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Journal of the History of the Neurosciences
Basic and Clinical Perspectives

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/njhn20

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To cite this article: Ian Bone & James L. Stone (2023) The advent of epilepsy directed neurosurgery: The early pioneers and who was first, Journal of the History of the Neurosciences, 32:4, 470-490, DOI: 10.1080/0964704X.2023.2207598

To link to this article: https://doi.org/10.1080/0964704X.2023.2207598

Published online: 18 May 2023.

JOURNAL OF THE HISTORY OF THE NEUROSCIENCES
2023, VOL. 32, NO. 4, 470–490
https://doi.org/10.1080/0964704X.2023.2207598

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The advent of epilepsy directed neurosurgery: The early pioneers and who was first

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ABSTRACT

Efforts to treat epileptic seizures likely date back to primitive, man-made skull openings or trephinations at the site of previous scalp or skull injuries. The purpose may have been the release of "evil spirits," removal of "cerebral excitement," and "restoral of bodily and intellectual functions." With progressive discoveries in brain function over the past 100 to 300 years, the cerebral cortical locations enabling voluntary movements, sensation, and speech have been well delineated. The locations of these functions have become surgical targets for the amelioration of disease processes. Disease entities in particular cerebral-cortical areas may predispose to the onset of focal and or generalized seizures, which secondarily interfere with normal cortical functioning. Modern neuroimaging and electroencephalography usually delineate the location of seizures and often the type of structural pathology. If noneloquent brain regions are involved, open surgical biopsy or removal of only abnormal tissue may be undertaken successfully. A number of the early neurosurgical pioneers in the development of epilepsy surgery are credited and discussed in this article.

KEYWORDS

Cortical localization; David Ferrier; epilepsy surgery; Hughes Bennett; Hughlings Jackson; Rickman Godlee; Victor Horsley; vivisection; William Macewen

Introduction

The iconic Harvey Cushing (1869–1939) of Boston has become the de facto "father of modern neurosurgery," but the specialty's roots owe much to earlier pioneers, William Macewan (1848–1924) and Victor Horsley (1857–1916). Both were knighted for services to medicine, and their particular roles have been overlooked by some. In a recent monograph Aminoff (2022) claimed Horsley as the world's first neurosurgeon, and although acknowledging his earlier contributions, relegated Macewen from the position of a prime innovator on the grounds of his lack of legacy and solitary personality. Although Paul Broca (1824–1880) has been attributed with the first localization based craniotomy (Stone 1991), Rickman Godlee (1849–1925), also knighted, remains considered by many as the leader. The early cases of Macewen, Godlee, and Horsley, described in this article, involved cerebral localization based on the observations of the form and nature of clinically observed seizures. Their endeavors represent milestones in the history of localized cortical brain anatomy,

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related functionality, and the location and possible eradication of identifiable neuropathology, with the possibility of surgical control of epilepsy as well. Macewen and Horsley did not restrict their surgery to the nervous system, and Godlee operated on the brain just once. Who can claim priority in performing localization-based epilepsy surgery by means of seizure semiology is discussed and, of interest, there is a particular Scottish connection throughout.

Cortical localization

By the late-nineteenth century mapping of the cerebral cortex by clinical observation, and experiments in animals and subhuman primates, laid the foundations for modern neurosurgery. The history of this and the individuals involved have been detailed elsewhere (Finger 2000; Wickens 2015), but certain names and dates are critical to the unfolding story of who were the earliest or perhaps first surgeons to operate by clinically applying the knowledge of cerebral cortical localization.

In 1825, French physician Jean Baptiste Bouillaud (1796–1881) first described focal brain lesions associated with speech loss (Stookey 1963), but it was left to his compatriot, surgeon Paul Broca (1824–1880), in a landmark case to consolidate this and draw attention to the role of the left hemisphere. His patient with epilepsy, a subsequent loss of speech, and right-sided paralysis was shown at autopsy to have predominant focal softening in the third frontal convolution of that hemisphere in addition to other areas (Broca 1861). In 1868, Broca traveled to speak at the British Association for the Advancement of Science, where he met the particularly gifted emerging English neurologist John Hughlings Jackson (1835–1911). (Finger 2000, 149). Jackson had studied similar cases of aphasia associated with right-sided limb weakness, suggesting not only a left hemisphere location but also middle cerebral artery embolism from rheumatic heart disease vegetations, as a mechanism with half of the 32 patients described by him having rheumatic heart disease (Jackson 1864). Jackson was to make many further clinical observations on the localization of function, including the association of left-sided hemiplegia with "mental affectation" and inattention (agnosia; see Jackson 1872).

Jackson's studies of seizures are most pertinent to the case histories that follow. In 1863, he noted the manner in which partial (focal) seizures could start and spread (Jackson 1863). In 1868, he published a series of papers documenting the sequence of involuntary movements or sensations he had observed during the course of unilateral seizures (York and Steinberg 2011). These collective observations led to the publication of his treatise, "A Study of Convulsions" (Jackson 1870), in which he described focal seizures as being a symptom of a localizable discharge within the cerebral cortex. In 1873, Jackson published on the localization of movements in the brain, subsequently dedicating this to fellow scientists Hitzig and Ferrier (Jackson 1875). In this he combined observations of both convulsions and paralysis to consolidate the concept of the motor cortex and its topographical organization.

Awareness of Bouillaud and Broca's observations were not confined to London. In Glasgow, William Gairdner (1824–1907), professor of physic, and Alexander Robertson (1834–1908), physician to the Town Hospital and City Asylum, had written on right-sided hemiplegia and aphasia, reported post-ictal speech arrest and were quoting from and communicating with their London counterparts, including Jackson (Gairdner 1866; Robertson 1867). Robertson developed a concept of epileptogenesis similar to Jackson's

and predating him, although his contributions on both aphasia and epilepsy have been largely forgotten (Eadie 2015). The nature of the journals in which these two clinicians published meant that their work did not reach a wide audience, and their provincial location may have been a drawback, but they clearly provided the highly thoughtful and respected Macewen with a stimulating milieu in which cerebral localization was understood and accepted.

Paralleling these clinical observations, the experimentalists were studying cortical function in the laboratory. In 1870, Gustav Fritsch (1838–1927) and Eduard Hitzig (1838–1907), working in Berlin, published studies on dogs showing that galvanic stimulation of the frontal cortex caused movement in the limbs opposite and that excision of the stimulated area subsequently lessened the response (Walker 1957). Sir David Ferrier (1843–1928), the Scottish neurologist and physiologist—based initially at West Riding Lunatic Asylum in Yorkshire and later at the National Hospital for the Paralyzed and Epileptic in London—was to play a major role in establishing international acceptance for cortical localization. Working in Yorkshire under the directorship of James Crichton Browne (1840–1938)—a fellow Scot and psychiatrist, neurologist, and eugenicist—Ferrier established a laboratory for animal work and published in the asylum's Medical Reports. In 1873, he began electrically exciting cortical areas in cats and dogs and subsequently with monkeys (Ferrier 1875). The fruit of these experiments was the publication of *The Functions of the Brain* (Ferrier 1876). Prosecuted unsuccessfully by antivivisectionists thereafter, there can be no doubt that Ferrier's research was fundamental to the human brain surgery that followed.

Crucial to the scientific community's acceptance of localized brain function was a debate between Ferrier and German physiologist Freidrich Goltz (1834–1902) at the Seventh International Medical Congress of 1881 (Tyler and Malessa 2000). Goltz questioned whether the cerebral cortex could be divided into specialized regions, whereas Ferrier contended that it could. Here, Ferrier's arguments and demonstration of loss of function in his lesioned monkeys carried the day over Goltz's dogs, with their relatively smaller and lesser traumatized cerebrums. Both Macewen and Robertson presented papers at the conference, although it is uncertain whether they witnessed Ferrier's triumph (MacCormac 1881).

Following Ferrier, brain mapping was further extended by the likes of Charles Sherrington (1857–1952) and Victor Horsley (1857–1916). Horsley, experimentalist and early neurosurgeon, and his collaborators conducted studies on the motor and other cortical regions at London's Brown Institution. This work, carried out between 1886 and 1890, involved electrical stimulation of the monkey brain and produced more refined maps of both motor cortex function and the function of other cortical areas (Horsley and Schafer 1888).

Otfrid Foerster (1873–1941), a German neurologist and neurosurgeon, further investigated cortical localization, producing more detailed maps of the human cortex and collaborating with the young Wilder Penfield, who had visited his Breslau laboratory (Feindel, Leblanc, and Nogueira de Almeida 2009).

Influenced by Foerster, Harvey Cushing (1869–1939) in Boston, and Wilder Penfield (1891–1976), now in Montreal, were able to stimulate the brain intra-operatively, as had Horsley initially, creating an even more detailed map of the human cortex and heralding in the dawn of modern neurosurgery for epilepsy (Penfield and Erickson 1941; see Figure 1)

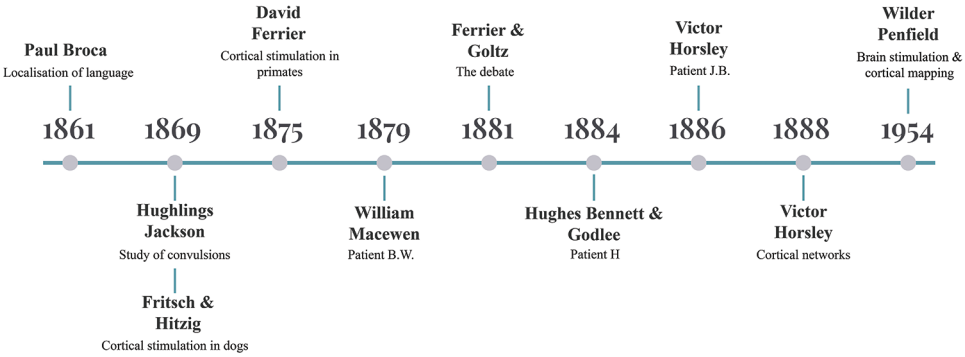


Figure 1. Timeline: Cerebral localization and the first localization based surgery.

Surgeons and their surgery

Sir William Macewen (1848–1924)

William Macewen was born on the Isle of Bute in the West of Scotland. He gained his medical education at the University of Glasgow and remained in the city throughout the entirety of his medical career. Influenced as an assistant surgeon under Joseph Lister at Glasgow's Royal Infirmary, Macewen practiced and developed antisepsis techniques and became, across a range of specialties, regarded as one of the most innovative surgeons of his generation. He was appointed Regius Professor of Surgery in 1882, knighted for services to medicine in 1902, and his life and works have been the subject of both biography (Bowman 1942) and memoir (Duguid 1957).

The evidence for Macewen's surgery is taken from his private journals, in which the details of patients and operations were recorded (1876–1886); the ward records of Glasgow Royal Infirmary; published presentations to local medical societies; and articles in medical journals. The private journal entries were often dictated by Macewen to a junior doctor. These journals occasionally contained illustrations of site and findings at operation and sometimes photographs of the patients; photography was his hobby. Ward records contain little more than patients' details, including admission and discharge dates with outcomes. To interrogate Macewen's earliest application of seizure-related cerebral localization to clinical practice, it is necessary to examine first a case in which surgery was planned although not carried out.

Case 1. John. McK., male, aged 11 years

Macewen's private journal (vol. 1. pp. 32–33) outlines J. McK's' admission on the July 20, 1876, to Glasgow Royal Infirmary. Fourteen days previously, he had fallen from a height, sustaining a cut over the left eyebrow that became infected. Two weeks afterward, he was observed to have had a convulsion "confined entirely to the right side and implicating the face and limbs." Macewen reviewed the boy's case on August 2 and deduced "that the symptoms pointed to inflammation of the brain and most probably to the formation of pus on the left hemisphere at the frontal portion at least." Colleagues counseled against surgery and the parents refused. The patient died and Macewen, with parental permission,

performed the intended surgery at postmortem, finding an abscess "about the size of a pigeon's egg which was situated in the 2nd and 3rd frontal convolns (sic)."

Macewen provided greater detail in his published accounts. In 1881 he asserted that the case was clearly that of an abscess, "the probable locus being the third frontal convolution," and described the patient as "decidedly aphasic" during the post ictal state (Macewen 1881, 581–583). In his 1888 address to the Annual Meeting of the British Medical Association, Macewen stated that, "trusting to these localising symptoms it was proposed to open the abscess aseptically by exposing Broca's lobe," and then described the postmortem, in which "an instrument was introduced through the third frontal convolution for half an inch when pus flowed." He stated that this spot had been "accurately determined from the localising phenomena induced by a focal lesion" (Macewen 1888, 303) and provided an illustration taken from his private journal to show the location of the abscess that he had "diagnosed from symptoms exhibited" (Figure 2a).

In his book on pyogenic infective diseases of the nervous system, Macewen described J. McK as "Case XXXIV; Cerebral abscess in the left frontal lobe of traumatic origin." Here he again claimed that "the localization was arrived at entirely from the data furnished by the symptoms, those of temporary aphasia and post-convulsive right-sided paralysis." He wrote that he had personally witnessed the symptoms, noting:

> [T]his case furnished an instance of an abscess situated at a distance from the seat of injury in the skull, and apparently not arising from distinct cerebral bruising. Had the skull been trephined at the part where the bare bone was situated, the abscess would not have been found directly underneath. The post-mortem proved the accuracy of the diagnosis, both as to the existence of the cerebral abscess and also as to its exact localization. (Macewen 1893, 189–193)

In his detailed account of Macewen's early brain surgery cases and the resultant controversy, Macmillan was certain it was his use of localizing signs in 1876 that led him to plan to operate on Broca's lobe (Macmillan 2005, 32)

Although evidence is spread over many years and the contemporaneous record is the least detailed, it appears that by 1876 Macewen—possibly with the support of his colleagues Robertson and Gairdner—had a sufficient knowledge of cerebral localization to plan surgery in a patient with focal seizures and aphasia.

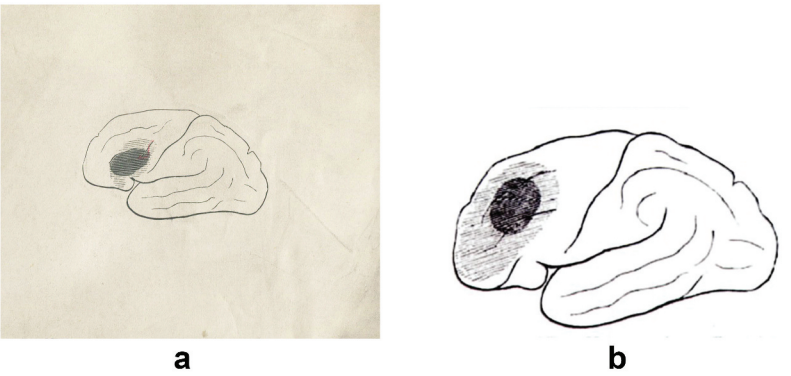


Figure 2. a. Abscess in the vicinity of Broca's lobe diagnosed from symptoms exhibited (Macewen 1888, 303). b. Tumor of the dura mater pressing on frontal lobe (Macewen 1888, 304).

Case 2. Barbara W., female, aged 14 years

Macewen's private journal (vol. 1. pp. 246–252) outlines B.W.'s admission to Glasgow Royal Infirmary on July 21, 1879. The patient complained of pain and swelling over the left eye at the site of the removal, a year previously, of a supraorbital periosteal growth. He described a "tumour over the upper side of the orbital cavity about the size of a kidney bean firmly attached to the periosteum" and, about two and a half inches above the supraorbital ridge, a prominence "about the size of a large barley grain" also with periosteal attachment. He determined to remove the recurrent growth over the eyeball, but before this could be done, "she took a series of convulsions." These were witnessed by nursing staff and documented by Macewen as "twitching of the right side of the face and arm," with the "first lasting 2–3 minutes and entirely confined to the right side" and minutes elapsing before further episodes. Seizures that had started as "a mere twitching of the eyelids" were now almost continuous, with it being "evident that a fatal issue was imminent." Macewen deduced that "there must be other tumours on the inside of the cranial cavity" and selected "the barley like node over the frontal bone to be the seat of operation."

Operating antiseptically, he cut into the node, noting it to be of a similar consistency to the supraorbital tumor removed previously and extending over the frontal bone connected to the periosteum. He described the bone beneath as soft and roughened, and a trephine "an inch in diameter was chosen." The journal outlines the removal of two and a half square inches of tumor from the surface of the dura overlying the frontal lobe. Macewen was uncertain if all had been completely excised, noting that its consistency was similar to that encounter outside the skull. He next turned his attention to the supraorbital mass, finding this extending into the orbit, and scooped it out. Postoperatively, B.W. was described as conscious and answering questions intelligently. On the fifth day, B.W. had a further right-sided seizure that left her with a resolving aphasia and right hemiparesis. There were no further events thereafter, apart from minor herniation at the trephine aperture. Macewen later speculated that tight dressing around the head might have precipitated the seizure (Macewen 1881). He next described her recovery as full; she was walking around and assisting in ward work. By June 1883, she was noted as being in excellent health and a photograph was taken. At review in March 1884, B.W. was well and in work, with no seizure or tumor recurrence. Her death, some seven years later, was ascribed to Bright's disease (nephritis), although there are no confirmatory records.

In November 1879, Macewen, writing in the third person, published the case report in the Glasgow Medical Journal (Macewen 1879, 211). Here the convulsions were described in greater detail and their localizing value emphasized. Although noting the supra-orbital periosteal tumor, "Dr Macewen who had been noting the progress of the case since the beginning of the attack concluded that the convulsions depended on pressure on the brain on the left side in connection somehow." Writing in *The Lancet* (1881, 581–583), Macewen gave an account of his experiences in localizing intracranial lesions and the advantages of antiseptic trephining. B.W,'s case is among the four presented, with her left pupil described as small and poorly reactive preoperatively. He claimed that this and the pains over the left brow "raised the possibility of intracranial pressure as a small tumour in front of the orbital cavity could scarcely produce these." He provided a fuller account of the seizures here than can be found in the private journal, describing this as an indicator of "the probable locus of brain pressure."

In his 1888 address to the Annual Meeting of the British Medical Association, Macewen brought greater clarity to B.W.'s surgical management. He commented that she was "placed under the observations of an educated skilled nurse" and described the witnessed seizures. He stated, "these phenomena were construed as indicating extension of the irritation to the lower and middle portions of the ascending convolutions and ... it was concluded that an irritative lesion existed in the left frontal lobe." He asserted that, on these grounds, he "resolved to trephine midway between the centre of the ascending convolutions and the anterior aspect of the cranium." Here for the first time, nine years after the surgery, was a clear indication of the trephination site, with seizures seeming to have defined it (Macewen 1888, 304), and he provided an illustration of the surgery taken from his private journal (Figure 2b).

Between 1879 and 1884, Macewen carried out cranial surgery on a further five patients but, because of incomplete documentation, it is uncertain how many were conducted on the basis of localization alone. Clearer evidence of knowledge of his ability to clinically apply cerebral localization can be found in his account of a patient with a syphilitic history who developed a left hemiplegia. (Macewen 1884). Writing toward the end of his life, Macewen claimed that his interest in cerebral localization dated back to his days as a medical student (Macewen 1922).

Sir Rickman John Godlee (1849–1925)

Rickman Godlee completed his medical degree at University College, London, before continuing surgical training in Edinburgh. Here he worked under his uncle, Lord Joseph Lister, who had recently moved from Glasgow, and was later to be his biographer. On returning to London, he became surgeon to the Brompton Hospital, where he pioneered chest surgery. In 1892, he was appointed emeritus professor of surgery at University College Hospital, served as the president of the Royal College of Surgeons (1911–1913), and was president of the Royal Society of Medicine (1916–1918). He was surgeon to the Household and Queen Victoria and Kings Edward VII and George V, created a baronet in 1912, and was made Knight Commander of the Royal Victorian Order (KCVO) in 1914 (British Medical Journal 1925). Godlee performed his one and only brain operation at the Hospital for Epilepsy and Paralysis in Regent's Park, London. Alexander Hughes Bennett (1848–1901), physician to the Hospital for Epilepsy and Paralysis, guided the neurologically inexperienced and junior surgeon into operating. Bennett had trained in Edinburgh, becoming a ship's doctor with the Peninsular and Orient Line (P&O), before specializing in neurology. He never collaborated again with Godlee and retired early and died at the age of 53 (Ireland 1909). Queen Square Library, UCL, Queen Square Institute of Neurology, has no archival record of the operation, and the description that follows is taken from the medical publications of the time.

Case 3. Henderson, male, aged 25 years

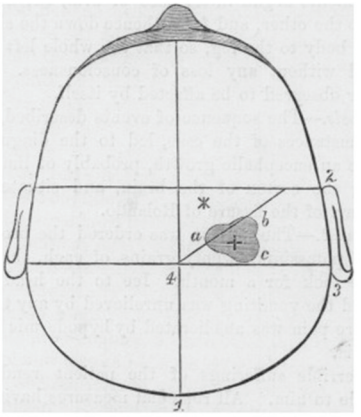
In December 1884, Bennett and Godlee published their case of "excision of a tumour from the brain" in *The Lancet*, commenting that "this operation performed, we believe, for the first time in the history of medicine has naturally attracted much notice amongst the profession and numerous enquires as to the truth of reports" (Bennett and Godlee 1884, 1090–1901). They described a 25-year-old Scottish farmer, Henderson, who, four years

earlier in Canada had suffered a blow to the left side of his head from falling lumber and subsequently experienced episodes of twitching of the left side of his face. Next he experienced episodes in which a sensation in his face spread into his arm and leg followed by a generalized convulsion. Six months before surgery the attacks became more frequent, involving the hand and arm, but the generalized seizures had ceased. He then came under the care of Dr. Bennett, whose examination revealed normal intelligence; slight weakness of the left side of the face; complete paralysis of the left hand, less so the forearm; and mild weakness of the left leg. Seizures "usually began in the fingers and thumb of the left hand . . . occasionally they began in the face and from there extended to the arm and down the leg on the same side." Bennett diagnosed a brain tumor he believed to be small and localized in "the neighbourhood of the upper third of the fissure of Rolando" and recommended surgery on the basis of his patient's "intolerable" symptoms.

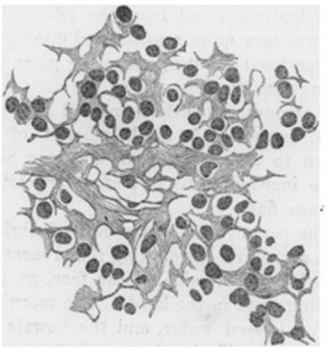
On the November 25, 1884, at the Hospital for the Relief and Cure of Epilepsy and Paralysis, London, having explained the risks of operating to the patient, Godlee trephined over the proposed site. On exposing the cortex no tumor was visible, but the ascending frontal cortex seemed distended. Cutting down into the gray matter some quarter of an inch, "a morbid growth was found . . . .this was carefully removed and proved to be a hard glioma about the size of a walnut." By December 15, the patient was described as free of seizures, but the paralysis of the leg had worsened and the wound was now fatally infected. Henderson's demise, along with his postmortem findings, were promptly reported in the Lancet (Bennett and Godlee 1885a).

The case was presented at the meeting of the Royal Medical and Chirurgical Society on the May 12, 1885 (Bennett and Godlee 1885b). The history of motor seizures commencing in the face and arm with spread to the whole left side without loss of consciousness and failure to respond to bromide as well as paroxysmal attacks of lancination headache were set out, along with the findings of optic neuritis (assumed papilledema) with retinal hemorrhages. The two-hour operation was conducted under chloroform, with antiseptic precautions. External scalp markings were used to locate the middle third of the fissure of Rolando (Figure 3a), and three overlapping trephines made. A thinly encapsulated solid tumor was identified a quarter of an inch below the cortical surface at the predicated site and removed, the surrounding brain being described as healthy. On the fifth postoperative day, the wound became swollen and smelled of putrefaction and "hernia cerebri" had developed. The patient continued to worsen, dying four weeks after surgery. Postmortem confirmed intracranial infection with brain herniation through the skull aperture. Pathological examination of the tumor removed at surgery showed this to be glioma (Figure 3b).

Discussion of the case—involving Godlee, Bennett, Jackson, Ferrier, Macewen, and Horsley—took place at the Royal Medical and Chirurgical Society in May 1885, and was reported in the *British Medical Journal Report of Societies* (Bennett and Godlee 1885b, 988–989). Jackson began by congratulating Bennett on his accuracy of diagnosis and Ferrier, "from whose researches the tumour was localised." Ferrier, who had been present at the operation, described it as "a wonderful success" in spite of the fatal outcome. Macewen described his 1876 case (J. McK.), in which he had correctly localized the site of an abscess confirmed by postmortem. He next outlined a case in which the "researches of Hughlings Jackson, Professor Ferrier and M.M. Charcot had greatly assisted in localisation" and claimed to have conducted 17 operations for the "relief of intracranial pressure," 14 by



External surface of scalp. 1, 2, 3, 4. Lines to determine position of fissure of Rolando. + Theoretical and actual position of tumour. ⁎ Tender spot on scalp. *a*, *b*, *c*. Position and order of trephine openings.



Structure of glioma, from section by Dr. Hebb, about 400 diam.

a **b**

Figure 3. a. External surface of the scalp 1, 2, 3, 4. Lines to determine position of fissure of Rolando (Bennett and Godlee 1885b, 248). b. Structure of glioma, from section (Bennett and Godlee 1885b, 251).

trephining and three by "elevation of bone." In 11, he had reimplanted portions of excised bone at the operation site and, unlike Godlee, had never used cautery or witnessed significant hernia cerebri.

Bennett expressed interest in Macewen's cases and was quoted saying that he "felt obliged to say, with all due deference, that they did not appear to him completely analogous," as his case was about a small lesion that had to be cut down upon, whereas in Macewen's cases, the "injuries were much more extensive." Godlee congratulated Macewen "on his interesting and successful cases" and wondered in his own case if more care in cleansing the head preoperatively with carbolic might have prevented putrefaction and death. With prolonged soaking of the scalp before surgery, he said, he "should not hesitate to undertake a second similar operation." He was never to operate on the brain again or to collaborate with Bennett.

Sir Victor Horsley (1857–1916)

Horsley graduated in medicine from University College, London, before studying in Berlin and returning to London to complete his surgical training. From 1884 to 1890, he was professor-superintendent at London's Brown Institute while also becoming the first fully practicing neurosurgeon at the National Hospital of Epilepsy and Paralysis in 1886. He subsequently became professor of clinical surgery at University College and was knighted in 1902 for his services to medicine. As well as being a surgeon and scientist, Horsley championed women's suffrage, campaigned against alcohol, and played prominent roles in the formation of the British Medical Association, insurance for doctors, and improving standards of medical practice. At the outbreak of World War I, he volunteered for active duty and died of heatstroke in Mesopotamia. The neurosurgical unit at the National Hospital is named for him. Horsley's complex personality and myriad achievements are

the subject of a recent biography (Aminoff 2022), and his life and works are the subject of another, written soon after his death (Paget 1919).

The account that follows is taken from clinical records archived at Queen Square Library, UCL, Queen Square Institute of Neurology (Horsley 1886b), and published medical articles.

Case 4. James B., male, aged 22 years

James B., a Scot residing in London, was admitted with seizures to the National Hospital for Paralysis and Epilepsy[1] on the April 27, 1886, under the care of Dr. Hughlings Jackson. At the age of seven in Edinburgh, he had been struck by a cab, sustaining a comminuted depressed skull fracture. Removal of bone fragments was complicated by wound infection, brain herniation, and a resolving hemiplegia. At 15 years old, he developed seizures of variable frequency, punctuated by episodes of status epilepticus (Horsley 1886a).

Medical records (Horsley 1886b) documented that James B. had been under Dr. Jackson's care for some months, with worsening stereotypical seizures in which

> [T]he right lower limb was extended and the seat of tonic spasm. The right upper limb then slowly extended at right angles to the body, the wrist and fingers being flexed; the fingers next became extended and clonic spasms of flexion and extension affected the whole limb followed by turning of the head and eyes to the right.

Based on this, it was felt that the "focus of discharge was situated around the posterior end of the superior frontal sulcus" matching the site of scar (Figure 4a) and skull defect; this being measured as at the center of the upper third of the ascending convolution. Multiple daily seizures persisted, despite frequent treatment with paraldehyde and on May 25, he underwent surgery, which was documented in detail (Horsley 1886b, 29–34). The head was "scrubbed" with 1 in 20 carbolic and chloroform administered. The center of the quad radiate scar was "roughly estimated to lie just in front of the upper end of the fissure of Rolando." Horsley, with trephines, created a bone flap (Figure 4b) and, after excising underlying dura, encountered the scar on the cortical surface (Figure 4c). By making a vertical incision around this, including a half-a-centimeter perimeter of adjacent brain, he was able to remove the scar, leaving only a deep seated residue felt to be connected with the "roof of the third ventricle."

Postoperatively, there was no evidence of infection and good wound healing. Neurologically, there was resolving right-sided weakness of wrist flexion, thumb and fingers and foot eversion associated with loss of tactile sensation of the hand. A few twitching episodes of the right thumb were documented as being nothing like the presurgical seizure severity or frequency of "never out of a fit day or night." At discharge on August 23, James B. was described as "cured," the only complaint being that he could not hold a knife as well as previously (Horsley 1886a, 670–675).

The following year, in a landmark paper focusing on the topographical relationship of the cortical motor region to the exterior of the skull and the technique and localizing role of intra-operative cortical excitation by faradism, Horsley mentioned James B. but made no comment on his current seizure status (Horsley 1887). Thereafter, Horsley operated on six further cases with epilepsy, combining three of these in an analysis of six such cases through adding others published by colleagues. In three, seizures were described as arrested; in two,

[1]The hospital's subsequent change of name is detailed in S. Shorvon and A. Compston's (2018) *Queen Square: A History of the National Hospital and its Institute of Neurology*. Cambridge, UK: Cambridge University Press.

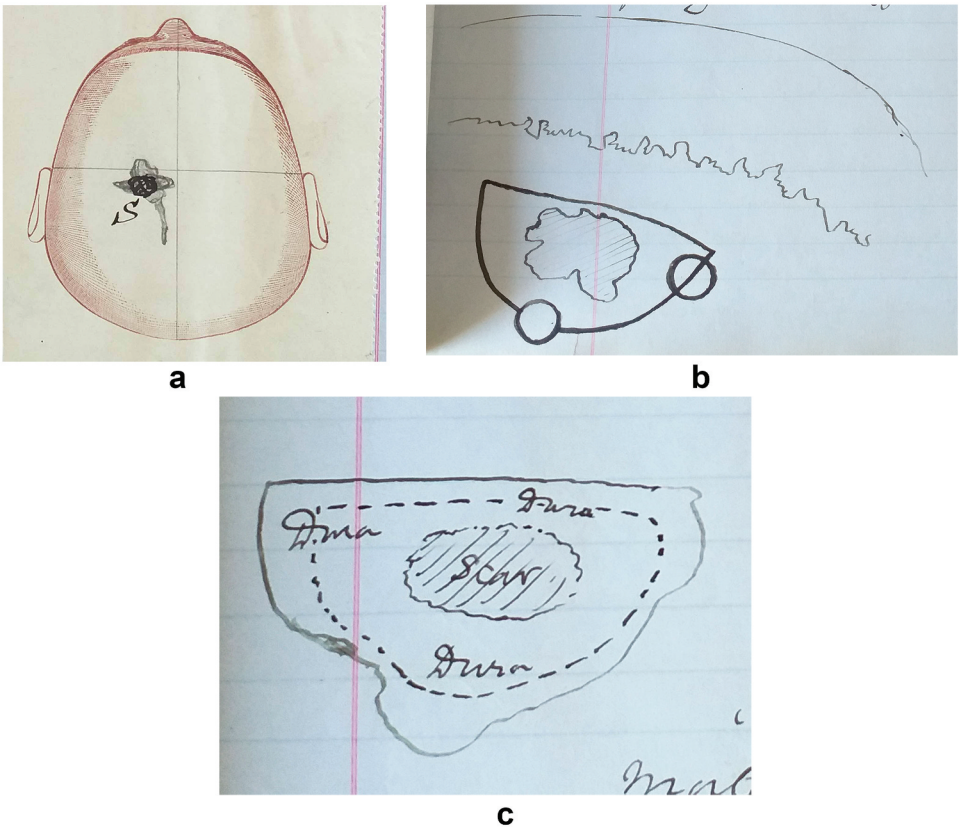


Figure 4. a. View of skull vertex (Horsley 1886b, 17). b. Bone flap and trephines (Horsley 1886b, 31). c. Exposed scar on the cortical surface (Horsley 1886b, 32).

diminished; and in one, following brief improvement, unaltered. In five cases, electrical stimulation was used to identify the focus. He concluded, "personally I do not think that a final answer can be given on the permanency of the freedom from epilepsy until each case has been observed for about five years" (Horsley 1890, 1291). When addressing the 1906 Annual Meeting of the British Medical Association on the techniques involved in brain surgery, he made no mention of Macewen, Godlee, or others and stated that "the massing together of cases treated by different surgeons under different conditions of operative technique with different clinical histories has always seemed to me an unscientific proceeding" (Horsley 1906, 490).

The controversies

Macewen vs. Godlee

Barely three weeks after Godlee's operation, a letter to the editor of the *Times of London* ignited controversy. Entitled "Brain Surgery" and anonymously signed by F.R.S, the letter was intended as a riposte to those who had opposed vivisection (Crichton Browne 1884a). F. R.S. described the operation as "unique," inaugurating "a new era in cerebral surgery" and

hailing Ferrier's animal experiments in localizing brain lesions critical to making the operation possible. Being unaware at the time of the writing of Henderson's tragic outcome, F.R.S described him as being "saved from prolonged torture and death" by "the sacrifice, under anaesthetics, of a few rabbits and monkeys."

F.R.S's identity, unknown for years, later proved to be Sir James Crichton Browne, a colleague of both Godlee and Hughes Bennett (Trotter 1934). His letter was reprinted in the *Glasgow Herald* the following day and an exchange between James Whitson, an assistant surgeon working with Macewen, and Crichton Browne ensued. Whitson (1884) praised Hughes Bennett for his localizing skills but added that "no doubt such operations are new to London; but they may almost be said to be old to us in Glasgow." F.R.S responded immediately through the *Times*, reprinted in the *Glasgow Herald* (Crichton Browne 1884b), writing,

> I was not ignorant of the fact that Dr Macewen of Glasgow had secured striking results with the operation of trephining [but he] has not published any reports of his cases and the brief notices that have appeared in some medical journals certainly create the impression that they were of a very different character than the recent case from the Regents Park Hospital.

He emphasized that the focus for surgery there had been determined by motor symptoms alone and thus "unique in the annals of surgery."

In early January 1885, correspondence continued with F.R.S (Crichton Browne) accusing Whitson of "an almost feminine jealousy" (Crichton Browne 1885) and Whitson replying that "the new era of cerebral surgery only dawning in London in the last few months has been for years an accomplished fact in Glasgow" (Whitson 1885).

By mid-January 1885, the *London Times* had received 64 letters about who was first or for and against vivisection (Macmillan 2004). Hughes Bennett brought the vitriol to an end by writing in the *London Times* that he had made no claim to priority and that the debate was the consequence of "a series of premature surmises and erroneous conclusions" (Bennett 1885).

The Royal Medical and Chirurgical Society received the written account of Henderson's operation on January 13 and it was presented, with Macewen in attendance, at its meeting in May. The written submission commented,

> [S]ince this (the operation) has been accomplished in the present instance, the public papers have asserted that the same has already been carried out on several occasions at the Royal Infirmary of Glasgow. To this it can only be said that up until the present date no report of such proceedings is to be found in medical or scientific literature. (Bennett and Godlee 1885b, 274–275)

This statement was absent in the published account of the meeting (British Medical Journal 1885).

Before the May meeting, on January 22, David Ferrier had written to Macewen regarding "the squabbles that have arisen in regard to your operations on the brain." He suggested that it would be desirable, in the interest of cerebral surgery, that Macewen publish an account of his experiences, commenting that "you are able to say that you have operated successfully on the brain several times but I cannot find any particulars." He suggested that Macewen should submit a paper to the journal *Brain*, cofounded by himself, Crichton Browne and Jackson. He finished by asking Macewen about his experiences of hernia cerebri and his antiseptic techniques (Ferrier 1885).

The following week Macewen drafted a reply (1885a) in which he asserted that he had "no part in the squabble." He wrote that F.R.S's letter was published the evening of a dinner at the Royal Infirmary at which Dr. Whitson undertook to respond but Macewen "said to him that I would prefer that he should not do so," expressing concern that a letter would "retard publication of anything on the subject by me." He expressed sorrow that London had been mentioned in the way it had and that in his view F.R.S's letter had "merely wished to advance the cause of vivisection" rather than to claim priority. The letter was incomplete and it is uncertain if it was sent, as there was no reply from Ferrier.

Macewen did not take up Ferrier's offer of having his cases published in Brain. It is surprising that Ferrier was so unaware of Macewen's work, given that he had visited his wards previously. Macewen recalled he

> had therefore much pleasure in describing to Professor Ferrier, when he visited my wards in Glasgow in the spring of 1884, some cases of the same nature as those here presented, and I was glad that he so soon afterwards had the opportunity of advising and assisting Dr Hughes Bennett and Mr Godlee in the case in which the latter removed a tumour from the brain. (Macewen 1885c, 935)

In early 1885, Hughes Bennett seems to have written to Macewen requesting details of his cases, as Macewan replied stating that he "hopes to be able to send you the details of the cases to which you refer and then with them judge for yourself concerning them." He went on to emphasize that all had been presented at various local medical societies (1885b). Two months later Macewen, at the invitation of Bennett and Godlee, attended and addressed the meeting of the Royal Medical and Surgical Society, where he presented his brain surgery and was congratulated "on his interesting and successful cases" (British Medical Journal 1885, 989).

Following Macewen's 1888 address on surgery of the brain and spinal cord at the Annual Meeting of the British Medical Association, an accompanying editorial commented,

> [A]ll these operations proved successful, and they all occurred before the case under the care of Dr Bennett and Mr Godlee, which attracted so much attention in London in 1884. With indisputable justice, therefore, may Dr Macewen claim the proud distinction of having been the leader in this country, and we believe in the world, of this great advance in our art. (British Medical Journal 1888, 323)

Four years later, while delivering the Cameron Lecture in Edinburgh, Ferrier said that "the honour of actually having led the way belongs to our countryman, Macewen of Glasgow" (Ferrier 1892).

On the 50th anniversary of Godlee's surgery the *Times of London* published a celebratory article titled, "Jubilee of the First Operation for the Removal of a Tumour of the Brain" (Anon. 1934) without mention of Macewen, thus stimulating a response from his son, Dr. James Macewen, drawing the author's attention to his father's 1879 account of removing, by trephination, a dural tumor (Macewen 1934). Wilfred Trotter, surgeon to University College Hospital London, delivered a validatory lecture titled "A Landmark in Neurology" to the Royal Society of Medicine in the November 1934. He confirmed Sir James Crichton Browne as F.R.S, the author of the incendiary letter (1884a), "which pointed out the direct dependence of the operation upon the results of animal experiments, and which led to some controversy," adding that Ferrier and Jackson were present at the operation although

Crichton Browne was not. There was no mention of Macewen's earlier surgery in his address (Trotter 1934, 1210).

Ferrier and Horsley vs. the antivivisectionists

At the conclusion of the International Medical Conference of 1881, during which Ferrier had triumphed, physiologist Michael Foster asserted that "experiments on living animals have in the past proved of great service to medicine, and are indispensable for its future progress" (Obenchain 2012, 144).

Ferrier's success was to be dented by an adversary in the formidable shape of Frances Cobbe, social reformer and activist. In 1875 she had established the Society for the Protection of Animals Liable to Vivisection (SPALV) and Ferrier presented her with a cause celebre. Cobbe noticed that Ferrier did not have a license for his animal studies on cerebral localization and was thus in breach of the Cruelty to Animals Act of 1876 (Cruelty to Animals Act 1876). This led to a criminal charge against Ferrier being heard in November 1881 at Bow Street Court (Stahnisch 2010). The British Medical Association instructed a solicitor to act on Ferrier's behalf and published the proceedings (British Medical Journal 1881). The defense disclosed that the operations on monkeys and dogs had been performed not by Ferrier but by George Yeo, his coinvestigator, who did indeed hold the required license. The prosecution then argued that all the animals experimented on should have been destroyed before the anaesthetic had worn off, whereas Ferrier had personally continued with his experiments for a while thereafter. The defense argued that Ferrier's research had been conducted in compliance with the law and—with Jackson, Lord Lister, Foster, Yeo, and other eminent medical supporters in court—the case was dismissed. Cobbe remained unconvinced, noting in her biography that Ferrier's name appeared first on the relevant publications and that he must have had a leading role in the experiments (Cobbe 1894, 300). Later, for Ferrier and his colleagues, Godlee's landmark operation was triumphed a resounding vindication of the vivisection that had preceded it.

Horsley and Cobbe had clashed before, but it was her involvement in the book *The Nine Circles of the Hell of the Innocent* (Rhodes 1892) that ignited matters. Styled on Dante's *Inferno* and compiled by Georgine Rhodes under Cobbe's supervision, it cataloged animal experimentations, called out vivisectionists, and frequently cited Horsley's work. Horsley, in correspondence in the *Times*, described the book as one of the "rankest impostures that for many years had defaced English literature being full of fraudulent misrepresentations" (Mitchell 2004, 339). Cobbe replied, apologizing for any minor inaccuracy but conceded little else (Cobbe 1892). Horsley responded by calling Cobbe a liar who had been accusing medical men of "murder, cruelty and falsehood" (Horsley 1892), resulting in the editor informing him that in polite society, "a gentleman should not call a lady a liar" (Obenchain 2012, 174).

Horsley later engaged in heated correspondence with Dr. Walter Hadwen, secretary of the British Union for the Abolition of Vivisection, through the pages of the *Daily Mail*. Through September 1908, in a hostile interchange, Horsley outlined the medical conditions in which animal experimentation had relieved human suffering, with Hadwen refuting each in turn. Horsley acerbically concluded correspondence with the comment that "the Daily Mail cannot be exploited as a means for filling up all the hiatuses in Dr Hadwen's medical education" (Horsley 1908).

Discussion

The expectation that surgery could ameliorate seizures dates back to Hippocratic surgeons. On the basis of the site of skull injury, they assigned unilateral focal motor features to injury to the middle portion of the brain on the opposite side and accordingly trephined there (Temkin 1971, 35). Espino et al. (2022) reviewed skull trephinations in pre-Columbian Peruvian cultures dating from 700 BCE and speculated on the application to epilepsy, concluding that religious mystical knowledge may have led to epilepsy being an indication but without certainty. It was only with the acceptance of cerebral localization that this ancient surgical practice of trepanation found its rationale. Flanigin, Hermann, and King (1991), reviewing the history of epilepsy surgery in North America, cited early pioneers such as Benjamin Dudley (1785–1870) and Stephen Smith (1823–1922), although their surgery was not based on symptom localization. In 1871, Paul Broca, by draining an epidural abscess presenting with nonfluent aphasia, could claim to be the first to operate on the basis of symptom localization (Stone 1991). Broca's pupil, Lucas-Championniere (1843–1913), had studied antisepsis under Lister in Glasgow and initially developed the indications for trepanation in traumatic lesions and later based upon cerebral localization (Lucas-Championniere 1878, 150; see also Garrison 1921, 596).

In the debate as to who was first to carry out localization-based surgery for the amelioration of epilepsy, each of the operations discussed here has its own uniqueness and all owe much to the collective brilliance of Ferrier and Jackson as well as being seen as vindication of the animal experimentation that preceded them. Feindel, Leblanc, and Villemure (1997), in outlining the nineteenth-century history of the surgical treatment for epilepsy, credited the roles of the experimentalists and clinicians such as Ferrier and Jackson while focusing on the pioneering surgery of Horsley and the contribution of Macewen through his adoption of Lister's antiseptic techniques. Horsley's surgery on James B. was detailed as was Godlee's but Macewen's was not. The authors also drew attention to the early surgery in the United States by Moses Allen Starr (1854–1932) and Charles Burney (1845–1913) that postdated their European counterparts.

The pioneering neurosurgeon Sir Geoffrey Jefferson, writing on Macewen's contribution to neurosurgery, noted that in the case of J. McK, he was probably the first surgeon to offer surgery on the basis of having localized the cerebral focus from seizures (Jefferson 1950). Harvey Cushing, in his Macewen memorial lecture, noted that in his 1879 case Macewen had operated on "a lesion presenting itself to view, whereas in the celebrated Godlee-Bennett case operated upon five years afterwards, the presence and location of the hidden lesion were determined solely by its neurological signs." He continued, "though Macewen had previously operated upon several correctly localized intracranial lesions; he had the ill fortune not to have happened upon a true brain tumour" (Cushing 1927, 14).

Eadie (2009) stated that, after 1875, cerebral localization had become well enough accepted for surgeons, beginning in 1879 with the 31-year-old William Macewen at the Glasgow Royal infirmary, to employ this knowledge to locate and then operate successfully on intracranial tumors. Finger and Stone (2010, 195) commented that, although many of his patients had scalp or skull abnormalities to guide surgery, "Macewen maintained that his hands were guided by localizing symptoms alone in several instances."

Malcolm Macmillan's seminal study provides an account of Macewen's wider surgical experience, its application to his brain surgery, and the controversies that resulted from this.

He noted that Macewen had carried out seven similar operations before Bennett and Godlee and, through reviewing the private journals and publications, interrogated whether localizing signs were used in surgical planning. Published in two parts (2004, 2005), Macmillan investigated the notion that Macewen had priority over Bennett and Godlee. Although he acknowledged that the use of localization is questionable in some of the cases and discrepancies are to be found in various publications, his conclusion was that localization allowed Macewen to plan surgery on J. McK. in 1876 and to carry it out on Barbara W. in 1879. Supported by this detailed examination of the early cases and Macewen's own published accounts, there would seem little doubt that by 1876, he was well able to apply localization to the planning of cranial surgery. But where did he acquire such knowledge, and why were his achievements so overlooked?

Two years before his death, in his President's Address on Brain Surgery at the annual meeting of the British Medical Association, Macewen set out the historical background to cerebral localization and how knowledge of this allowed him to successfully localize his cases (Macewen 1922). He reiterated his claim that, with Barbara W. (1879), it was the symptoms that enabled "the tumour to be located and removed by operation" (1922, 157). Macewen added, as a footnote to the address, that as a medical student, graduating in 1872, he was "given the means of studying lesions in the base of the third frontal convolution producing motor aphasia. Two such cases were in the medical wards during these years, the lesions afterwards being confirmed by autopsy" (1922, 157). This indicates knowledge of localization even as a fledgling doctor.

Supporting the claim that he was conversant with cerebral localization is the fact that two of his senior Glasgow colleagues, Gairdner and Robertson, who had been publishing on aphasia, worked in the same hospital (Glasgow Royal Infirmary) and attended the same Medico-Chirurgical Society meetings. Robertson's role in planning the surgery may have gone unrecognized, with the solitary Macewen invariably publishing as sole author. Bowman commented on the support Robertson gave the young Macewen in helping him "embark upon the surgical which he so much desired" (Bowman 1942, 16). Given his knowledge and their closeness, it seems improbable that Robertson's opinion was not sought after on Macewen's early cerebral cases.

The absence of detailed contemporaneous medical records has been a stumbling block to the acceptance of Macewen's brain surgery, as was his publishing locally before nationally. From the published and private journal accounts of Barbara W., for example, it is not possible to know whether her tumor was an intradural meningioma, as Cushing believed, or extradural, arising from bone, and thus a fibrous dysplasia of the skull with no record of pathology being retained. Bowman, in his biography, described the uncongenial atmosphere Macewen confronted in May 1885 on attending the Royal Medico-Chirurgical Society meeting, and commented that "the surgeons of the metropolis may have been relatively unacquainted with the work and personality of a surgeon from the north" (Bowman 1942, 261). Ferrier, present at the meeting, having previously visited his wards and aware of his fellow Scot's work, did not speak up for him at that time, leaving this to his 1892 Cameron Address in the safety of Edinburgh. There, referring to Macewen's 1879 case (Barbara W.), he said that there was "no more triumphant vindication than this could be given of the surgical value of cerebral localisation; for a reliance merely on external would have in all probability have sacrificed the life of the patient, or resulted in incurable infirmity" (Ferrier 1892, 890).

The failure to embrace Macewen's pioneering cranial surgery could simply be put down to not what he did but where he was. The National Hospital for the Relief and Cure of Paralysis and Epilepsy, later named the National Hospital at Queens Square London, was establishing an international reputation, with a glittering array of staff that included the likes of Jackson, Ferrier, Crichton Browne Gower's, and Brown-Squared. That Macewen did not work in such a heady environment, or have eminently connected colleagues to promote him, might explain the tardiness in acknowledging him and his achievements. On June 23, 1926, two years after Macewen's death, an oration was given in his honor. This was to be delivered by Harvey Cushing, but in his absence was read by Macewen's successor to the Regius Chair of Surgery. Revealingly, Macewen was described as an individualist, not a team player, and prone to working alone. Among his many diverse contributions to surgery, he was noted as having "achieved his greatest fame as the pioneer of brain surgery" and that any rivalry with Horsley was "less in their minds and more in the minds of their respective supporters" (Young 1926, 39).

Rickman Godlee, although being in the right place at the right time, became the first surgeon to operate on an intrinsic brain tumor. At the time, he was a junior surgeon and clearly a highly skilled technician who had been instructed in what to do (Kirkpatrick 1984). At Godlee's elbow were Bennett, the orchestrator, and Ferrier and Jackson, his supporters. Godlee progressed to become a distinguished and innovative thoracic surgeon with Henderson his one and only foray into brain surgery. It was ironic that the patient was to die of postoperative infection, given that Godlee was Lister's nephew and trainee. Bennett was also soon to leave the neurological stage, with his own long illness appearing to isolate him from his colleagues, possibly because the stigma of symptoms suggestive of tabes dorsalis. The Godlee–Bennett operation drew immediate worldwide attention as a clarion call for the emerging specialty, with others—such as Horsley, Keen, Krause, Foerster, Durante, and Cushing—soon to become its earliest pioneering practitioners. Few operations can claim to have had their jubilee announced so fully in national newspapers. The Godlee–Bennett case illustrated the courage of the clinicians involved but also that of their patient, Henderson, who tragically did not survive.

Horsley, unlike Macewen, was as at home in the animal laboratory as in the operating theater but also a collaborator. After being appointed, in 1886, as the first surgeon to the National Hospital at Queen Square, he thereafter restricted his practice to neurological surgery, whereas Macewen remained a generalist throughout his career and a single author in most of his publications. Horsley's full-time position resulted in great innovations, such as defining the relationship between surface markings and their underlying gyri (Northfield 1973), which he applied in James B.'s case, and devising with Robert Clarke the first stereotactic instrumentation (Jensen, Stone, and Hayne 1996).

Horsley's experimental work on localization started in 1884 and persisted well into his active surgical career, bringing him and Ferrier into contention with the antivivisectionists. Macewen avoided the controversy, making no supportive comment on behalf of the experimentalists, and this may well have further isolated him from his London contemporaries.

James B.'s clinical records describe his case in greatest detail (Horsley 1886b). The site of surgery was defined by the prior comminute fracture, with seizure semiology pinpointing accurate localization and a discrete cerebral scar found at the anticipated site and partially resected with a dramatic reduction in seizure frequency. Thereafter,

Horsley combined his cases with those of others in publishing the first case series of epilepsy surgery with outcomes (Horsley 1890); this despite his skepticism that different surgeons under differing circumstances could meaningfully combine their results. Having used electrical stimulation in his experimental work on monkeys, he was first to apply this technique intra-operatively in humans (Horsley 1884) and to use it in defining the epileptogenic cortex requiring excision. Horsley left an immediate legacy of neurosurgery at the National Hospital, whereas Macewen in Glasgow did not.

All three operations described in this article were unique in their own right, each was dependent on accurate clinical localization based on the features of focal motor seizures. Macewen's can make a strong claim to be the first localization based operation for epilepsy; Godlee's, the first removal of an intrinsic brain tumor manifesting as epilepsy; and Horsley's, the first detailed clinical record of a surgical approach to epilepsy. Horsley was also first to provide a collaborative case series of epilepsy surgery with outcomes and to use intra-operative stimulation to identify epileptogenic foci. All operations were widely regarded as vindication for the animal experimentations that preceded and made them possible.

Perhaps the last word on Macewen and Horsley's relative contributions is best left to their more modern contemporary, Harvey Cushing: "We merely stand on the shoulders of our predecessors, and the sturdy contemporary figures of Macewen on one side and Horsley on the other are what support the arch of modern neurosurgery" (Cushing 1927, 13).

Acknowledgments

We would like to thank Clare Harrison, library and heritage manager, and Kirsty Earley, digital heritage and engagement officer, both of the Royal College of Physicians and Surgeons of Glasgow, United Kingdom, for their help in the preparation of this manuscript. Also to Sarah Lawson, head of Queen Square Library, University College London Queen Square Institute of Neurology, for providing access to archive material and for her support.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

The authors reported there is no funding associated with the work featured in this article.

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References

Aminoff, M. 2022. *Victor Horsley: The world's first neurosurgeon and his conscience*. Cambridge UK: Cambridge University Press.

Anon. 1934 Jubilee of the first operation for the removal of a tumour of the brain. *The Times (London)*, November 28
Bennett, A. H. 1885. [Letter]. *The Times* (London), January 15.
Bennett, H. A., and R. J. Godlee. 1885a. Sequel to the case of excision of a tumour from the brain. *Lancet I* 1: 13.
Bennett, A. H., and R. J. Godlee. 1885b. Case of cerebral tumour: The surgical treatment. *Medico-chirurgical Transactions* 58:243–75.
Bennett, H. A., and R. J. Godlee. 1884. Excision of a tumour from the brain. *The Lancet* 124:1090–91. doi:10.1016/S0140-6736(02)29062-5.
Bowman, A. K. 1942. *Sir William Macewen: A chapter in the history of surgery*. London: William Hodge and Company Limited.
British Medical Journal. 1881 November 19. [Anon] The charge against Professor Ferrier under the vivisection act: Dismissal of the summons. *British Medical Journal* 2:836–42. doi:10.1136/bmj.2.1090.836-a.
British Medical Journal. 1885 May 16. [Anon] Report of societies: Royal Medico-Chirurgical Society. *British Medical Journal* 1:988–89.
British Medical Journal. 1888 August 11. [Editorial] The surgery of the brain and spinal cord. *British Medical Journal* 2:322–24.
British Medical Journal. 1925 April 25. [Anon]. Obituary. Sir Rickman John Godlee. *British Medical Journal* 1:809–10. doi:10.1136/bmj.1.3356.809.
Broca, P. 1861. Remarques sur le siege de la faculte du language articule suivies d'une observation d'aphemie (perte de la parole). *Bulletins de la Société Anatomique* 6:330–57,398–407.
Cobbe, F. 1892. [Letter]. *The Times (London)*, October 15th.
Cobbe, F. P. 1894. The claims of the brutes. In *Life of Frances Power Cobbe by herself*, Vol. 2, Boston: Houghton and Mifflin and Co.
Crichton Browne, J. 1884a. Brain surgery. *The Times (London) [letter]*, December 16th.
Crichton Browne, J. 1884b. Brain surgery. *Glasgow Herald*, [letter], December 29th.
Crichton Browne, J. 1885. Brain surgery. *The Times* (London) [letter], January 8th.
Cruelty to Animals Act. 1876. 39 & 40 Vict. c. 77. August 15th.
Cushing, H. 1927. *The meningiomas arising from the olfactory groove and their removal by the aid of electro surgery. Macewen memorial lecture*. Glasgow: Jackson Wylie and Co.
Duguid, G. 1957. *Macewen of Glasgow: A recollection of the chief*. London: Oliver and Boyd.
Eadie, M. J. 2009. The role of focal epilepsy in the development of Jacksonian localization. *Journal of the History of the Neurosciences* 18 (3):262–82. doi:10.1080/09647040802025136.
Eadie, M. J. 2015. Alexander Robertson (1834–1908): Glasgow's pioneer aphasiologist and epileptologist. *Journal of the History of the Neurosciences* 24 (3):292–302. doi:10.1080/0964704X.2014.1000065.
Espino, P. H., J. E. Toro-Perez, S. Shkrum, and J. G. Burneo. 2022. Cranial trepanation in pre-Columbian Peruvian cultures: Was it an option to treat epilepsy? *Brain* 145 (10):3335–38. doi:10.1093/brain/awac277.
Feindel, W. R., R. Leblanc, and A. Nogueira de Almeida. 2009. Epilepsy surgery: Historical highlights 1909–2009. *Epilepsia* 50 (supplement 3):131–51. doi:10.11.11/j.1528-1167.
Feindel, W., R. Leblanc, and J.-G. Villemure. 1997. History of the surgical treatment of epilepsy. In *A history of neurosurgery: In its scientific and professional contexts*, ed. S. H. Greenblatt, T. F. Dagi, and M. H. Epstein, 466–68. Park Ridge: American Association of Neurosurgeons.
Ferrier, D. 1875. Experiments on the brains of monkeys. *Proceedings of the Royal Society* 23:403–30.
Ferrier, D. 1876. *The functions of the brain*. London: Smith Elder and Company.
Ferrier, D. 1885. Letter to William Macewen. January 22nd. Sir William Macewen, (1848–1924). RCPSG GB 250 10/1A/43, Royal College of Physicians and Surgeons of Glasgow.
Ferrier, D. 1892. Cerebral localisation in relation to therapeutics. (The Cameron Lecture). *Edinburgh Medical Journal* 37:881–97.
Finger, S. 2000. David Ferrier and Eduard Hitzig: The experimentalists map the cerebral cortex. In *Minds behind the brain: A history of the pioneers and their discoveries*, 155–75. Oxford UK: Oxford University Press.

Finger, S., and S. L. Stone. 2010. Landmarks of surgical neurology and the interplay of disciplines. In *Handbook of clinical neurology*, ed. M. J. Aminoff, F. Boller, and D. F. Swaab, Vol. 95, 3rd series ed., 189–202. Edinburgh, Amsterdam: Elsevier. B.V.

Flanigin, H. F., B. P. Hermann, and D. W. King. 1991. The history of surgical treatment of epilepsy in North America prior to 1975. In *Epilepsy surgery*, ed. H. Luders, 19–35. New York: Raven Press.

Gairdner, W. T. 1866. A case of aphasia or speechlessness of cerebral origin without distinct paralysis and fatal with epileptic convulsions. *Glasgow Medical Journal* 1:1–13.

Garrison, F. H. 1921. The nineteenth century: The beginnings of organised advancement of medicine. In *An introduction to the history of medicine*, 3rd ed., 424–722. Philadelphia: WB Saunders.

Horsley, V. 1884. Case of encephalocele in which the correct diagnosis was obtained by means of the induced current. *Brain* 7:228–43. doi:10.1093/brain/7.2.228.

Horsley, V. 1886a. Brain Surgery. Proceedings of the fifty-fourth annual meeting of the British Medical Association. *British Medical Journal* 2:670–75.

Horsley, V. 1886b. Epilepsy resection. Ferrier, David: Case notes. National Hospital for Neurology and Neurosurgery. NHNN/CN/13/1, Queen Square Archives, UCL Queen Square Institute of Neurology.

Horsley, V. 1887. A note on the means of topographical diagnosis of a focal lesion affecting the so-called motor region of the cerebral cortex. *American Journal of the Medical Sciences* 93:342–69. doi:10.1097/00000441-188704000-00002.

Horsley, V. 1890. Remarks on surgery of the central nervous system. *British Medical Journal* 2:1286–92. doi:10.1136/bmj.2.1562.1286.

Horsley, V.1892. *The Times* (London): [Letter], October 20th.

Horsley, V. 1906. Address in surgery on the techniques of operations on the central nervous system. *British Medical Journal* 2:411–23. doi:10.1136/bmj.2.2382.411.

Horsley, V. 1908. The value of vivisection. *The Daily Mail* [letter], September 15th.

Horsley, V., and E. A. Schafer. 1888. A record of experiments upon the function of the cerebral cortex. *Philosophical Transactions of the Royal Society of London* 179:1–45.

Ireland, W. W. 1909. Alexander Robertson [notes and news]. *Journal of Mental Sciences* 55:228.

Jackson, H. J. 1870. A study of convulsions. *St Andrews Medical Graduates Association Transactions* 3:162–204.

Jackson, J. H. 1863. Convulsive spasms of the right hand and arm preceding (generalized) epileptic seizures. *Medical Times and Gazette* 1:110–11.

Jackson, J. H. 1864. Hemiplegia on the right side with loss of speech. *British Medical Journal* 1:572–73. doi:10.1136/bmj.1.177.572.

Jackson, J. H. 1872. Case of disease of the brain-left hemiplegia-mental affectation. *Medical Times and Gazette* 1:513–14.

Jackson, J. H. 1875. *On localisation of movements in the brain*. London: J and A Churchill.

Jefferson, G. 1950. *Sir William Macewen's contribution to neurosurgery and its sequel: Macewen memorial lecture*. Glasgow: Jackson. 1–36.

Jensen, R. L., J. L. Stone, and R. A. Hayne. 1996. Introduction of the human Horsley-Clarke stereotactic frame. *Neurosurgery* 38 (3):563–67. doi:10.1097/00006123-199603000-00029.

Kirkpatrick, D. B. 1984. The first primary brain-tumor operation. *Journal of Neurosurgery* 61 (5):809–13. doi:10.3171/jns.1984.61.5.0809.

Luas-Championniere, J. 1878. *La trépanation guidée par les localisations cérébrales*. Paris: Masson.

MacCormac, W. 1881. *Transactions of the 7th international medical congress*. London: J. W. Kolkmann.

Macewen, J. 1934. Letter to the editor of *The Times*. Sir William Macewen, (1848–1924), surgeon. RCPSG GB 250 10/1A/36, Royal College of Physicians and Surgeons of Glasgow.

Macewen, W. 1876–1886. Private journals of William Macewen. Sir William Macewen, (1848–1924), surgeon. RCPSG GB 250 10/9/1-6, Royal College of Physicians and Surgeons of Glasgow.

Macewen, W. 1879. Tumour of the dura mater – Convulsions – removal of the tumour by trephining – recovery. *Glasgow Medical Journal* 12:210–13.

Macewen, W. 1881. Intra-cranial lesions: Illustrating some points in connexion to with the localisation of cerebral affections and the advantages of antiseptic trephining. *The Lancet* 118:581–83. doi:10.1016/S0140-6736(02)36340-2.

Macewen, W. 1884. A case of a patient whose brain had been operated on for the relief of left hemiplegia. *Glasgow Medical Journal* 21:142–45.
Macewen, W. 1885a. Letter to D. Ferrier, 22 January. Sir William Macewen, (1848–1924), surgeon. RCPSG GB 250 10/1A/43, Royal College of Physicians and Surgeons of Glasgow.
Macewen, W. 1885b. Letter to H. Bennett, 20 February. Sir William Macewen, (1848–1924), surgeon. RCPSG GB 250 10/1A/11/1-2, Royal College of Physicians and Surgeons of Glasgow.
Macewen, W. 1885c. Cases illustrative of cerebral surgery. *The Lancet I* 1: 881–3, 934–6.
Macewen, W. 1888. An address on the surgery of the brain and spinal cord. *British Medical Journal* 2:302–09. doi:10.1136/bmj.2.1441.302.
Macewen, W. 1893. *Pyogenic infective diseases of the brain and spinal cord*. Glasgow: James Maclehouse and Sons.
Macewen, W. 1922. Ninetieth annual meeting glasgow: President's address on Brain Surgery. *British Medical Journal* 155–65. doi:10.1136/bmj.2.3213.155.
Macmillan, M. 2004. Localisation and William Macewen's early brain surgery Part I: The controversy. *Journal of the History of the Neurosciences* 13 (4):297–325. doi:10.1080/09647040490881659.
Macmillan, M. 2005. Localization and William Macewen's early brain surgery Part II: The cases. *Journal of the History of the Neurosciences* 14 (1):24–56. doi:10.1080/09647040590881793.
Mitchell, S. 2004. *Frances Power Cobbe: Victorian feminist, journalist, reformer*. Charlottesville: University of Virginia Press.
Northfield, D. W. C. 1973. Victor Horsley: His contributions to surgical neurology. *Surgical Neurology* 1:131–34.
Obenchain, T. G. 2012. Professor Ferrier and his monkeys. In *The Victorian vivisection debate*, 137–51. Jefferson, North Carolina: McFarland and Company.
Paget, S. 1919. *Sir Victor Horsley: A study of his life and work*. London: Constable.
Penfield, W., and T. C. Erickson. 1941. Seizure patterns and their localisation. In *Epilepsy and cerebral localization*, 60–160. Springfield, Illinois: Charles Thomas.
Rhodes, G. M. 1892. *The nine circles of the hell of the innocent*. London: Swan Sonnenschein and Co.
Robertson, A. 1867. The pathology of aphasia. *Journal of Mental Science* 12:503–21. doi:10.1192/bjp.12.60.503.
Stahnisch, F. W. 2010. The use of animal experimentation in the history of neurology. In *Handbook of clinical neurology*, ed. S. Finger, F. Boller, and K. L. Tyler, Vol. 95, 3rd series ed., 129–48. Edinburgh, Amsterdam: Elsevier B.V.
Stone, J. L. 1991. Paul Broca and the first craniotomy based on cerebral localization. *Journal of Neurosurgery* 75 (1):154–59. doi:10.3171/jns.1991.75.1.0154.
Stookey, B. 1963. Jean-baptiste Bouillaud and Ernest Auburtin. Early studies on cerebral localization and the speech center. *JAMA* 184:1024–29. doi:10.1001/jama.1963.73700260007011.
Temkin, O. 1971. Epilepsy in ancient medical science. In *The falling sickness: A history of epilepsy from the Greeks to the beginnings of modern neurology*, 2nd ed., (revised), 28–81. Baltimore: The John Hopkins University Press.
Trotter, W. 1934. A landmark in modern neurology. *The Lancet* 224:1207–10. doi:10.1016/S0140-6736(00)43902-4.
Tyler, K. L., and R. Malessa. 2000. The Goltz-Ferrier debates and the triumph of cerebral localizationalist theory. *Neurology* 55 (7):1015–24. doi:10.1212/wnl.55.7.1015.
Walker, A. E. 1957. The development of the concept of cerebral localisation in the nineteenth century. *Bulletin of the History of Medicine* 1:99–121).
Whitson, J.1884. Brain surgery. *Glasgow Herald*, [letter], December 22.
Whitson, J.1885. Brain surgery. *The Times* (London) [letter], January 5.
Wickens, A. P. 2015. Mapping the cerebral cortex. In *A history of the brain: From Stone Age surgery to modern neuroscience*, 216–41. London: Psychology Press Taylor Frances Group.
York, G. K., and D. A. Steinberg. 2011. Hughlings Jackson's neurological ideas. *Brain* 134 (10): 3106–13. https://dx.doi.org/10.1093/brain/awr219
Young, A. 1926. *Sir William Macewen: An oration*. Glasgow: Jackson Wylie and Co.