A history of cerebral localization

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The brain has been known to be the center of voluntary movement, sensation, and intelligence for centuries. Nevertheless, it was not until the latter third of the 19th century that the functions of its different areas were discovered. It was the labor of several key men that made possible the accurate localization and, furthermore, the resection of brain neoplasms.

KEY WORDS • brain lesion • tumor localization • seizure

OVERVIEW

Galen, physician to Marcus Aurelius (the Roman emperor who ruled in the middle of the second century AD), declared "Where the origin of the nerves is, there is the command of the soul." As Paget mentions in his biography of Horsley, by Galen's time it was accepted that the brain was the seat of voluntary movement, intelligence, and sensation.¹¹ Nevertheless, it was not until the last third of the 19th century that the specifics of cerebral localization began to be discovered. Induction of general anesthesia with the use of ether vapor was introduced by William Morton in 1846 at Massachusetts General Hospital. The following year, chloroform was used by Marie Jean Pierre Flourens in Paris. The specter of postoperative infection was addressed when Joseph Lister reported his concept of antisepsis in 1867 from the University of Glasgow.⁶ With the achievement of these two advances, only one major obstacle remained for surgeons in the quest for the resection of brain tumors, and that was the problem of localization of the lesion.

JOHN HUGHLINGS JACKSON

John Hughlings Jackson, one of the greatest early contributors to the current knowledge of anatomical cerebral localization, was born in England in 1835. After receiving his medical education and initial training in York, he came to London in 1859. There he was substantially influenced by an acquaintance, Dr. Charles Brown-Séquard, to pursue his interest in the study of neurology, particularly seizures. Jackson, an astute clinician, obtained finely detailed histories from and performed thorough examinations on his patients. Then, with tireless attention to minutiae, he observed the natural and clinical courses of diseases and carefully correlated these findings with the pathological findings at autopsy (see Horwitz⁷).

Until Jackson's time, seizures were thought to originate in the medulla oblongata. According to Horwitz,⁷ however, based on extensive study of patients with epilepsy, Jackson concluded that an abnormal electrical discharge from the cortical gray matter was consistently the origin of the seizures in his patients. He described individuals who had sustained a blunt injury to the head and in whom hemiplegia subsequently developed on the contralateral side of the body and face. When these patients experienced epileptic activity, with rare exceptions it began on the hemiplegic side. Jackson⁹ also noted that those whose external injury overlaid the posterior left frontal lobe usually had a degree of difficulty with speech at baseline or during their seizure. Extrapolating this information to other atraumatic scenarios, he was often able to predict with great accuracy the location of intracerebral lesions found at autopsy. The following excerpt is taken from "A Study of Convulsions," which appeared in the publication *Transactions St. Andrews Medical Graduates*, volume iii, in 1870 (see Horwitz⁷).

The great majority of chronic convulsions may be arranged in two classes.

1. Those in which the spasm affects both sides of the body almost contemporaneously.
2. Those in which the fit begins by deliberate spasm on one side of the body, and in which parts of the body are affected, one after another.

It is with the second class only that I intend to deal in the article...

Fits beginning unilaterally may doubtless begin by movement in any part of the region which is paralysed in hemiplegia, i.e. in the face, in the arm, or in the leg. But I know few cases of fits of this class which begin other than in the side of the face (usually the cheek), in the hand, or in the foot... The fit usually begins, it is to be observed, in that part of the face, of the arm, and of the leg which has the most varied uses.

Parts with the most varied uses will be represented in the

central nervous system by most ganglion cells. I say most varied movements, as it is not only a question of number of movements, but also of number of different movements.

The eponym “jacksonian seizure” or “jacksonian march” was derived from the foregoing description.⁷

DAVID FERRIER

In 1870, two German scientists, Gustav Fritsch and Edward Hitzig, reported their findings on the electrical excitability of the exposed cerebral cortex in dogs in which galvanic current was used. According to Horwitz,⁵ David Ferrier was impressed by these scientists’ work, and he refined their techniques. By using faradic current stimulation, Ferrier investigated even further the cortical functioning of many different animals, including primates. He constructed one of the first detailed cortical maps and confirmed many of the principles set forth by Dr. Jackson. Ferrier firmly established the location of the motor cortex, stating that it extended along the rolandic fissure medially to the interhemispheric area. Not all of his conclusions were correct, however. For example, he erroneously placed the center for vision in the superior temporal lobes, and similarly was unable adequately to determine the function of the occipital lobes from his studies. Ferrier summarized his results in the 1876 publication of *The Functions of the Brain*,⁴ and dedicated this work to Jackson, stating “To Dr. Hughlings Jackson, who from a clinical and pathological standpoint anticipated many of the more important results of recent experimental investigation into the functions of the cerebral hemispheres.” As discussed in Horwitz,⁵ 2 years later, Ferrier produced a second publication titled *The Localisation of Cerebral Disease*, and he dedicated it to a well-known French neurologist, Dr. Jean-Martin Charcot.

JEAN-MARTIN CHARCOT

Dr. Charcot, Jackson’s French counterpart, had observed in his practice and research many of the same patterns on which Jackson elaborated. In his 1881 work *Lectures on the Diseases of the Nervous System*, Charcot² had this to say concerning the insight provided by his colleague:

I believe I ought to mention to you, incidentally, that the mode of invasion takes place here in conformity with the rule established by the ingenious studies of Dr. H. Jackson.... when convulsions in partial epilepsy, commencing by the upper extremity, tend to become generalized, they only invade the lower limb after having first affected the face. If, on the contrary, the case be one in which the face is first affected, the upper extremity is the next taken; and, lastly, comes the turn of the lower limb. Finally, if ... the convulsions should first invade the lower extremity, they spread successively to the upper limb first, and then to the face. This order seems to be almost never inverted....

The benefits of this research had not been manifested at the bedside where it was needed. It was during this time that men such as Sir Victor Horsley, Hughes Bennett, and Rickman Godlee made significant contributions.

SIR VICTOR HORSLEY

Born and educated primarily in England, yet receiving most of his postgraduate training in Germany, Victor Hors-

ley was able to glean clinical applications from the landmark works of his predecessors. He was a brilliant clinician and researcher. An added facet, however, was the fact that he was a surgeon. This, in association with his interest in the nervous system, was a distinct advantage as he pursued research on neurological function and disease. He performed extensive experiments on the brain and spinal cord by using ablative as well as electrical techniques to create maps of the central nervous system. With associates Charles Beevor and Edward Schäfer, Horsley experimented on higher primates to approximate more closely the anatomy and physiology of the human brain. As stated in the biography by Paget,¹¹ Horsley coauthored eight papers, including “The Arrangement of the Internal Capsule,” “The Central Innervation of the Larynx,” and “Further Minute Analysis of the Motor Region.” Another meaningful contribution was a chapter in the Cunningham memoir, Volume VII, titled “Topographical Relations of the Cranium and Surface of the Cerebrum.” Horsley discussed the anatomical variations commonly related to age, race, sex, and cephalic indices as well as those secondary to elevated intracranial pressure, which also happened to be a subject of particular interest to him. Included in this chapter were detailed color drawings of cadaveric specimens from photographs of their plaster casts. According to Horwitz,⁸ these drawings illustrated the relationships of cortical gyri and sulci to the overlying cranial bones.

Nevertheless, others reported first on successful resection of intracranial neoplasms. In 1881, Dr. William MacEwen of Glasgow, Scotland, reported in *The Lancet* the successful removal of a left frontal meningioma in a 14-year-old girl 2 years earlier. His localization of the tumor, however, had been aided by hyperostosis of the skull above the left orbit. This cosmetic deformity had actually been the presenting complaint, but a few days after her admission to the Glasgow Royal Infirmary the patient began experiencing seizures that rapidly progressed from intermittent focal, to secondary generalized, to status epilepticus finally, at which point they became life threatening. Dr. MacEwen operated using the external deformity as a marker for the point of entry. The tumor was removed, and the young girl survived. This was no small task at this time in the history of brain surgery, and over several months the patient regained much of her strength from the postoperative right hemiplegia, and her seizures ceased.¹⁰

Contemporarily, in Italy, Francesco Durante reported a similar case of intracranial neoplasm resection performed in May 1884. A 35-year-old woman with a 3-month history of anosmia and a lowered and outward-drawn left eye came seeking help. Once again, the obvious visible abnormalities provided the necessary insight for surgical approach and tumor localization. Durante performed a large left frontal craniotomy and removed an “apple-sized sarcoma.” The patient recovered from the surgery without incident.³ This success notwithstanding, surgeons had still not succeeded in localizing and removing an occult neoplasm.

In November of 1884, a cerebral tumor was diagnosed by Dr. Hughes Bennett and resected by Dr. Rickman Godlee in London. The patient, a 25-year-old farmer, had experienced mouth twitching on the left side, which had started 3 years before presentation. These occasional episodes evolved into “fits” that began with a strange feeling in the left side of the mouth, progressed to involve the left upper

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and lower extremities, and finally culminated in loss of consciousness and full body convulsion. These seizures continued with intermingled twitching of the mouth and hand. Then, 6 months before presentation, weakness was noted in the hand and fingers on this side and also progressed to produce a limp in the left lower extremity. The physical examination was remarkable for the left hemiparesis as well as multiple small retinal hemorrhages on fundoscopic examination of the right eye. Based on these findings, a diagnosis of a right-sided cerebral tumor was made and the lesion was localized to the cortex near the middle third of the of the rolandic fissure. By using various external landmarks and their relationship to underlying cerebral structures, Dr. Godlee was able to make a surprisingly small craniotomy in this area. The tumor was found directly under the open dura mater. The operation was initially successful; the patient began to recover with reasonable preservation of function. Nevertheless, less than 1 month later, he died of a persistent and overwhelming wound infection. Despite the outcome, this case was highly publicized because it illustrated the ability to locate accurately and excise a tumor based solely on the patient's history and the findings on physical examination.¹

The ability to localize a lesion was expanded in 1895 by Wilhelm Roentgen with his discovery of x-rays. Cushing believed that a plain x-ray study was of limited value but did mention its help in localizing lesions in the vicinity of the sella turcica. The development of the pneumoencephalogram by Dandy in 1918 ushered neurosurgeons into the modern age of radiological localization of lesions of the central nervous system. Jackson, Ferrier, Horsley, and Charcot will always be remembered for their contributions to cerebral localization. Nevertheless, their work is now largely overshadowed by innovations in the field of radiology.

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