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The Horsley-Clarke Stereotaxic Instrument: The Beginning

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Dr. Marshall received her Ph.D. in 1935 from the University of Chicago, where she also met and married Wade H. Marshall, and developed her lifelong interest in the Neurosciences. She was in the Aviation Medicine program at the NIH from 1943-46 and as a research physiologist from 1946-65. From 1965-75, she was a professional associate at the National Research Council with executive responsibility for the Committee on Brain Sciences which spearheaded the drive to found the Society for Neuroscience. She served as Acting Secretary-Treasurer for the Society in 1969-70. From 1975 to the present, she has been associated with the Brain Research Institute Neuroscience History Program in collaboration with Dr. Magoun. Dr. Magoun has in preparation a book on the history of the anatomy of the brain and played an active role in the revival of the Horsely-Clarke Stereotaxic instrument in Ranson's Institute of Neurology at Northwestern University in 1928. Dr Marshall can be reached at 213-825-3191.

INTRODUCTION

The encumbrance of a lack of precision in the placement of a lesion or stimulus in brain tissue delayed progress in neuroscience from the time when significant experimental neurophysiology commenced. Without knowing where the knife or electrode tip rested within the brain substance, replication and interpretation of findings were haphazard and inconclusive. There were other methodologic obstacles to be overcome as well, such as tissue hardening, sectioning, and staining, but imprecise experimentation was the great deterrent. Writing of the nineteenth century, that towering medical historian, Max Neuburger (1868-1955), stressed "In its efforts to attain precision, medical science...has achieved a 'rebuilding from the very foundations' " (1981, p.l). And again, "...everywhere there will be manifested a trend towards precision...the point of intersection between empiricism and speculation" (p.2).

Pierre Flourens was fully aware of the handicap of imprecision, writing in 1823 regarding the properties and functions of the vertebrate nervous system. He acknowledged that one could understand why Redi, Haller, Zinn, Lorry, and others had such contradictory results, "...observed such confusing phenomena in the animals which they mutilated so blindly and without knowing which part bore the mutilation..." (p.370). As the nineteenth century progressed, explorations of the surface of the living brain became commonplace but any success in trauma-free penetration below the surface and confidence in the findings was impossible until a method utilizing three-dimensional coordinates firmly grounded on the anatomic substrate became available. The events that delayed the widespread use of the Stereotaxic solution of the problem of imprecision constitute a fascinating historical inquiry.

MAPPING THE CORTICAL SURFACE

The traditional view that the brain surface was nonexcitable or that it responded en masse to stimulation (Flourens's holistic theory of equivalence of excitability) was shattered by the publication in 1870 of the work of two young German physicians, Eduard Hitzig (1838-1907) and Gus-tav Theodore Fritsch (1838-1927). They found a few discrete areas on the dog brain where galvanic stimuli produced contraction of muscles on the opposite side of the body. Although he was the junior author, Hitzig continued the work alone, extending it to the monkey. He summarized his subsequent life-work on the brain in the Hughlings

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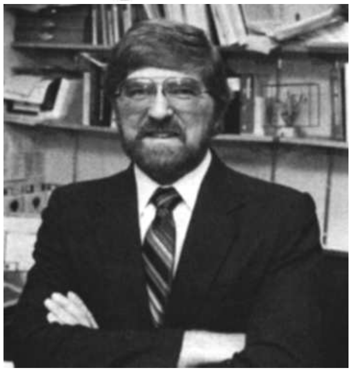

Editor's Column

Last year at the 1989 Society for Neuroscience Convention, we had the honor and enjoyment of displaying the second original Horsely - Clarke Stereotaxic Instrument. It had just been restored by David Kopf Instruments and was provided for the display by Drs, H. W. Magoun and L. H. Marshall. Dr. Marshall, with Dr. Magoun's help, has since written a wonderful monograph on the history of Stereotaxy and the Horsley-Clarke Instrument in particular. She has graciously consented to have parts of that history published as issues of the Carrier. The first part of the history appears here, and others will be published later.

The story of the development of the stereotax-ic method and instruments is a fascinating one and a real part of our heritage, although one of which most of us know little. We tend to take the Stereotaxic instrument for granted, not realizing that this vital instrument and technique did not always exist, but was developed over many years with great effort.

I believe that you will thoroughly enjoy the historical perspective that Drs. Marshall and Magoun bring to this narrative, and that as other parts of the history appear, they will become necessary reading for graduate students, and perhaps for practicing neuroscientists. We want to thank Drs. Marshall and Magoun very much_.fQr..shat_ ing the account given here of the development of the first Stereotaxic machine, and look forward to other parts of this history in future issues.

Dr. Marshall will be at the David Kopf Instrument booth at various times during the upcoming Society for Neuroscience Convention and we invite you to stop by to talk with her. She has many fascinating insights into the history and development of our science.

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Jackson lecture of 1901.

Cortical localization or mapping of function became a major experimental interest of the distinguished group of neurologist-surgeons centered in London in the last quarter of the nineteenth century. David Ferrier (1843-1928), appointed at the National Hospital (Queen Square), London and working at the West Riding Lunatic Asylum which had facilities for what were called recovery experiments, not only verified and extended Hitzig's results to primates but also had the audacity to superimpose a map of the responsive loci on the outline of a human brain, thus rashly extrapolating (and erroneously it turned out) from lower forms to man.

The first systematic exploration of the cerebral surface was by two other affiliates of the National Hospital, Victor Horsley (1857-1916), surgeon, and his associate, Charles Beevor. They plotted on a millimeter grid the silent areas as well as points posterior and anterior to the central sulcus from which they obtained contralateral muscular responses to electrical stimulation in an orangutan.

Victor Horsley's family was wealthy, socially influential, and talented, and he could not be other than a high achiever. His colorful career made him the ideal subject of biographies of which there have been several (see, for example, Paget, 1919; Jefferson, 1957; Lyons, 1966). A deft and quick surgeon, canny experimenter, and generous collaborator, Sir Victor (he was knighted at the age of 45) was the first surgeon to successfully remove a spinal tumor and to propound the concept that voluntary movement depends not only on the integrity of the corticospinal but also .on the extrapyramidal systems. Toward the end of his life Horsley became an ardent crusader, principally against alcohol, which he carried to extremes, and for reform of medical education. Although too old for military service at the outbreak of World War I, Horsley requested and received assignment to an active billet. He died from a combination of heat exhaustion and a sudden tropical infection while on duty with the Mediterranean Expeditionary Force.

Horsley's professional stature at the turn of the century is attested by his invited communications. In 1891 he and Francis Gotch presented the Croonian Lecture, England's most prestigious lectureship. The title was "On the mammalian nervous system, its functions, and their localization determined by an electrical method," and they claimed to be"...the first to determine by use of the electrical method the localization and quantitative estimation of either centripetal [afferent] or efferent impulses issuing from

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nerve centers in functional activity...." (p. 278-279). This was followed the next year by a chapter on the topographic relations of cranium and cerebral surface in Cunningham's influential text (1892). In that publication Horsley showed, in graphic detail, changes in the surface of the human brain from fetal stages to 111 years of age and also included comparative drawings of brain surfaces of monkeys and apes. In 1909 Horsley delivered the Linacre Lecture at St. John's College, Cambridge, titled "The function of the so-called motor area of the brain." The high caliber of those major writings justified the great esteem with which his peers regarded the successful neuro-surgeon.

Horsley had many collaborators, two of whom became distinguished in their own right. Geoffrey Jefferson (1886-1961), in his lecture celebrating the centenary of Horsley's birth and with whom he was associated for several years, gave a perceptive account (1957) of Horsley's life that stressed the broadness of scientific inquiry of his subject Sir Victor has been credited with a distinguished list of important early contributions to neurological science. In addition to those already mentionedintradural spinal tumor removal and the quantitative estimation of stimulation effects on function-Horsley proved that myxoedema and cretinism are due to thyroid gland destruction (MacNalty, 1957, p. 911); and confirmed in England Pasteur's method of immunizing animals against rabies (ibid., 1957, p. 912).

A second long-term collaborator was Robert Henry Clarke (1850-1926). Older by seven years, Clarke's relation to Horsley and his family was warm and personal, and "he was...the most treasured of the friends who used to come and stay...in the holidays" (letter P. Robinson to R.A. Davis, quoted in Davis, 1964, p. 1337). The two men were opposites; whereas Horsley achieved in scholarly pursuits, Clarke's schooling was marked by athletic successes, both in team sports and in horsemanship as well. As a biographer pointed out (ibid., p. 1333), Clarke was born into the best of Victorian times and had the personality to thrive "in this keen and stimulating environment." Clarke published some veterinary work carried out at the Brown Institution, of which Horsley was superintendent, and then became a collaborator after Horsley established (in 1896; see MacNalty, 1957, p. 913) a private laboratory behind the anatomy amphitheater at UniversityCollege London.

Horsley's research then centered on the cerebellum, which was attracting the attention of many investigators at that time. In collaboration with Clarke, he was utilizing electrolytic lesions and Marchi staining of degenerating axons in the study of that enigmatic organ's direct connections with the peduncles or spinal cord, begun in 1903 and published in 1905. Although not expressed in that 1905 paper, Horsley and Clarke later stated that theirs and others' results justified a "systematic enquiry into the function of the cer-ebellar cortex and nuclei, respectively....An essential preliminaryto further progress was to find...a means of producing lesions...which should be accurate in position, limited to any desired degree in extent, and involving as little injury as possible to other structures"(1908, p.47). It was clear that an improvement in technique was necessary before precise studies on cerebral function could go forward.

THE FIRST MODEL

The initial completely stereotaxic instrument did not suddenly emerge in full bloom and without antecedents from its inventor's mind. After the interest in cortical localization of muscle action was invigorated by Hitzig and Fritsch's stimulation experiments, transection and ablation of tissue in the central nervous system became important adjuncts to the experimental armamentarium, first for relating brain anatomy to muscle function and later for tracing fiber tracts. Knives mounted singly or in pairs and under micrometer rack and pinion control were inserted into brain tissue at predetermined depths. Variations were developed until in 1907 an innovative German physician-surgeon and experimentalist, Frederich Trendelenburg (1845-1925), whose name is immortalized in several contributions to medicine and surgery, described the myelotome, a multi-jointed and pivoted frame carrying a knife that could be moved in all planes. The knife handle projected to a brass sheet on which a stencil had been cut of the proposed lesion; by tracing the stencil outline, a small degree of reproducibility was possible. Tigerstedt's Handbuch (1912) described a two-coordinate system for guiding a needle, used by Carl Ludwig (1816-1895) and his school, for stimulation.

With frustration as catalyst, and a period of enforced leisure as opportunity, Robert Clarke developed a solution to the problem of precision and reproducibility. While recovering from pneumonia, Clarke occupied himself by planning a device based on geometric principles utilizing three coordinates to overcome the inadequacies of previous methods. Encouraged by Horsley's approval, Clarke designed and supervised the construction of a rectangular stereotaxic "machine" by James Swift, a machinist at Palmer and Company in London. As they explained in the first published report of the device (Clarke and Horsley, 1906), the problem in studying the structure and function of the cerebellum was two-fold: "...localizing deep centres and conveying

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sthe stimulation on electrolytic needle to them" (p. 1799).

In that short "preliminary communication," after a relatively unclear presentation of the stereotaxic principles on which the design was based (see Kreig, 1975, pg. 2 for a lucid explanation); four parts were described; the frame, the carrier, the vulcanite needle holder and the needle, a nickel-plated 24- to 26-gauge steel wire insulated to within 1 millimeter of the tip by "a glass vaccine tube about two sizes larger." The ease with which the device could be converted from stimulation to making a lesion whose locus could be later confirmed histologically was emphasized. The results of a few stimulation experiments were described, the most interesting being that " [t]he effects produced on the muscles are the same as those obtained by direct excitation of the [cerebellar] nuclei."

In spite of its purely English origins, the machine was not presented to the medical community in England but in Canada. A year before the preliminary note (1906), Horsley demonstrated the new device at the 74th annual meeting of the British Medical Association, held in Toronto. The report of the section of Physiology stated: " [T]he next item was a demonstration by Sir Victor Horsley and Dr. R.H. Clarke (London) of an apparatus for localizing and stimulating or destroying by electrolysis points inside the cerebellum. By means of this instrument localized areas of grey matter in the deep nuclei of the cerebellum were destroyed, and as a result of investigations thus made they concluded that the only efferent motor centres in the cerebellum are those for movements of the head and eyes. The cortex cerebelli was relatively inexcitable, and was a sensory receptive apparatus" (Anonymous, 1906, p.633).

Five years elapsed between first identification of the need for a better method and publication (Horsley and Clarke, 1908) of the specifications for the frame, the cerebellar electrode carrier, several types of "needles," and a hand saw for cutting slices of frozen cat or monkey brains in 1-or 2-millimeter thicknesses. That 79-page article presented sections on rectilinear topography, electrolysis, and stimulation in addition to the detailed, fully labeled drawings of the instrument itself. At the time of publishing the paper, they had been testing the instrument for three years which was developed, they wrote, "[t]o meet our immediate necessities...." (p.49). To satisfy the anatomical reference requirements, three series of stained, 2-millimeter-thick sections cut in sagittal, frontal, and horizontal planes were prepared and photographed, on which a superimposed grid provided the coordinates of individual brain structures. Horlsey was an accomplished photographer and much of this work was carried out in his residence; the special microtome they used was developed by Clarke. As in the preliminary report, a future publication of their results was promised but never materialized, perhaps because the authors were exhausted by the attention to detail with which they examined every technical facet of their "new method".

The use of electrolysis to produce precisely placed, circumscribed lesions is especially interesting. At least two authors, MacNalty (1957, p. 913) and Paget (1919), claimed that Horlsey was the first to do so. The 1908 paper disproves this, however as with characteristic thoroughness, the authors presented the previous work of which they were aware before describing their own studies (see Horsley and Clarke, 1908, p. 86 ff.). They assigned priority to Golsinger in St. Petersburg (1895) but were unable to see the original report, which was quoted by Gustav Roussy, who in 1907 had five of twenty operated animals survive with successful thalamic lesions produced by electrolysis. The British workers also described the prior description of biopolar electrolysis (1898) of Sellier and Verger in Bordeaux, and its use in an experimental study on five dogs with localized lesions of the thalamus (1903). The significant contribution of Horsley and Clarke in 1908 was their experimental analysis of several methods of producing the lesions (for example, sparks or constant current) and their reasons for choosing from many observations the "rough average quantities and proportional effects as follows: Kind of Lesion-simple anodal; Size of lesion-2.7 mm.; Quantity of current-3 ma.; Duration of electrolysis-1.8 min. The 1908 paper presented an abundance of histologic sections demonstrating the degree of necrosis and edema at various times after production of the lesion.

The full impact of this monumental develop-ment-the apparatus itself-was not realized until much later. The instrument has been compared (Tepperman, 1970) to Leeuwenhoek's microscope and Galileo's telescope as a technological innovation that made possible new fields of scientific research and was catapulted far beyond its immediate application.

Perhaps its most colorful evaluation was that of Horsley's authorized biographer, Stephen Paget. He wrote that the stereo-taxic apparatus "devised by Clarke [was]... probably the most complex of all the mathematical instruments of physiology, for the exact

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directing of an insulated electrolytic needle by graduated movements in three planes. Thus moving by hairbreadths, and on planes exactly determined, they were able to produce a minimal electrolytic lesion...." (1919, p. 189). One can only marvel at the meticulous validation of its utility that was lavished on it by the instrument's developers and wonder why its adaptation by other investigators was delayed so long.

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Recently, we received a question from a reader and want to help him get an answer. Have you or anyone you know about impaled liposomes with microelectrodes to study membrane potentials of these artificial cells? If so, please write or call:

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A number of years ago, L.A. Geddes wrote a book entitled Electrodes and the Measurement of Bioelectric Events. Unfortunately the book went out of print. We have been informed that the information in that book and much more is available in the book Principles of Applied Bio-medical Instrumentation by Geddes and Baker (1989) published by Wiley. This would be a good source of information on microelectrodes, recording and stimulation.