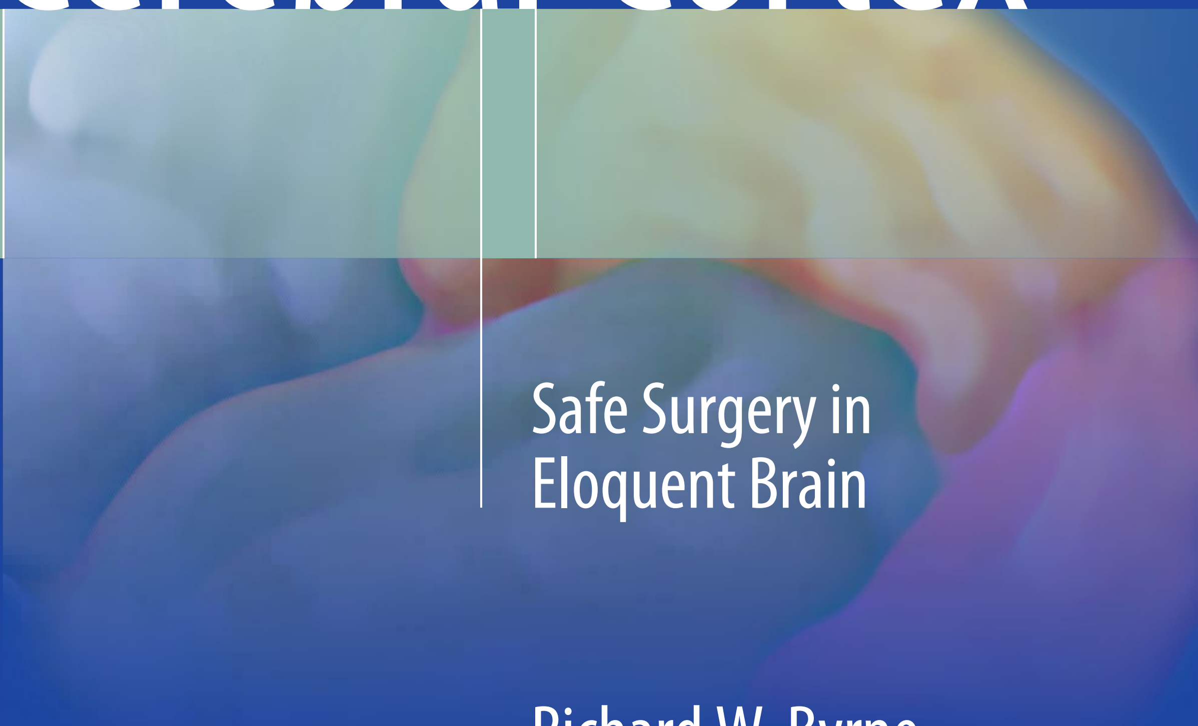
Functional Mapping of the Cerebral Cortex



Safe Surgery in Eloquent Brain

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Richard W. Byrne, M.D.

Foreword

It is an honor and pleasure to be asked to write a foreword to this splendid volume on *Functional Mapping of the Cerebral Cortex*.

After having spent 35 years performing resections of epileptic foci, and trying in each case to determine with precision where we are over and within the brain, it is refreshing, instructive, and useful to see such an updated gathering of practical information on this important topic.

Techniques of cerebral mapping were developed mostly for resection of epileptic foci and brain tumors. While the early history of the brain motor responses upon stimulation reflects the collective and cumulative efforts of many neurosurgeons, the confirmation of the sensory strip resulted from the work of a single man, Harvey Cushing, in 1909.

If one had to pick a single work on cerebral mapping characterized by its thoroughness and usefulness, it should be that of Penfield and Boldrey of 1939. It illustrates the early and systematic work of Penfield and collaborators at the Montreal Neurological Institute. Over the years, the so-called Montreal procedure was used for all types of resections but mostly for temporal lobe epilepsy. Stimulation studies were systematically carried out under local anesthesia to identify the sensory strip, mainly the tongue area, to determine the position of the central sulcus and the extent of the resection along the Sylvian fissure. Identification of speech centers was more complicated, giving rise often to negative responses and anxiety. The parameters used became of paramount importance.

There came a point in time where enough physiological data gathered could be transposed to morphology. To what extent the surgeon can nowadays rely on morphological landmarks and preoperative data only is of crucial importance. With the advent of three-dimensional reconstruction and the integration of physiological findings, the process of cerebral mapping starts before the actual surgical procedure. Using navigation, the preliminary identification of the motor, sensory, and speech centers can be used for centering the craniotomy and zooming on the areas to be visually recognized and stimulated. This approach has led to smaller craniotomies often to the detriment of electrocorticography. However, in spite of their usefulness and precision, these techniques have not replaced the need for peri-operative confirmation. They rather serve to optimize the whole process of localization.

A significant advantage of peri-operative stimulation is the need to have the patient awake and cooperating, which allows not only for the acquisition of physiological data but also for the detection of an eventual early and reversible deficit. Close collaboration with anesthesia is essential and the expertise in conducting awake procedures cannot be overemphasized.

A safe removal does not relate strictly to the extent, compactness, and cruciality of the tissue resected but also to the consequence of vessels occlusion deliberate or not, venous or arterial, in the actual process of resection.

The various techniques described in this book will help the young neurosurgeon interested in the resection of epileptic foci and brain tumors to develop his own way of finding out precisely where he is over and within the brain, recognize eventual pitfalls, and avoid complications.

Montreal, QC, Canada André Olivier, M.D., Ph.D.
June 2015

Preface

The purpose of this book is to give practical guidance to clinicians and scientists (neurosurgeons, neurologists, neuroradiologists, neurophysiologists, neuropsychologists, and those in training in these disciplines) in their encounters with the difficult and commonly encountered problem of treating patients with lesions in eloquent cortex. These cases represent some of our greatest challenges in clinical medicine, but they also represent our opportunity to potentially make the greatest positive impact for our patients. Through careful consideration of the indications for an intervention, proper choice of brain mapping technology, and proper execution of brain mapping techniques, we are now able to offer some of our most challenging patients a safer and more effective intervention. This is made possible through a combination of advantages that brain mapping offers. First, brain mapping techniques may identify the cases in which we should not offer an invasive procedure, saving patients from operative morbidity. Second, brain mapping can show us when we can offer a more radical procedure than indicated by our imaging technology and by presumed functional localization. Finally, brain mapping can show us when we need to stop in order to avoid permanent morbidity by giving preoperative localization clues and intraoperative immediate feedback on the impact of our intervention.

The art and science of brain mapping once was the purview primarily of epilepsy surgeons. In fact, it is in this aspect of my practice that I learned and became comfortable with the various techniques of brain mapping. As both brain mapping and operative technology have advanced over the past 25 years since I first participated in a brain mapping operation, it has become more clear that this discipline could be adopted more widely by practitioners who rarely encounter operative epilepsy conditions, but rather commonly encounter intra-axial lesions such as glioma, metastasis, and congenital and vascular lesions. In fact, intra-axial lesions have become a common indication for brain mapping. Widespread acceptance and adoption of brain mapping techniques has occurred over the past 10 years. However, many practitioners have not had extensive training in brain mapping techniques and lack an understanding of the advantages and limitations of the various brain mapping techniques available. As such, many clinicians seek training in brain mapping in order to bring the advantages of brain mapping to their patients. While teaching and training residents and practicing clinicians in brain mapping, it became apparent to me that there was a need for a practical guide to brain mapping, bringing together the extra- and intraoperative techniques and technologies. This textbook is our effort to provide this guide. In doing so, I have partnered with many of the most respected leaders in this field who have generously given their clear and careful practical guidance in their particular expertise. I am grateful for their generosity in sharing their time and experience.

The structure of the textbook emphasizes the progression of the various ways that eloquent cortex can be identified. First and foremost is anatomy. In this chapter the classic anatomic-functional correlations essential for any neurosurgeon, neurologist, or neuroscientist to achieve an understanding of brain mapping are described. As neuroanatomy is highly conserved in evolution, knowing the sometimes subtle but reliable nuances of neuroanatomy is all that is necessary to proceed with safe treatment in many cases of nonlesional or lesional neurosurgery remote from eloquent cortex. This may also be the case in a limited number of well-circumscribed lesional cases located at the surface in and around eloquent cortex. There are, however, limits to this anatomical localization. Certainty of anatomic localization is often limited in identifying areas necessary for speech function. Variable localization and in some cases even lateralization of speech function introduces uncertainty in an area that requires near certainty. Furthermore, the nature of lesional neurosurgery necessarily causes distortions in normal anatomy, and in some cases neural plasticity may cause relocation of function. Because of this, preoperative and intraoperative adjuncts in functional localization are often necessary.

The various forms of image-based functional localization have evolved over time to become more reliable and more available to practitioners. This has paralleled rapid advances in imaging technology. The history of the development of functional localization highlights the necessary reliance of brain mapping on the progress of applied technology. Early mapping efforts focused on direct recording of evoked potentials and direct cortical stimulation. Indirect noninvasive forms of mapping based on functional metabolic, electrical, and magnetic signals have continued to expand our understanding of brain function. Their ability to display all brain regions involved in a cerebral function has been their strength, but also their weakness. From a research perspective, this high level of sensitivity is ideal. From an operative decision-making standpoint, this is a weakness.

The ideal mapping technique from the standpoint of a clinician balances sensitivity and specificity for localization of truly essential cortex, as opposed to all merely involved cortical areas. Because of this, a major focus of this textbook is intraoperative and extraoperative cortical stimulation mapping techniques and practical decision-making. The described technique of "negative mapping" is described extensively in one chapter and emphasizes the advantages of this technique in brain tumor cases. Cortical stimulation mapping, with or without the awake technique, remains our gold standard in cases of lesional and nonlesional pathology involving eloquent cortex. This mapping may be done intra- or extraoperatively and can be combined with extra-operative imaging and metabolic mapping technologies. Because cortical stimulation mapping identifies essential cortex, and imaging technologies display the wider areas of diffusely involved functional cortex, the techniques are complementary. We have gathered several chapters with slightly different points of view on indications, protocol, and technique to highlight the variety of ways cortical mapping can be used in both lesional and nonlesional epilepsy and brain tumor surgery. These chapters along with chapters highlighting indications, extraoperative mapping, intraoperative evoked potential monitoring, and anesthetic techniques offer the clinician and scientist a guide to the various options available for modern brain mapping. We have highlighted key points and have provided illustrative cases demonstrating practical applications of brain mapping.

We have also included chapters hinting at what may become a growing part of the future of brain mapping. Intra- and extraoperative techniques of gamma frequency EEG mapping and extraoperative transcranial magnetic stimulation are quickly advancing through the research phase and may soon become a routine part of clinically applied brain mapping. Although today's practitioners are becoming well versed in the accepted techniques and technology available now, we will all welcome the day when these and other technologies will mature and help us make caring for patients with pathology in eloquent cortex safer and more effective.

Finally, I would like to end with a word about clinical judgment. No matter what technology is available to clinicians treating patients with pathology in eloquent cortex and eloquent white matter connections in the brain, it must be emphasized that it takes experienced clinicians working in multidisciplinary teams with a well-informed patient to weigh decisions to operate, or not operate in these cases. The same applies to the choice of which technique or technology to employ. No technique that we describe here completely guards against operative morbidity. In fact, operating in eloquent cortex commonly leads to temporary morbidity that must often be accepted and anticipated by the practitioner and patient alike. A judicious balancing of the risks of an intervention versus the risks of the natural history of a pathological process, whether it is epilepsy, tumor or other, is the proper starting point. The final decision to intervene will in turn be made based on the wide variety of clinical factors that treating clinicians routinely encounter in treating these patients, upon their comfort level with the techniques, the resources available at their institution, and upon the wishes of the patient.

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Historical Perspective on the Development of Cerebral Localization, Cerebral Cortical Motor Stimulation, and Sensory Evoked Potentials

James L. Stone, Ashley N. Selner, and Vimal A. Patel

John Hughlings Jackson (Fig. 1), often called the "The Father of Neurology" was a keen-eyed observer with a passion for detail and brooding intelligence, which enabled him to see general laws emerging from details [1]. This remarkable British theorist by 1861 deduced motor activity to be the basic function of all nervous systems, proposed the anterior and posterior cerebrum being predominately motor and sensory respectively, and that motor and sensory brain centers represent sensorimotor movements not muscles. His thoughtful analysis based on the study of seizure patterns and neurological abnormalities demonstrated the somatotopic distribution of human motor and sensory functions across the human cerebral cortex [1, 2]. He further believed that higher levels of integration evolved to exert more extensive and progressively finer control … the cerebrum and cerebellum invariably work together … coordination being a function of the entire nervous system [1, 2].

Also in 1861, *Paul Pierre Broca* of France demonstrated clinicopathologically that the third left frontal convolution was necessary for motor/articulate speech and based on such localization 10 years later trephined and drained a traumatic abscess [3]. However, the concept of cerebral localization of function remained controversial for the next 10–15 years although evidence accumulated in animals including lower primates and man.

In 1869 or early 1870 *Eduard Hitzig* a budding neurologist and electrotherapist in Berlin, Germany found that delivering galvanic currents between the ear lobe and mastoid process of patients induced involuntary ocular movements and vertigo [4]. Believing he had electrically stimulated a brain center (later work disclosed this was probably peripheral vestibular in origin) he sought the help of *Gustav Fritsch*, a young physician with research experience [4]. During the year 1870 Fritsch and Hitzig in Berlin working with dogs, and following their lead in 1873—*David Ferrier* in England working with monkeys—proved electrical stimulation applied directly to the pre-central frontal cortical surface produced contralateral motor movements. Conversely ablation of this area resulted in contralateral paralysis [5–8]. Fritsch and Hitzig evidently used galvanic current (they talk of a chain of batteries, anode, and cath-

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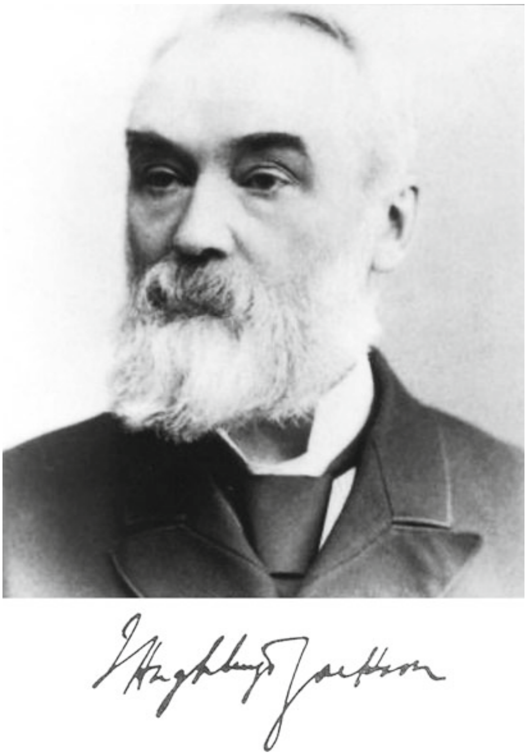

Fig. 1 John Hughlings Jackson (1835–1911). From David W. Loring, History of Neuropsychology Through Epilepsy Eyes, Archives of Clinical Neuropsychology, 2010, by permission of Oxford University Press

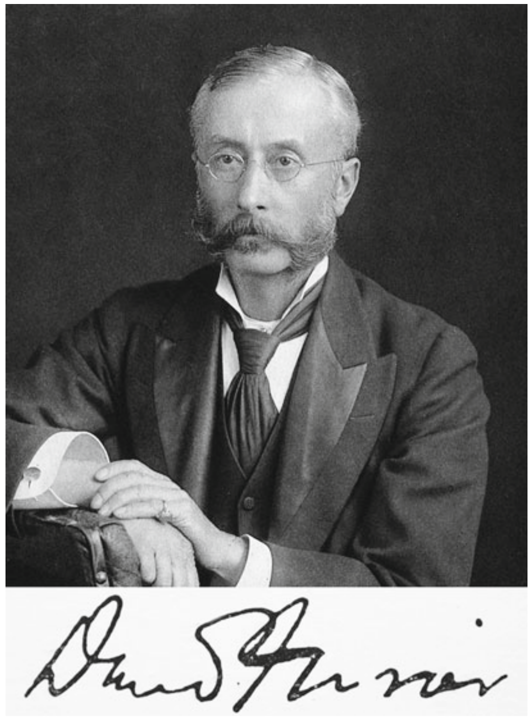

Fig. 2 David Ferrier (1843–1928)

ode, but also used a secondary induction "spiral") and only the frontal (anterior) cortex produced motor responses which they mapped out with precision [9]. Ferrier's choice of faradic over galvanic stimuli was considered an important advance over the earlier work in elicitation of sustained and deliberate, instead of twitch-like or tetanizing movements [10].

In 1874 *Roberts Bartholow* of Cincinatti, Ohio, a neurologist familiar with electrotherapeutic methods and the above research, delivered faradic currents through insulated needles placed in the postcentral/parietal lobes of a consented volunteer with carcinoma of the scalpand erosion of the skull. He obtained contralateral sensory phenomena, motor movements, and seizures [11–14].

David Ferrier (Fig. 2) went on to extend his convincing cerebral localization work to studies on apes [5, 6, 10, 15], and tremendous research activity ensued world-wide to elucidate the physiology and anatomy of the nervous system. Ferrier, additionally a highly respected London neurologist predicted "the unfailing safety of experiments upon animals made it clear that similar results would soon be achieved on man himself" [16]. Charles Sherrington (see below) a noted British neurophysiologist working several decades later remarked "(Ferrier's) work was the actual pioneer-step leading to modern cerebral surgery … (and thus) to Ferrier rather than to the surgeons is primarily due the origin of modern cerebral surgery" [17].

In the 1880s *Victor Horsley* (Fig. 3a), an academic London surgeon, began extensive cerebral cortical motor mapping and pyramidal tract studies in the monkey and higher apes using direct cortical stimulation. Horsley like Jackson came to believe the pre- and postcentral gyri were functionally sensorimotor and obtained similar motor responses from each region [18–20]. In early 1886, Horsley was given a surgical appointment to London's National Hospital for the Paralyzed and Epileptic at Queen Square.

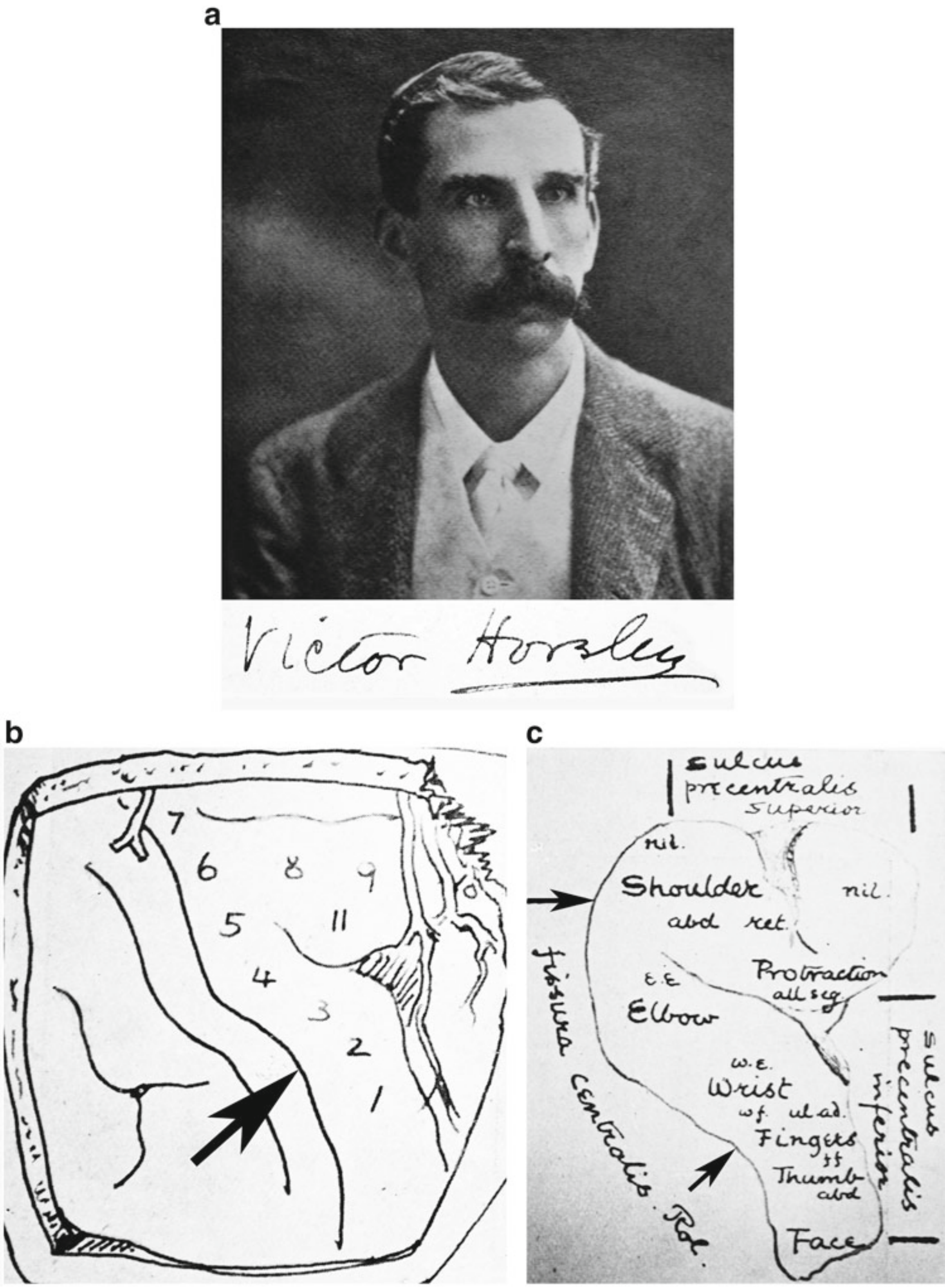

Fig. 3 (**a**) Victor Horsley (1857–1916). (**b**) Sketch of a right-sided craniotomy in 1908 showing areas of faradic motor stimulation of the pre-central gyrus. *Arrow* shows central sulcus. (**c**) Sketch of the gross, excised central gyrus. Focal seizures of the left arm ceased, and 1 year later partial recovery of left arm voluntary function, astereognosis, and slight tactile anesthesia of the left hand [18]. Reproduced from (The British Medical Journal, The Linacre Lecture on the function of the so-called motor area of the brain, Victor Horsley, volume 2, 1909) with permission from BMJ Publishing Group Ltd

Hughlings Jackson, a senior Queen Square neurologist visited Horsley's laboratory and was "greatly impressed by the certainty and precision with which Horsley by gently faradizing a small part of the cortex could bring a monkey's thumb and forefinger into opposition. At once Jackson recalled a patient … who developed epilepsy, each attack commencing with such a movement as he now saw evoked in the monkey by electrical stimulation." [21].

Beginning in 1886 electrical stimulation of the cortex during operations on patients was extensively performed by Victor Horsley in London (Fig. 3b), and the following year by *W.W. Keen* in Philadelphia who was the first to obtain a response in the leg [22–27]. Horsley's first three craniotomy patients at Queen Square had intractable seizures. Each had a lesion within or near the motor cortex—a cortical scar, small tumor, or cyst—and responded favorably to localized excision [21]. Excision of cortical "motor points," was then believed to be a promising treatment for focal motor seizures. Additionally, Horsley considered the identification of cerebral motor points a definitive aid to localizing subcortical lesions in patients with motor findings [28]. Consequently cortical motor stimulation was highly instrumental in initiating and building confidence in the new special field of neurological surgery [29]. From this work Horsley, as well as Jackson who reached his conclusions from close clinical observations, were convinced the pre- and postcentral gyri were functionally sensorimotor and similar motor responses could be obtained from each region [18, 19].

Beginning in the mid 1880s the neurophysiologist *Charles S. Sherrington* (Fig. 4) and associates began extensive experimental study of brain and spinal cord reflexes in regard to the pyramidal tract, motor control, and feedback, and about 1900 began cerebral cortical stimulation studies utilizing about 20 great apes (anthropoids—gorilla, orangatang, chimpanzee) [30, 31]. Using unipolar faradization by induction coil stimulation they obtained clear motor responses in the higher apes they believed were more distinctive and easier to elicit from the pre-central cortex composing the anterior wall of the central sulcus of fissure of Rolando and adjoining surface of the pre-central gyrus [31, 32]. The young, recently trained American surgeon *Harvey Cushing* (Fig. 5a) visited Sherrington for the month of July 1901 and assisted with the surgical exposure and cerebral cortical stimulation studies on these anesthetized but arousable great apes [7]. Sherrington explained to Cushing "the disparity of his and the old observations is that Ferrier, who did the earliest work on the monkey expecting wide areas [of representation], used strong currents and succeeded in calling out responses which, [Sherrington says], however, were not as distinctive as the ascending frontal (pre-central) convolution responses" [7]. In regard to Cushing's question as to the primary cortical area for cutaneous sensation, Sherrington suggested it was the postcentral gyrus and Cushing in a letter to his father went on to say "the chimpanzee yesterday

Fig. 4 Charles S. Sherrington (1857–1952)

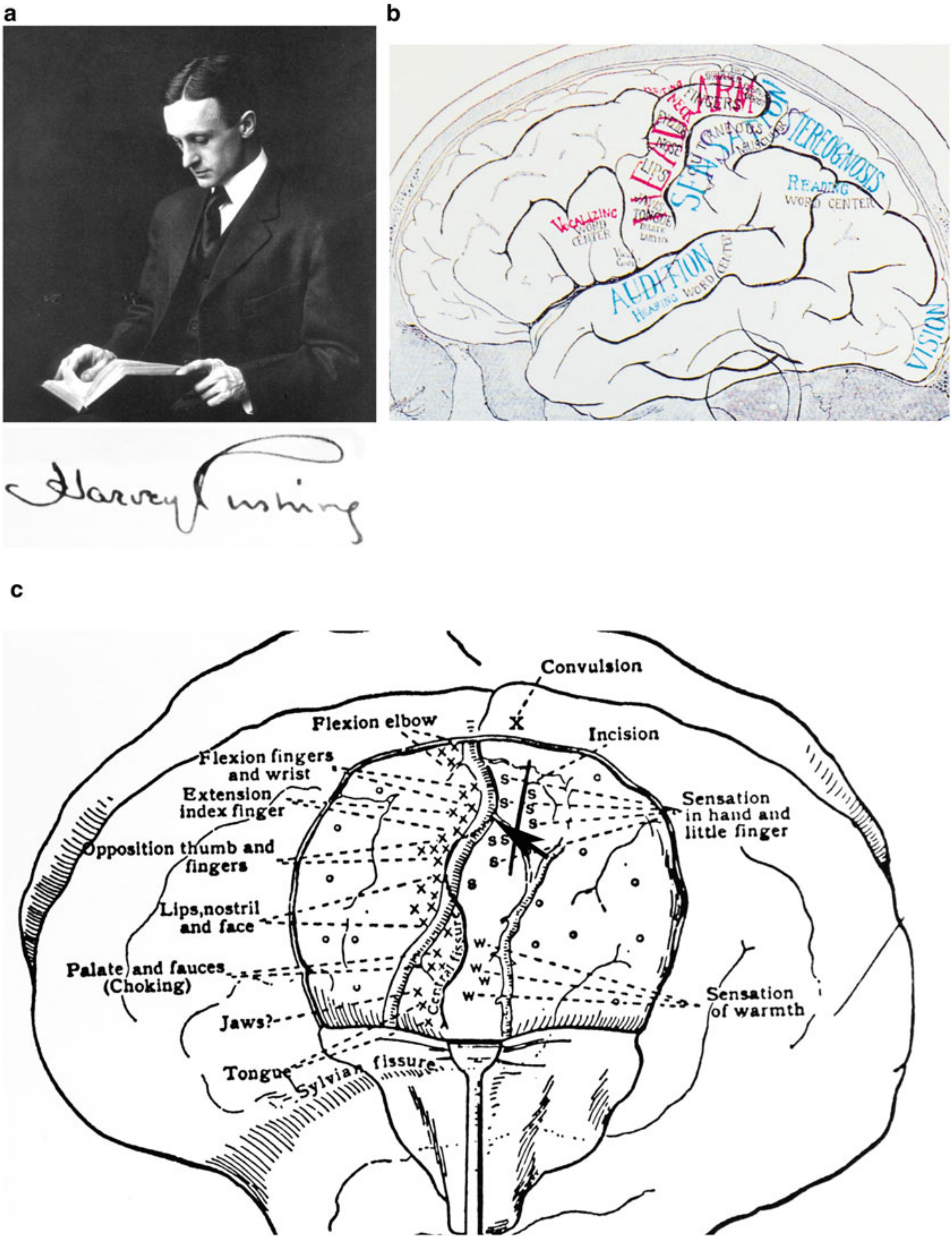

Fig. 5 (**a**) Harvey Cushing (1869–1939). (**b**) Drawing of primary motor and sensory cortex, 1908 [33]. (**c**) Drawing of pre- and postcentral gyrus, showing central sulcus of Rolando (*arrow*) and genu [34]

responded like a sensory response when this area was stimulated. The motor responses are slow and different from the motor cortex ones, but each time when the animal was stimulated there it opened its eyes … evidently the recipient of some great stimulus." [7].

Cushing returned to Johns Hopkins, gained further experience in neurological surgery and human cortical stimulation (Fig. 5b) [34]. At that point in his career he had performed cortical stimulation for motor point mapping and central sulcus localization in more than 50 anesthetized patients in the removal of tumors or other lesions [34]. A few years earlier an unanesthetized awake patient, during preliminary palpation of the exposed postcentral region, surprised Cushing by reporting a "focal sensory attack" or sensory paresthesia [35]. This prompted Cushing to report two epileptic patients with focal sensory auras who underwent unipolar faradic stimulation of the postcentral gyrus, in the hope of improving the operative localization of the central fissure of Rolando, as well as improve localization and removal of "subcortical irritative lesions of the immediate postcentral field" (Fig. 5c) [34]. Both were operated awake in a second stage under local anesthesia. Very brief faradic stimulation was applied, and with the same current strength—motor and somatosensory impressions (numbness, tactile feeling) were obtained only from the pre- or postcentral gyri respectively. Although focal and generalized seizures occurred during stimulation, and in one patient stimulation of the postcentral gyrus produced transient focal/partial sensory phenomena identical to their typical sensory seizure aura—Cushing was unable to clearly delineate or remove a lesion in either patient [34].

Several of Cushing's above observations are of particular note despite being among the earliest human cases of clear somatosensory responses from postcentral gyrus stimulation. In his first case, Cushing comments upon "the characteristic configuration of the central fissure," and stimulation of the precentral gyrus gave "an opposing movement of thumb and fingers from points opposite to the unmistakable genu," and "below the evident middle genu" stimulation produced contraction of the contralateral face [34]. If not obscured by sulcal veins, this "omega-shaped landmark or genu" is consistently seen between the superior and middle frontal gyri bulging into the central sulcus (convex posteriorly). The gyral banks of this sulcal region were noted by Broca and represent the pre- (primary motor) and post- (primary sensory) central cortical hand areas [36, 37].

In these two cases the evoked sensations were limited entirely to the hand and arm, and Cushing questioned whether this means there is an "especially wide cortical representation for afferent impulses from this region" or whether their hand and arm were unduly excitable owing to their seizure tendency in these particular patients [34]. At that time motor and sensory cortical homunculi had not yet been constructed. In the second case, the central sulcus was less typical and obscured by a prominent vein but Cushing obtained motor responses from the gyrus anterior to the vein. This additional recording of sensory responses on the posterior gyrus stimulation for Cushing confirmed the correct location of the central sulcus [34].

Fedor Krause (Fig. 6) was a well-known late nineteenth and early twentieth century general and neurological surgeon from Berlin, Germany who was strongly influenced by the classical cortical stimulation work of Fritsch and Hitzig, Ferrier, and Sherrington [38–40]. Krause as early as 1893 began human cortical stimulation under partial anesthesia and used monopolar faradic stimulation, at the lowest possible current for motor stimulation to avoid unwanted stimulation of adjacent cortical regions [38–40]. Krause had extensive experience with human motor stimulation and produced a quite detailed motor map. Being highly supportive of Sherrington's work in the higher apes, it is likely any human motor responses from stimulation posterior to the central sulcus would have been considered by Krause secondary to current spread. With neurologist Hermann Oppenheim they very carefully documented the clinical results of many cortical excisions including complex sensory and perceptual findings, agraphias, and noted lesion variability in producing aphasia [39, 40]. Krause elevated an old frontal depressed skull fracture in a patient with frequent seizures beginning with head turning to the opposite side. Cortical stimulation of

Fig. 6 Fedor Krause (1857–1937)

the second frontal gyrus anterior to the precentral region reproduced the aversive head motion heralding the attack, and the patient was greatly improved after decompression. Krause corroborated the fact that the central region contains separate motor and sensory centers "the relation of the anterior central convolution to the posterior is that of one twin to its fellow" [40]. Krause mapped cortical motor function to aid with the safe removal of cerebral tumors, and in cases of refractory epilepsy to reproduce the focus of Jacksonian seizure onset [40]. By 1910 he reported 29 patients in whom he had identified and excised a cortical focus or "primary spasmic center," thereby "diminishing the seizure tendency" [38].

Like Cushing, Krause was concerned over uncertainty in locating the central sulcus of Rolando related to venous variability or obscuration of the sulcus. Krause more definitively concluded "at the operating table we possess in faradic simulation of the cerebral cortex an indispensable method of great diagnostic value. It offers the only possibility for exact localizations in the anterior central convolutions [40].

An extraordinarily talented German neurologist and neurological surgeon *Otfrid Foerster* (Fig. 7a) of Breslau, Germany, gained experience in electrical stimulation of the human cortex beginning in 1905. He was a highly trained neurologist and self-taught neurosurgeon who began by operating on peripheral nerves during World War I. Many of his earlier patients were war veterans with intractable posttraumatic epilepsy. By 1931 he had gathered information on more than 150 cases of cerebral cortical stimulation and his experience exceeded that of any other neurosurgeon [42–46]. Foerster operated predominately under local anesthesia to facilitate cortical mapping using unipolar galvanic stimulation to reproduce the subject's clinical seizure, and excised a clear cortical focus or scar. Foerster and Krause both emphasized the importance of keeping the cortical surface dry and draining or sponging away any pooling of cerebrospinal fluid or blood [40, 43].

In regard to pre-central gyrus stimulation, Foerster noted that the motor threshold current to elicit a response in area 4 (0.3–6.0 mA, average about 0.5–1.5 mA) was lower than that of motor area 6a, but there was much individual variation. He determined the effects of stimulating either area 4 and area 6a both depend on the integrity of the pyramidal tract, but he came to believe area 6a was dependant on a relay utilizing area 4 [43, 44].

Postcentral gyrus, area 3,1,2 stimulation usually produced paresthesias and seldom pain. Here Foerster found a detailed somatotopic distribution similar to the pre-central gyrus. In addition, areas 3,1,2 reacted to stimulation not only with sensory effects, but motor effects as well. These motor effects additionally resembled those of pre-central convolution stimulation as each focus responded with an isolated movement of a single segment of the extremities or single part of the body. However, the electrical current threshold to evoke motor responses from the postcentral convolution was markedly (2.0–4.0 mA) higher than that of the pre-central gyrus (average motor threshold: postcentral—3.0–4.0 mA; pre-central—0.5–1.5 mA). The higher the threshold of area 4, the correspondingly higher the motor threshold of areas 3,1,2 [43, 44].

Foerster reminds us that destruction of the postcentral area is followed not only by defects in sensibility but also a disturbance in motility. Coordination of movements depends on the