, Germany’s leading neurosurgeon, published a five-page article on Die operative Behandlung der Epilepsie in a Berlin medical journal. He followed this with more extensive exposiciones of the surgical treatment of epilepsy, during the course of which he produced detailed maps of the human motor cortex (Krause, 1912; Krause & Schurn, 1932).

Before Harvey Cushing went to Budapest to attend the International Medical Congress, his seminal paper in
Brain (Cushing, 1909a) reported for the first time sensory responses and the sensory auras of focal attacks, produced by electrical stimulation of the postcentral cortex, in two patients awake under local anesthesia during the operations.

Therefore, by the time the ILAE was founded in 1909, neurosurgeons were already breaking new ground in the surgical therapy and scientific understanding of epilepsy.

**History of Epilepsy Surgery**


Readers are referred to these sources for definitive discussions on important historical aspects of epilepsy surgery, such as hemispherectomy, corpus callosotomy, corticectomy for dysplasia, and stereotaxic approaches, which we have excluded from this selective review.

**The Pioneer Work of Horsley**

The observation by Paul Broca (1824–1880) that focal cerebral lesions can produce speech deficits (Broca, 1876) and the demonstration by Gustav Fritsch (1838–1891) and Eduard Hitzig (1838–1907) that selective sites on the cerebral cortex can be excited by electrical stimulation to produce specific motor responses (Hitzig, 1900), led Hughlings Jackson to consider focal epilepsy as a manifestation of cortical irritation. He suggested treatment by removal of the irritating focus (Jackson, 1870, 1873), and prevailed on his neurosurgical colleague, Victor Horsley, to perform craniotomy to effect a cure of epilepsy (Horsley, 1886). It was a challenge for a young doctor just starting surgical practice (Taylor, 1987).

The patient, James B., a 22-year-old Scotsman, had been run over by a cab in Edinburgh when he was a child. He sustained a depressed comminuted skull fracture with local brain damage, which at age 15 led to episodes of fits and occasional attacks of life-threatening status epilepticus. The focal motor seizures affected, in order, the opposite leg, the upper arm, the wrists and fingers, and face. Before operation the patient was given a quarter grain of morphine and put under chloroform anesthesia. Horsley mentions that brain operations can be performed under local anesthesia, using a very strong solution of cocaine to block the pain from the dura. He enlarged the bone defect resulting from the prior injury. The scarred dura, adherent to the scalp, was raised with the skin flap to expose a highly vascular 3 × 2 cm scar, which he excised along with a border of cortex. The presence of a discrete cortical vascular scar and the arrest of the focal motor seizures following its excision provided direct support for Jackson’s concept of the etiology of focal epilepsy.
Horsley presented this and two similar operative cases of focal fits to the British Medical Association (Horsley, 1886). After hearing Horsley’s lecture, Professor Jean-Martin Charcot (1825–1893) remarked, “Not only had English surgeons cut out tumors of brain, but here was a case in which it was probable that epilepsy had been cured by operative measures.” Hughlings Jackson stated, “there was in every case of epileptiform seizures a persisting discharging lesion.” He believed the starting point of the fit was a sign of the seat of the “discharging lesion,” and advocated cutting out that lesion, whether it was produced by tumor or not. These auspicious beginnings of epilepsy surgery broadened into a wider field of brain surgery, an area in which Horsley made frequent reports over the next decade (Horsley, 1906, 1909).

Horsley’s results from epilepsy surgery were initially favorable; all patients survived. Localization of the site for surgery was obvious in the two patients with skull defects from head injuries. But the focal onset of the seizure in the third case was correctly interpreted by Jackson to point to the motor cortex as the site of the epileptogenic lesion, which proved to be a tuberculoma. Horsley and Charles E. Beevor (1854–1908) had observed thumb and finger responses from cortical stimulation in their experiments on monkeys: it was the comparison of these findings with the patient’s focal seizure onset that led Jackson to advise an exploratory operation that disclosed the lesion.

Unfortunately not all neurosurgeons had the skill of Victor Horsley, or the benefit of Hughlings Jackson’s adroit guidance. More significantly, identification of the motor strip, in the absence of cortical electrical stimulation, depended on external landmarks that were notoriously unreliable, despite studies by Broca that related the central fissure to the coronal suture (Broca, 1876). Further advances in the surgical treatment of focal epilepsy awaited the development of local anesthetic agents with better asepsis and hemostasis. But the close collaboration of the neurologist–epileptologist, the epilepsy surgeon, and the experimentalist, exemplified by Jackson, Horsley, Ferrier, and Beevor would serve as a model for the surgical treatment of epilepsy (Jackson, 1888; Horsley, 1892, 1906).

Sir William Osler (1849–1919), the Regius Professor of Medicine at Oxford, had been well aware of Horsley’s report on the first three patients that he had operated upon for Jacksonian seizures. “One of the most interesting aspects of modern surgery” Osler stated, “relates to the treatment of epilepsy, Jacksonian and idiopathic” (Osler, 1889). Osler became an early protagonist for the role of surgery for epilepsy and, in addition, strongly influenced the neurosurgical careers of Cushing and Penfield (Feindel, 2003a, 2003b). In discussing the early instance of brain tumor performed by Rickman Godlee (1849–1925) in 1884 in London, William Osler referred to his own observation of a postmortem examination at Montreal in 1883, which had disclosed a small frontal glioma in the leg center. The patient, a physician’s child, had intermittent Jacksonian seizures for 12 years and died eventually in status epilepticus. This was “an instance,” Osler wrote, “in which an operation would have been justifiable and possibly have been the means of saving life” (Osler, 1885). A vindication of Osler’s positive views for epilepsy surgery is provided by a similar case report of a patient with surgical cure of focal seizures caused by a small glioma (Feindel, 2009).

In 1907, after hearing William Macewen and Donald Armour (1869–1933) review their experiences in brain surgery, Osler (by then the Regius Professor of Medicine at Oxford) commented, “a great deal of skepticism in regard to the value of operation in cases of cerebral tumor was a result of the bicapital condition of neurology.” Osler added that he “would prefer to see neurology a special department so that there would not be neurological physicians and surgeons, but medico-chirurgical neurologists, properly trained in the anatomical, physiological, clinical and surgical aspects of the subject” (Osler, 1907). This dictum could well serve as a directive for neurosurgeons who take up epilepsy surgery.

### Early Surgery for Epilepsy in the United States

The patients reported by Victor Horsley were the first examples where the sites of the operation and cortical ablation were informed by experimental cortical stimulation results, combined with the astute interpretation of the focal seizure pattern to indicate the appropriate area of the epileptic focus. But as Herman Flanigin (b. 1920) and his associates point out (Meador et al., 1988; Flanigin et al., 1991) in their thorough review of the surgical treatment of epilepsy, it was Benjamin W. Dudley (1785–1870) in Lexington, Kentucky, who in 1828 was among the first in North America to report the results of trephination for posttraumatic epilepsy. He operated on five patients; three became seizure-free and two improved.

Flanigin et al. (1991) also refer to Stephen Smith (1823–1922), who listed 27 cases of trephination for epilepsy in the United States (Smith, 1852). They note that in 1861, John Shaw Billings (1838–1913) credited Ephraim McDowell (1771–1830) of St. Louis for operations on more than 100 patients for epilepsy. In these pre-Listerian times, sepsis presented as the major complication.

### Fedor Krause and Epilepsy Surgery

During the 19th century some surgeons suggested that epilepsy is the result of an increased production of cerebrospinal fluid and that seizures are produced by sudden
changes in cerebral blood flow resulting in an acute rise in intracranial pressure. Measures were devised to equilibrate the assumed elevation in intracranial pressure in epileptics, most notably the valve operation devised by Theodor Kocher and adopted by Fedor Krause.

After a large craniectomy, the resected dura was replaced by a galeal flap that partially covered the brain, thereby creating a “valve” through which, it was considered that cerebrospinal fluid could escape (Krause, 1909). This type of operation was abandoned when laboratory investigation failed to demonstrate that intracranial hypertension or cerebral hyperemia produce seizures, and when the results of surgery, analyzed by Krause and others, proved unsatisfactory. Nonetheless, a possible causal relationship between circulatory factors and epileptic seizures would remain a persistent problem for investigation by Krause (1912), Foerster and Penfield (1930a, 1930b), and Penfield (1933, 1937).

From 1893 to 1912 Fedor Krause operated on 96 patients for the treatment of epilepsy (Leblanc, 1990). In many of these operations he used faradic stimulation to map the motor strip and identify epileptic areas, which were more excitable to the electrical current. Krause thereby confirmed the demonstration of Horsley (1909) that the central dogma of discrete functional localization applies to man. These observations led to the production of detailed maps of the human motor strip and established cortical resection as a safe and effective treatment for focal epilepsy (Krause, 1909, 1912).

**CAUSES OF FOCAL EPILEPSY**

Krause recognized that focal epilepsy could be caused by a variety of conditions affecting the brain and its coverings. With regard to the surgery of focal epilepsy he recognized three important conditions: tumors involving and irritating the motor area, infantile cerebral palsy, and those cases with a cortical scar. He paid special attention to posttraumatic phenomena as a cause, astutely postulating that epilepsy could produce changes beyond the primary spasmic center. This led him to believe that “operative intervention will favorably influence the atrophic and sclerotic metamorphoses known to flourish in the cortices of so many epileptics” (Krause, 1912). Krause believed that a posttraumatic scar could be related to epileptogenicity: “the leptomeninges may be found in a condition of cicatrical transformation and united with the cerebral cortex; or, scars may even be discovered within the substance of the latter” (Krause, 1912).

According to Krause (1912), posttraumatic scars could produce “adhesions with the arachnoid, pia, and the surface of the brain” and these changes “could affect the cortical blood vessels present within bands of cicatrical tissue.” Krause shared with Adolf Kussmaul (1822–1902) the view that anemia of the cerebral cortex bears an important relation to the origin of epileptic spasms, and suggested that focal epilepsy could be produced in a reflex manner by the traction of scars on the encased blood vessels. Krause thus recognized all the elements that Wilder Penfield (1891–1976) would later demonstrate within a postruptional meningeal cerebral cicatrix, such as produced by him in experimental animals, or examined in the laboratory of Pio Del Rio Hortega (1882–1945), or as observed in Otfrid Forester’s (1878–1941) resected specimens.

Krause also recognized that the primary spasmic center, the epileptogenic area, may be distant from the structural lesion. He considered the operative strategy in such cases, addressing “the question whether the morbid focus only should be excised, or in conjunction with it the primary spasming field as well” (Krause, 1912). He stressed that “in a few instances I have adopted the latter plan with excellent result.” This foreshadows the current concept of an “epileptogenic border zone,” Penfield’s term for cortex so severely disrupted by tumor or scar that it cannot generate electrical activity itself. Krause’s advice to resect both the structural lesion and the epileptic area is now currently accepted practice.

**CORTICAL STIMULATION AND RESECTION**

Krause operated without the aid of contrast radiology or electroencephalography (EEG). Because the basis of localization was the patient’s clinical presentation, most of his cases were of Jacksonian epilepsy. The seizure focus could not be precisely identified preoperatively; therefore, he stressed the necessity of a wide surgical exposure. If no etiology such as a tumor was identified, then faradic stimulation could be employed to locate the primary spasming point.

During stimulation of the brain Krause had three physicians observe the patient: one to inspect the face, a second the upper part of the trunk and upper extremities, and a third the lower part of the trunk and lower extremities. Observations of muscular contractions of face and extremities were dictated to the recorder, while the located centers were noted on a sketch of the cerebral surface by the artist (Krause, 1912). With the aid of these extensive and labor-intensive techniques of observation and drawings of the operative field to record results, Krause was able to produce one of the first detailed human brain maps localizing the motor strip to the precentral gyrus (Fig. 2). As Horsley (1909) and others had shown clearly in primates, Krause concluded that:

The anterior central convolution contains all the [motor] foci located. Their arrangement on the cortical surface is such that the centres for the lower extremity occupy the uppermost portion of the convolution near the sinus
longitudinalis . . . the lower extremity engages as its locus approximately the upper one-fourth of the central convolution. About one-half of the middle portion responds to stimuli with contralateral muscular contractions of the upper extremity, from the shoulders down to the fingers. The lower one-third of the convolution discloses, upon irritation, the foci of the muscles of the face and those of mastication. Here should also be found the centres of the muscles of the larynx, the platysma myoides, and the muscles of the tongue (Krause & Schurn, 1931).

Although cautioning surgeons that the primary spasming center of the right hand should be excised with great delicacy and that Broca’s cortical field for speech is even more sensitive than the center of the arm, Krause nonetheless recognized that preoperative pareses and paralyses frequently improved, in some cases of perinatal injury producing infantile hemiplegia, after resection of the epileptogenic area, even if this included the central region. In this way Krause anticipated Penfield’s concept of nociferous epileptic cortex exercising a deleterious effect on the remainder of the brain, producing neurologic symptoms that are improved with resection of the epileptogenic area. This predates the now common observation that hemispherectomy in previously paralyzed patients frequently improves their motor function.

Krause was aware that advocacy of cortical resection for epilepsy ran counter to the opinion of his contemporaries; he, therefore, paid special attention to the follow-up of his patients to determine the results of surgery. Taking advantage of the efficient Prussian postal system, his patients were requested to answer a specific questionnaire that addressed their general condition, and specific features such as the presence or absence of epileptic seizures and, if present, their nature and frequency; the state of their memory and intellectual faculties; the nature and duration, if any, of their current medical treatment; and the patient’s own appreciation of his condition (better, worse, or the same) following surgery.

Of 55 patients undergoing cortical resection for Jacksonian epilepsy, 29 answered his questionnaire. Four others died from status epilepticus within 6 days after surgery. Of the other 29, 11 were the same as before the operation, 3 became aggravated, and 8 showed a marked improvement and amelioration of the symptoms and seizures. Very good results were obtained in three cases; four cases were completely cured. Aware that epilepsy can have a fluctuating course, Krause did not consider patients permanently cured until they had been seizure-free for 5 years.
Harvey Cushing and the Sensory Cortex

In 1901, on a visit to Charles Sherrington’s (1857–1952) physiologic laboratory in Liverpool, Harvey Cushing helped to map the motor cortex in three primates, including that of a gorilla. His sketches, used by A. S. F. Leyton (1869–1921) and Sherrington in a report of 1917, showed motor responses from a narrow precentral strip, rather than the wider territory described by Horsley and his associates. Later, at the Johns Hopkins Hospital, Cushing (Thomas & Cushing, 1908) reported on stimulation of motor cortex in more than 50 operations, confirming the results of Krause.

The next year, Cushing described operations involving faradic stimulation of the postcentral gyrus on two patients with focal sensorimotor attacks. The patients were kept awake under local anesthetic during the operations, while Cushing utilized a stimulating probe created after the design of Sherrington (Cushing, 1909a, 1909b). The sensory responses in the hand and arm were likened by the patient to the feeling of weakness or “goneness” that initiated the attacks. Lower in the postcentral gyrus a sensation of warmth in the arm, rather vague and indescribable, was reported (Fig. 3).

In the second patient, stimulation behind the postcentral vein was described as though someone had touched or stroked the finger or the back of the hand. Incision into the upper part of the postcentral gyrus in the first patient revealed no lesion; no resection was made. In the second case, further exposure disclosed a lesion of the superior part of the postcentral convolution, which was thought to be irremovable. In these cases, Cushing thus demonstrated, for the first time, the sensory function of this postcentral area. In a footnote to his Linacre Lecture, Horsley (1909) acknowledged Cushing’s discovery of the sensory nature of the postcentral area. These studies of cortical localization evidently influenced Cushing’s later classification of a large series of meningiomas, by relating them to cortical regions with specific functions (Cushing & Eisenhardt, 1938).

Writing in August 1932 to Wilder Penfield in Montreal, Cushing noted, “... I, too, just thirty years ago was extirpating a cortex [sic] for epilepsy. If I had had the industry and ability that you and Foerster combine, I might have gone ahead with it and made something out of it. But I soon dropped it for things I thought I could do better” (Preul & Feindel, 2001).

Otfrid Foerster and Cerebral Localization

After World War I many soldiers with posttraumatic epilepsy made their way to Otfrid Foerster in Breslau to seek relief of their affliction. Like Krause, Foerster initially had few technologic means to localize the seizure focus. He depended almost entirely on the chance observation of a seizure to exhibit a focal onset. To better study the onset and spread of seizures Foerster was the first to report, in 1924, on the use of hyperventilation to precipitate an epileptic attack. He was also one of the first to apply pneumoencephalography for the preoperative

Figure 3.
Stimulation points that evoked motor and sensory responses and reproduction of patient’s aura (sensation of warmth) from the postcentral gyrus (Cushing, 1909a).
Epilepsia © ILAE
lateralization and location of the focal lesion in patients with posttraumatic epilepsy (Foerster, 1925).

Foerster, trained in neurology with J. Jules Dejerine (1849–1917) and Carl Wernicke (1848–1905), took up the scalpel commenting, it is said, that he could do no worse than his previous surgical colleague since, after Foerster localized the cerebral lesion and indicated where to operate, all the patients died.

Foerster operated on patients who were under local anesthesia and, perhaps reflecting his early interest in archaeology, he opened the cranial vault by piecemeal ronguering. The epileptogenic area was identified by electrical stimulation in an attempt to reproduce the patient’s usual seizure, by traction on the epileptogenic scar, and by intraoperative hyperventilation. These rudimentary techniques would eventually be enhanced in 1934, by the first use, with his coworker Hans Altenburger (1902–1938), of intraoperative electrocorticography (ECoG) (Foerster & Altenburger, 1935). They also investigated the physiologic use of ECoG, in a manner akin to evoked potentials, by recording the effects of visual stimulation, of stimulation of the plantar response, or of mental activity.

Foerster benefited greatly from his collaboration with Oskar Vogt (1870–1959) and Cécile Vogt (1875–1962), who were investigating cortical localization in animals. This resulted in a more detailed human cortical map (Foerster, 1934). On the 100th anniversary of the birth of Hughlings Jackson in 1936, Foerster summarized his experience with cortical stimulation in the IXth Hughlings Jackson Lecture of the Royal Society of Medicine (Foerster, 1936).

Between the wars, the clinic of Foerster was briefly visited by a host of North American neurosurgeons such Alfred Adson (1887–1951) from the Mayo Clinic, Max Minor Peet (1885–1949) and Edgar Kahn (1900–1945) from the University of Michigan, Leo Daviddoff (1898–1975) from New York, Paul Bucy (1904–1993) from Chicago, and the physiologists John Fulton (1899–1960) and Margaret Kennard (1891–1976) from Yale.

In 1930 Foerster was invited by Cushing to be “Surgeon-in-chief, pro tempore” at the Peter Bent Brigham Hospital in Boston. Foerster’s contributions to neurosurgery would also be recognized by the British Association of Neurological Surgeons who visited his Breslau clinic in 1937, where he discoursed on brain tumors, and was elected an emeritus member of the association.

Foerster benefited from the generosity of the Rockefeller Foundation to establish a neurologic institute, under his directorship, in Breslau; he continued his work through the Weimar years, through the rise of National Socialism (Zülch, 1969, 1973). His death, in 1941, in the darkest days of the war, after the blitz and the Battle of Britain, would be noted by his British colleagues Hugh Cairns (1896–1952), Lord Russell Brain (1886–1961), and Sir Geoffrey Jefferson (1886–1961), the latter commenting “It will be a grief to many to learn that they will not meet Otfrid Foerster again” (Jefferson, 1941).

**Foerster and Penfield**

One of Foerster’s earliest and most productive collaborations had been with the young Wilder Penfield, who had become interested in cerebral scars as a factor in focal epilepsy. This had taken Penfield in 1924 from New York to the laboratory in Madrid of Pio Del Río Hortega, with whom he studied the reaction of neuroglia and microglia to brain wounds (Del Río Hortega & Penfield, 1927; Penfield, 1927). So it was with a prepared mind that he visited Foerster in 1928.

During a 6-month stay in Breslau, Penfield applied Spanish gold and silver staining techniques to study the reaction of the neuroglia to cerebral trauma (Penfield, 1977). From their detailed study of 12 operative cases, came the first systematic histologic examination of lesions in posttraumatic epilepsy, the first testable hypothesis of the etiology of this phenomenon, and a therapeutic rationale for exchanging an epileptogenic meningoencephalic cicatrix for a clean surgical wound (Foerster & Penfield, 1930a, 1930b) (Fig. 4). Penfield’s examination of these resected posttraumatic scars revealed fibrous bands projecting inward from the meningeal surface, penetrating the cortex, and extending deep into the white matter in more or less parallel lines. These bands of blood vessels and collagenous fibers intermingled with neural and glial filaments; the three components intertwined like “strands in a rope.”

Penfield (1933) noted:

> An outstanding feature of all these scars is the rich plexus of newly-formed vessels in and about the cicatrix. This vascular plexus anastomoses very freely with the large vessels which enter the scar from without. It also anastomoses freely with intracerebral vessels in as much as the surface of the dura continues to bleed after it is completely exposed and cut free from surrounding dura . . .

Foerster had observed that epileptic seizures can be initiated by electric stimulation around the meningoencephalic cicatrix, as well by gentle traction on the cicatrix itself. He and Penfield proposed that the resultant traction on the encased blood vessels might set up a “vaso-motor reflex secondary to this traction,” which could be “responsible for the initiation of the convulsive seizures” (Foerster & Penfield, 1930a, 1930b).

**Penfield and the Montreal School**

After his return to Montreal in 1928, Penfield further investigated this vascular hypothesis in the first series of
epileptic patients that he operated on, thus for the first time characterizing the vascular physiology of the epileptic brain (Penfield, 1933, 1937). He observed that the most frequent sequela of an epileptic seizure is “the appearance of focal areas of cortical anaemia,” which he considered might be responsible for postictal paralysis.

In other operations, Penfield observed vasoconstriction of pial arteries that was sufficiently severe to interrupt blood flow. Less frequently he observed dilation of the vascular bed characterized by bright red arterial blood shunting into veins (Penfield, 1937). However, further observation of epileptic patients at the time of surgery and judicious use of newly available technology in the form of the “Gibbs blood flow thermocouple, the Matthews electrocardiograph, operative photography and running descriptive dictation” would lead him to abandon this concept of reflex vasoconstriction as the cause of posttraumatic epilepsy (Penfield, 1937). Nonetheless the investigation of this hypothesis by his students Everett Lyle Gage (1901–1972) (1931), Jerzy Chorobski (1902–1986) (Chorobski & Penfield, 1932), and Francis McNaughton (1906–1986) (1937) led to the demonstrations of the innervation of meningeal and cerebral blood vessels and produced the first study of cerebral vasospasm, by Francis Echlin (1906–1988) (1939).

**Wilder Penfield’s Early Career**

Wilder Penfield had been introduced to the nervous system through his studies with Charles Sherrington at Oxford in 1915–1916 and again in 1920–1921. Explaining how he was led into neurosurgery, Penfield later wrote “It was the inspiration of Sherrington. He was, so it seemed to me from the first, a surgical physiologist, and I hoped then to become a physiological surgeon” (Penfield, 1977).

From his work at Oxford, Penfield became familiar with the observations on cortical localization by electrical stimulation in animals by Ferrier (1876) and in primates by Leyton and Sherrington (1917) (Feindel, 2007). Penfield centered his main career on the science and surgery of epilepsy (Penfield, 1930, 1967; Penfield & Erickson, 1941; Penfield & Jasper, 1954; Lewis, 1981). His experience with Foerster came at a critical period in Penfield’s career. While in Germany, freed from his busy surgical practice in New York, Penfield also took on the substantial task of organizing an authoritative compendium by international authors that appeared in three volumes as the *Cytology and Cellular Pathology of the Nervous System* (Penfield, 1932), an enduring classic reprinted in 1965.

Penfield became familiar with Foerster’s use of local anesthesia and electrical stimulation to map motor and sensory areas of the human cortex exposed at operation, so that these could be protected during surgical excision of epileptogenic brain (Foerster & Penfield, 1930a, 1930b). But Penfield would go beyond Foerster by mapping other areas of cortex that subserve speech, hearing, vision, and, perhaps most crucial of all, memory function. He recorded these observations on cortical localization in a long series of publications with many associates (Penfield, 1975; Eccles & Feindel, 1978 [includes bibliography of Penfield’s writings]; Feindel, 1977).

Recurrent analyses were also reported on the follow-up results of surgical excision in controlling seizures. In 1937, Penfield and Edwin Boldrey (1906–1988) analyzed results from 163 craniotomies in which electrical stimulation of the exposed cerebral cortex in humans was carried out under local anesthesia (Penfield & Boldrey, 1937). The motor and sensory maps thus obtained provided no evidence for area 6a beta, the tertiary motor area, as described in the monkey by the Vogts, or for the existence of various “extrapyramidal motor areas” reported by Foerster.
These cortical maps, like those of Horsley, Krause, and Foerster, gave the topographic localization for different parts of the body. The Montreal results were synthesized for visual purposes into a “homunculus,” which cartooned the relative size and order of the cortical representation (Penfield & Boldrey, 1937). They found an overlap in the function of the so-called sensory and motor cortex so that some sensory responses were obtained from the precentral or “motor” gyrus whereas, conversely, a number of motor responses were obtained from the “sensory” postcentral gyrus. In addition, they noted a large overlap of the cortical areas from which stimulation evoked responses relating to different parts of the body, an important finding in considering the mechanisms of “plasticity” of the motor cortex in recovery from focal lesions (Fig. 5).

Penfield’s early operations for epilepsy were based primarily on an intense study of the clinical seizure pattern and by cortical mapping and stimulation at operation to evoke the patient’s aura (Penfield, 1930). The focal lesion, often a meningocerebral scar from trauma or infection, could also be epileptogenic cortex bordering a brain tumor or angioma (Penfield & Erickson, 1941), as first surmised by Krause (1912).

**Figure 5.**
Overlap of cortical zones relating to movement and sensation evoked from the rolandic region (Penfield & Boldrey, 1937).

*Epilepsia* © ILAE

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**Penfield’s First Temporal Lobectomy**

Shortly after they arrived in Montreal, in November 1928, Penfield and his surgical partner, William Cone (1897–1959), performed their first operation utilizing the Foerster method. The patient, a young man previously treated for a subdural hematoma and contusion, had as many as 20 seizures each day. Three operations eventually led to improvement (Feindel, 1991). At the third operation, the thin scarred cortex of the temporal lobe was widely resected (Fig. 6). Afterward the patient exhibited a greatly reduced number of seizures, which were still further decreased to four in the 13 years after he began to take Dilantin.

Penfield referred to this operation as his first temporal lobectomy (Feindel, 1993). Stimulation in the midfrontal cortex caused the patient’s eyes to blink; Penfield noted a local blanching of the pial arteries at the same site. This was the earliest of many observations, including arterial constriction and arterialized blood in veins draining epileptic zones, which supported the concept of a cerebral vascular mechanism for epilepsy (Foerster & Penfield,
1930a, 1930b). Focal hyperemia, especially after focal seizures or in relation to vascular shunts in tumors and cysts (Penfield, 1933, 1937, 1971), eventually led to the concept of “red cerebral veins,” a feature that still demands more exact physiologic explanation (Feindel & Perot, 1965).

**The Montreal Neurological Institute**

The Montreal Neurological Institute (MNI) opened in 1934, fulfilling Penfield’s dream to combine in the same edifice a hospital for patients with neurologic disorders, a research center for the scientific study of the nervous system, and a teaching Department of Neurology and Neurosurgery for McGill University. By this time Penfield had fully prepared himself by scientific studies and by developing his eclectic surgical technique derived from Percy Sargent (1873–1933), Harvey Cushing, Walter Dandy (1886–1946), Charles Frazier (1870–1936), and Otfrid Foerster (Feindel, 1977; Penfield, 1977; Preul & Feindel, 1991). The institute provided a fertile setting for the work on epilepsy, where surgical physiology, cellular pathology, radiology, and, later, neuropsychology, EEG and neurochemistry were all applied to advance the understanding of the pathophysiologic processes underlying focal seizures.

From the beginning, Penfield and his team attracted diverse and international groups of associates. Many returned to lead university departments of neurosurgery in the United States and abroad, where they set up units for the scientific study and surgical treatment of epilepsy (Feindel, 1977, 1993; Flanigin et al., 1991). In the early operative series for epilepsy, surgical exposure of a region suspected of causing focal seizures sometimes revealed no visible lesion, so that no surgical removal could be made. However, negative explorations became less frequent with the advent of EEG.
introduced in 1937 at the Institute by Herbert Jasper (1906–1999).

**Jasper Joins Penfield at the MNI**

In 1937, a chance encounter at Brown University led Penfield to bring Herbert Jasper and EEG to Montreal. Although Penfield was initially skeptical about this new technology, his opinion changed when Jasper applied the technique to investigate the MNI patients on whom surgery was being considered. EEG had been developed by Hans Berger (1873–1941) in 1929, (Gloor, 1969) but was only acknowledged by the international community after Adrian and Matthews (1934) confirmed Berger’s original results (Adrian, 1934). Jasper took a doctorate in psychology then changed to research in neurophysiology. A pioneer in the use of EEG, he later became an outstanding leader in the neurosciences (Feindel, 1999). Jasper and Carmichael (1935) published the first report in America on research application of EEG, in the same year that the Boston group led by Frederic Gibbs (1903–1992) had noted its clinical value in epilepsy (Gibbs et al., 1935).

**Surgery for Temporal Lobe Seizures**

The surgical treatment of epilepsy attracted more attention in the decade from 1945 to 1955, when seizures arising from the temporal lobe became a subject of increasing interest. Until that time, surgery had been directed mainly to the convexity of the cerebral hemispheres and most often for removal of traumatic scars or tumors.

In 1936, Frederic Gibbs and William Lennox (1884–1960) of the Boston school of EEG, classified psychomotor seizures as a separate entity from petit mal and grand mal for the first time. They considered epilepsy to be a paroxysmal “disordered functioning of the rate-regulating mechanism of the brain” (Gibbs et al., 1936). Accordingly, the presence of a structural lesion was more often than the rule, and the various types of seizures would be considered only as variations on the pattern of dysrhythmia (Gibbs et al., 1938). Their approach promoted EEG into a strategic position for diagnosis of epilepsy. Nevertheless, the authors failed to localize the origin of the psychomotor seizure because the reference electrode linked to the ears distorted temporal activity (Gibbs et al., 1935). Using this method, most of their “localized dysrhythmias” were found in the frontal and occipital regions (Gibbs et al., 1936).

By contrast, Jasper had long suspected that the mesial temporal structures played a role in the origin of seizures, although available technology could give only an “indication, not the localization, of deep lying disturbances.” In his words, although “localized potentials were obtained from surface aspects of the frontal, precentral, parietal, and occipital areas . . . discharges originating subcortically or from underlying distant cortical areas, e.g., the cornu ammonis, might spread to the surface and give apparent localizing signs in these areas” (Jasper & Hawke, 1938).

During his early days at the MNI, Jasper commuted weekly from Brown University, Providence, Rhode Island to Montreal in order to carry out EEG investigation on patients on whom Penfield would then operate (Jasper, 1958). Penfield’s recognition of the importance of neurophysiology in the evaluation of epileptic patients led him to provide in 1939, through support from private citizens and the Rockefeller Foundation, a new EEG laboratory at the institute. It was dedicated to the selection of patients for surgery and to provide the techniques for recording from the cortex during operation (Jasper, 1941, 1991). The EEG work enhanced the neurophysiologic research that flourished under Herbert Jasper’s vigorous leadership to add greatly to the recognition of the institute as an international center for training in the neurosciences.

From the 1940s onward, the close integration between neurophysiology and neurosurgery, a mirror of the friendship between Penfield and Jasper, made the MNI a leading world center for the surgical treatment of epilepsy (Fig. 7). Other centers, such as the epilepsy surgery program at the University of Illinois began later, in 1945, when Frederic Gibbs moved to Chicago to work with Percival Bailey (1892–1973) (Hermann & Stone, 1989).

In 1941, Jasper and John Kershman (1906–1951) proposed a classification for epilepsy based on forms and
patterns of EEG waves, localization of the activity, and clinical characteristics of the fits (Jasper & Kershman, 1941). The classification emphasized localization of the focus and was particularly applicable for surgeons looking for cerebral lesions (Penfield & Erickson, 1941; Lennox, 1949). Regarding psychomotor epilepsy, Jasper and Kershman (1941) wrote:

It seems clear from the nature of these disturbances that the temporal lobe and subjacent structures, probably in the archipallium, are the regions primarily involved. This is in accord with the electrographic localization, which so frequently seems to be deep to the temporal lobes (e.g., the hippocampus) near the midline or to involve an area first in one temporal lobe and then in the other.

Although by 1941 Jasper was already aware that mesial temporal structures might play a role in the origin of psychomotor epilepsy, one of the major obstacles for removing these structures was the lack of knowledge about their function. For example, it was believed that the hippocampus was an area devoted to olfaction. But in his critical analysis, Alf Brodal (1910–1988) (1947) exonerated the hippocampus from any connection with the olfactory system; it then became a well known (and captivating) anatomic structure looking for a function. Furthermore, Heinrich Klüver (1897–1979) and Paul Bucy (1904–1992) (Klüver & Bucy, 1939) published results of experiments on monkeys in which they resected both temporal lobes. The resultant syndrome, named after the authors, was characterized by psychic blindness, compulsion, loss of emotional reaction, and increase in sexual activity, a syndrome that obviously would be disastrous if produced by surgical resection in patients. The findings in monkeys led Bailey to restrict his excisions in patients to the anterior aspects of the temporal lobe. Like Penfield, Bailey was an expert neuropathologist and also looked for anatomic structure looking for a function. Moreover, the abnormal tissues of the mesial temporal regions were often removed by suction, and thus not available for pathologic examination. This was later remedied by Murray Falconer (1910–1977) by providing the neuropathologist Alfred Meyer (1895–1990) with en bloc excisions (Meyer et al., 1954).

In 1950, Penfield and Flanigin reviewed 68 patients who had surgery for temporal lobe seizures from 1939 to 1949 at the MNI (Penfield & Flanigin, 1950). All subjects had at least one year of follow-up. In this series, 10 patients had the uncus removed; 2 also had hippocampal removal. The seizures were controlled in half of the patients. Electrophysiologic abnormalities, such as spike activity and slow waves, were often recorded from the temporal cortex in this series (Jasper, 1949; Jasper et al., 1951), but an anatomic substrate had not yet been properly substantiated (Fig. 8). In one case, Penfield stimulated the uncinate region and produced an attack of automatism recorded from electrodes he placed over the temporal cortex (Jasper et al., 1951) (Fig. 9).

Meanwhile, at the University of Illinois in Chicago, Frederic Gibbs et al. (1948) by EEG studies assigned the origin of psychomotor seizures to the anterior and lateral cortex of the temporal lobe. In 1951, Percival Bailey and Frederic Gibbs reported their first 25 operations from 1947 to 1950. These were guided by EEG and ECoG. The resections were confined to gyrectomies in the lateral and anterior aspects of the temporal lobe. Like Penfield, Bailey was an expert neuropathologist and also looked for visible lesions at the epileptogenic sites localized by ECoG (Bucy, 1974). In their initial series, Bailey reported opaqueness and thickening of the leptomeninges, atrophy of the convolutions, and scarring of old contusions in the
removed tissue. In no instance did his extirpation extend to the insula or to the upper bank of the lateral fissure; he also carefully avoided the hippocampus. Bailey was concerned to avoid the severe deficits demonstrated after mesial bitemporal resections in monkeys (Klüber & Bucy, 1939).

In regard to surgery for seizures related to the temporal lobe, Penfield started the MNI series in 1939 (Penfield & Ward, 1948; Penfield & Flanigin, 1950), which was followed later by Bailey’s studies in Chicago in 1947 (Bailey & Gibbs, 1951). Arthur A. Morris (b. 1917), a neurological resident at the MNI from 1944 to 1946, reported from Washington, DC, five patients that he operated upon in 1948 and 1949, in “whom there was no specific alteration in gross or histologic pathology of the tissue removed” (Morris, 1950). These first resections, as described by Morris, were based on the operating procedure he learned at the MNI while studying with Penfield and Jasper from 1945 to 1946, which did not include excision of the uncus or hippocampus (Feindel et al., 1996; Almeida et al., 2008). Morris (1956) reported a later series with longer follow-up, in which he carried out larger removals to include these mesial structures, as in the operative procedure published previously from the MNI by Penfield and Baldwin (1952) and taken up earlier by Falconer (1953) and his associates (Meyer et al., 1954).

**The Amygdala and Hippocampus**

In the early 1950s, clues from experimental animal studies pointed to the mesial and inferior surfaces of the temporal lobe for the origin of the epileptic attack. Birger Kaada (1951) produced attacks of arrest of movement, licking, chewing, and swallowing by stimulating the amygdala, the head of hippocampus, and the pyriform region in animals. Henri Gastaut (1915–1995) and his coworkers produced experimental epileptogenic lesions by injecting alumina into the mesial temporal structures (Gastaut & Vigouroux, 1952). In order to understand seizure propagation, other laboratory studies investigated the
connections of anterior temporal cortex with the rest of the brain (Ajmone-Marsan & Stoll, 1950; Stoll et al., 1951; Green & Shimamoto, 1953). Feindel and Gloor (1954) produced epileptic discharge from stimulation of the amygdala and the reticular formation of the brainstem in cats, which resembled the findings at operation on humans.

Convincing physiologic evidence that the mesial temporal region was a crucial zone for the generation of temporal lobe seizures came from the systematic reproduction in 16 patients of habitual auras and other typical features of their attacks, by depth stimulation at operation within and around the amygdala, involving also sometimes the ventral claustrum and the anterior insula (Feindel et al., 1952). The responses were emotional (such as fear), visceral (epigastric aura), impaired consciousness and confused memory, or brief seizures with automatism and amnesia for the ictal period. During this amnesic period, there was blockage of the input to memory but retention of older memories, a feature well described by Hughlings Jackson (Jackson & Colman, 1898) for his patient "Z."

The resulting seizure discharges on corticography spread rapidly, often with low-voltage fast activity, engaging much of the temporal cortex (Fig. 10). These findings called for a meticulous excision of the amygdaloid region to ensure relief from attacks (Feindel & Penfield, 1954). The juxtaposition and overlap of the amygdala and hippocampus, and the contiguity of the amygdala with the globus pallidus, present anatomic features that make it difficult to separate these two structures in depth recording and stimulation and, in addition, to ensure adequate resection of the amygdala, while sparing the hippocampus. These observations drew attention to the significance of the human claustroamygdaloid complex in short-term memory, consciousness, and emotions (Feindel & Penfield, 1954).

Curiously, in the MNI experience, stimulation of the hippocampus directly exposed at operation rarely
produced such auras or ictal responses, even though epileptic abnormality might be recorded from the anterior part of the structure. Depth stimulation of the amygdala in cats reproduced these electrographic features of widespread cortical seizure activity, similar to responses produced by stimulation of the brainstem reticular formation (Feindel & Gloor, 1954). These findings demonstrated that the epileptic activity recorded from the lateral and anterior temporal cortex might be secondary to an epileptic focus deep in the claustroamygdaloid complex (Feindel & Penfield, 1954).

The group from the MNI also proposed that "incisural sclerosis," the gross scarring and atrophy of the mesial temporal structures encountered by the surgeon, could result from an ischemic injury caused by tentorial herniation, with compression of the uncinate region and hippocampus, or compromise of their blood supply, associated with either difficult birth or childhood brain injury (Earle et al., 1953). They based their theory on focal pathologic abnormalities found in a series of 157 patients with temporal lobe epilepsy operated upon by Penfield.

As resection of the anteromesial structures became the accepted treatment for temporal lobe epilepsy, a function for the hippocampus became elucidated. A syndrome of defect in recent memory but preservation of intellectual function was reported by Milner and Penfield (1955) from the MNI series, in two patients after unilateral temporal excision in the presence of what later became recognized as bilateral mesial temporal pathology, involving especially the hippocampus (Penfield & Milner, 1958; Penfield & Mathieson, 1974).

William Scoville (1906–1984) and his group at Hartford, based on neurophysiologic studies (Lieberson et al., 1951), carried out bilateral resections of the mesial temporal regions in a few patients with epilepsy. One patient, H. M., now famous in the annals of neuropsychology, developed a similar deficit in recent memory, which confirmed the MNI report that the hippocampi were especially involved in the "retention of new experiences" (Scoville & Milner, 1957). These findings, together with the previous observation by Feindel and Penfield (1954) that stimulation in the region of the amygdala evoked ictal amnesia with separation between short-term and long-term memory, directed attention to the important role of the mesial temporal structures in memory mechanisms (Milner, 1958; Feindel, 1964). Later studies showed that unilateral resection of the amygdala resulted in no memory deficit, but larger extent of resection of the hippocampus was associated with detectable memory impairment (Leonard, 1991).
Anteromesial Temporal Lobe Resection

In 1952, based on the above evidence, Penfield and Maitland Baldwin (1918–1970) published their now classical report describing the technique for subtotal temporal lobectomy that included the amygdala and hippocampal complex. They concluded that “the abnormal, sclerotic area of the cortex, which must be removed in most cases, lies in the deepest, most inferior and mesial portion of the [temporal] lobe...” (Figs. 11 and 12).

Their report laid out the resection that would serve as the model for temporal lobe surgery, going more mesial than the anterolateral procedure carried out by Bailey and Gibbs (1951) and Morris (1950). From 1953 onward, other neurosurgical centers, often involving surgeons and scientists who had studied at the MNI, took up anteromesial temporal lobe resection for the treatment of seizures (Morris, 1956; Baldwin & Bailey, 1958; Van Buren & Ajmone-Marsan, 1960). Falconer (1953), as noted, introduced the important modification of en bloc resection, which allowed his pathologists to examine the hippocampus and amygdala in toto (Meyer et al., 1954). Falconer (1953) also emphasized that temporal lobe pathology in his cases was sometimes associated not only with a difficult birth, but also with febrile seizures of infancy (Falconer & Taylor, 1968).

The importance attained by this topic spurred several meetings devoted to the study of psychomotor epilepsy. In 1954, Gastaut and his associates organized in Marseilles a colloquium on advances in the treatment of temporal lobe epilepsy. This gave an opportunity for Penfield to provide an overview of the early experimental and surgical results of his team at the MNI that established the important role of the mesial temporal region in the pathogenesis and surgical treatment (Penfield, 1956).

Another colloquium sponsored by Baldwin and Bailey (1958) at the National Institutes of Health, U.S.A., extended and confirmed the significance of subtotal temporal lobectomy, including particularly the mesial temporal structures, for treating temporal lobe seizures. Rasmussen and Jasper (1958), using electrodes combining stimulation and recording, confirmed and extended the earlier findings of Feindel and Penfield (1954) that clinical and electrographic features of temporal lobe seizures could consistently be initiated by stimulation in the amygdaloid region. Attending this colloquium, a Brazilian neurosurgeon, Paulo Niemeyer (1914–2004) presented his innovative surgical approach of selective resection of the amygdala and hippocampus with preservation of the temporal neocortex (Niemeyer, 1958).

The ingenious application of stereotactics for implanting depth electrodes used by the Paris school of Talairach and associates offered a new dimension for the preoperative analysis of seizure localization that became widely adopted from the early 1960s (Talairach et al., 1958; Crandell & Babb, 1993; Lüders, 2008).

Conclusions

Over the last 50 years, in neurosurgical centers throughout the world, thousands of patients afflicted with...
temporal lobe seizures have been treated with increasing success by operation (Engel, 1987; Lüders, 1991; Lüders et al., 2008). The standard anteromesial resection as detailed by Penfield and Baldwin (1952), and taken up in most centers, was based mainly on the original procedure introduced by the MNI group, often referred to as “The Montreal Procedure,” which distinguished it from the anterior-lateral gyrectomies performed by Bailey and associates in Chicago (Green et al., 1951).

In 1991, a report compared two long-term follow-up series of 100 patients each, operated upon between 1961 and 1980, with anteromesial resections. One series had a large and the other a minimal hippocampal removal, but both had resection of the amygdala. A 65% success rate was achieved in both series (Feindel & Rasmussen, 1991; Rasmussen & Feindel, 1991). This evidence indicated that the standard subtotal lobectomy, as originally described by Penfield and Baldwin (1952), could be more limited in terms of the amount of neocortical tissue removed (Fig. 13). This study also confirmed the importance of radical resection of the amygdala (Feindel & Penfield, 1954) and showed that satisfactory outcome can result without major hippocampectomy.

Selective removal of the amygdala and hippocampus, introduced by Niemeyer, 1958, was modified by Wieser and Yasargil (1982), André Olivier (b. 1938) (1991) and many others, with up to 80% successful control of seizures in selected patients (Wieser, 1991). These results indicate that the anterolateral temporal cortex, which first directed the attention of Gibbs and Jasper to the temporal lobe because of its epileptic spiking, need not be excised in many cases (Feindel et al., 1996). The role of the amygdala in the generation and propagation of temporal lobe seizures was confirmed in extensive studies by Gloor and reported in his monograph on the temporal lobe and limbic system (Gloor, 1999).

Since the 1970s, the advent of the revolutionary technology of computerized neuroimaging, particularly magnetic resonance imaging (MRI), has resulted in the detection of lesions in 25% of patients examined for temporal lobe seizures (Fig. 14). In another 30%, atrophy of the hippocampus, amygdala, and entorhinal cortex has been well documented and correlated with the local tissue pathology (Kuzniecky et al., 1987; Feindel, 1991; Berkovic et al., 2004). The exactness of anatomic depiction of the temporal resection by MRI now makes it possible to evaluate more precisely the postoperative results in comparison to the pathology and to the anatomic pattern of the surgical excision; thus the series of cases from different neurosurgical centers can be compared.

The widespread success of anteromesial temporal lobe resection renders this one of the most effective operations in the field of neurosurgery (Falconer, 1974; Feindel, 1974; Engel, 1987; Lüders, 1991; Engel 1993a, 1993b; Feindel et al., 1996; Lüders et al., 2008). But many substantial questions remain to be answered (Feindel, 2008, 2009). Can the attractive hypothesis of tentorial herniation as a cause for incisural sclerosis be validated? How do infantile generalized febrile seizures lead to focal, unilateral pathology? What is the specific epileptogenic role of juxtaposed structures such as the amygdala, entorhinal cortex, subiculum, hippocampus, insula, and claustrum in the origin and propagation of temporal lobe seizures? What are the physiologic and cognitive deficits resulting from focal surgery involving these structures and their circuitous connections? And how might these deficits be minimized by “tailoring” the pattern of resection in the individual patient, commensurate with successful relief of seizures? How much of the hippocampal region must be excised to obtain a seizure-free outcome without compromise of memory function? An extensive review by Schramm (2008) addressing patterns of resection of the temporal lobe, reported from 53 neurosurgical centers, confirms the efficacy of surgery but offers no adequate evidence to answer these basic questions.

Epilepsy was Penfield’s great teacher, as it was for so many of the pioneer surgical figures noted in this review (Penfield, 1967). The excitation from the neuronal

Figure 13.
Hatched lines indicate anterior cortical and amygdalar resection (large arrows) and a more posterior resection to include 2–4 cm of the hippocampus (small arrows). Both types of resections yielded a long-term follow-up rate of 65% in two series of 100 patients who were seizure free, or who had rare seizures (Feindel & Rasmussen, 1991).

Epilepsia © ILAE
substrate in the lateral temporal cortex of past experiences ("flash-backs") during surgical treatment was an almost startling phenomenon that enthralled Penfield to the end of his long career (Penfield, 1975). The automatism and amnesia characteristic of some temporal lobe seizures, noted by Jackson and Colman (1898) and evoked by stimulation in the region of the claustroamygdaloid complex, involves a temporary but striking interference with memory recording and absence of higher mental activity or mind, that still demands further elucidation (Feindel & Penfield, 1954). The function of the nondominant parietal lobe (Hécaen et al., 1956) and the extensive findings on lateralization and localization of speech function (Penfield & Roberts, 1959), were building blocks upon which some of the modern views of separable functions of the two halves of the human brain became established. The assessment of frontal lobe function after large excisions by Penfield (Penfield & Evans, 1935; Hebb & Penfield, 1940) presaged the clinical neuropsychology studies by Milner and her train of graduate students. Her orderly and scholarly evaluations of surgical patients of Penfield and Scoville identified the critical role of the hippocampal region in short-memory memory function (Milner & Penfield, 1955; Scoville & Milner, 1957; Penfield & Milner, 1958). The temporary and partial paresis of one cerebral hemisphere by injection of intracarotid sodium amytal, a technique introduced by Wada, became a useful test for determining the laterality of speech function (Wada & Rasmussen, 1960) and for evaluating memory responses in patients with bitemporal seizure activity (Milner et al., 1962). Many technical advances in the selection and investigation of patients with seizures have been developed, such as the computerized monitoring of ictal and interictal EEG (Ives & Gloor, 1978; Gotman, 1985, 1989).

Over a period of 80 years Penfield and his associates authored a rich canon of literature on the surgical and scientific aspects of epilepsy. Many of their publications became classics in the field of neurology (for Penfield bibliography see: Eccles & Feindel, 1978). Rasmussen’s meticulous long-term follow-up studies with his associates of the surgical patients treated at Montreal since 1928 now extend to more than 6,000 dossiers. These have provided invaluable documentation of the expectations, success rates, pitfalls, and questions still to be answered about the surgical treatment of epilepsy (Penfield & Rasmussen, 1950; Penfield & Jasper, 1954; Gloor & Feindel, 1963; Feindel, 1975; Rasmussen, 1983; Anderman, 1987; Feindel & Rasmussen, 1991; Olivier, 1991; Lüders, 1991; Almeida et al., 2008; Feindel, 2008, 2009).

The surgical cure of epilepsy has offered relief for countless patients, as confirmed from many neurosurgical centers world-wide (Engel, 2005; Lüders et al., 2008). Future directions of this special field of neurosurgery have been sagely discussed by other authors, who have offered sensible guidelines based on historical perspectives (Rasmussen, 1983; Engel, 1993a,b, 2005; Andermann & Harkness, 2008). Three major global challenges face the field of epilepsy surgery: the development of additional comprehensive epilepsy centers, the more effective use of existing epilepsy centers to provide surgical treatment, and intensified research into basic mechanisms of epilepsy so that the need for surgery might ultimately be eliminated.

As Penfield optimistically pointed out in his last book, The Mystery of the Mind (1975), “Epilepsy, though she wears the frightening mask of tragedy in her approach to each patient, takes off the mask at times before the physician who has the wit to stop and ponder her riddles.” His statement stands as a fitting comment for this centennial celebration of the founding of the ILAE.
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