



8 History of Stereotactic Surgery in Great Britain

E. A. C. Pereira · A. L. Green · D. Nandi · T. Z. Aziz


The Horsley–Clarke Apparatus


Stereotaxis was the name given to a procedure and apparatus invented in London by the Englishmen, Horsley and Clarke. Before then, the German Dittmar had used a guided probe to transect rodent medulla in 1873 [1], and Zernov in Russia had described an encephalometer enabling brain surface localization in 1889 [2]. Neither technique enabled targeting with respect to a fixed three-dimensional Cartesian coordinate system.

Sir Victor Alexander Haden Horsley (1857–1916;  *Figure 8-1a*) was the first neurophysiologist who was also a neurosurgeon, pioneering a Great British tradition of such hybrid scholars particularly prevalent in the stereotactic community. His uniquely deft approach to neurosurgery – derived from experiments upon over 100 primates – made a reputation such that “the Staff intended to have Horsley and nobody else” when tenure became available at the National Hospital for the Paralyzed and Epileptic in Queen Square in 1886 [3,4].

Robert Henry Clarke (1850–1926;  *Figure 8-1b*) studied medicine at St. George’s Hospital in London before surgical training in Glasgow. He worked with Horsley in London in the late 1880s [5]. Throughout the following decades, they became intellectually consumed by the experimental challenges of cerebral localization of motor function following the seminal work of Hughlings Jackson and others.

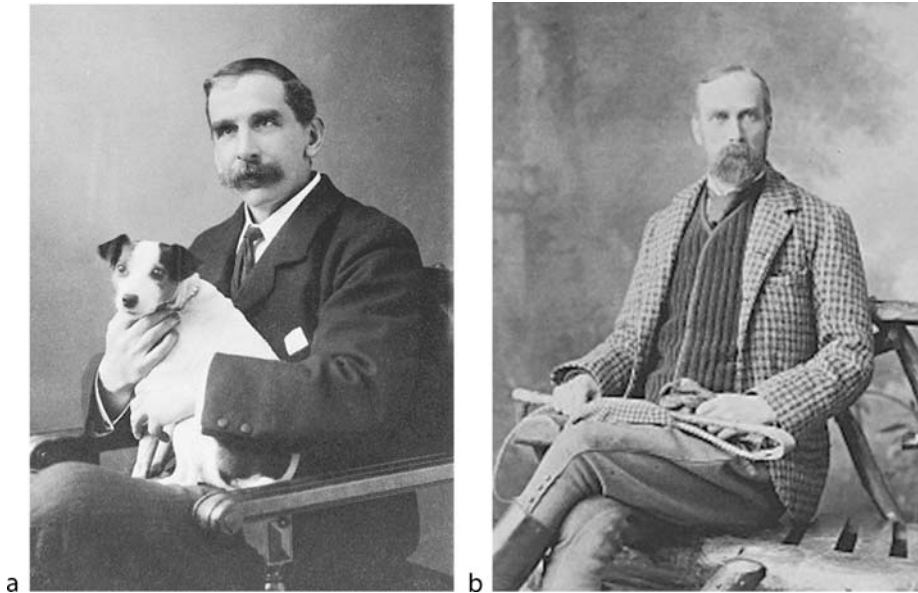
Clarke traveled to Egypt in the early 1890s to convalesce after developing aspiration pneumonia from aspirin inhalation. While there, gazing up at the stars, he conceived an apparatus through

which probing intracranial instruments could be inserted that could be clamped to an animal’s head fixing it to a Cartesian co-ordinate system by skull pins placed laterally, bars attached to plugs inserted into the external auditory meatus and further bars resting upon the nose and orbital margins. The idea was presented to Horsley on return to England [6]. A decade later in 1905 James Swift, a machinist at Palmer & Company in London, was commissioned to construct the first machine from brass, “Clarke’s stereoscopic instrument employed for excitation and electrolysis,” comprising frame, carrier and needle holder and costing £300 ( *Figure 8-2*) [7]. Results were published in 1906 from experimental use of the first instrument for targeting electrolytic lesions in the deep cerebellar nuclei of non-human primates [8]. In 1908 they described the apparatus and its use in greater depth, coining the term “stereotaxic” from the Greek “stereos” meaning “solid” and “taxis” meaning “arrangement,” commenting that “by this means every cubic millimeter of the brain could be studied and recorded” [9].

Although Clarke suggested that the apparatus might be useful in humans, neither he nor Horsley pursued the idea and shortly afterwards they ceased collaboration. Yet Clarke patented the apparatus including its proposed use in humans in 1914 and devoted much time to its improvement. By 1920, a rectilinear modification enabling needle inclination at different angles in an equatorial frame enabling 360° of movement were described ( *Figure 8-2*) [10]. Three others used the original apparatus in London for experimental work; first the visiting

■ **Figure 8-1**

(a) Sir Victor Alexander Haden Horsley; (b) Robert Henry Clarke (courtesy of the Wellcome Library, London)



American surgeon Ernest Sachs who studied the optic thalamus [11], then the neurologist S.A. Kinnier Wilson who studied the basal ganglia of 25 monkeys using the “Clarke-Horsley machine” [12]. Clarke’s original instrument was last utilized by Barrington, a London urologist who used it to study the effect of brain lesions upon micturition in cats [13]. Barrington died suddenly in 1956. Among the contents of his laboratory, “in true British fashion, was a biscuit tin” that contained parts of the original apparatus. After several inquiries, a technician in the Royal Veterinary College where Barrington had once worked produced a mahogany box containing the original model and it was returned to University College London in 1970. It now resides in the Science Museum in London, having been promoted from closed storage to prominent display by Tipu Aziz in 2000 (▶ *Figure 8-3*). Two further apparatus designs were made for Clarke by machinists Goodwin and Velacott also of Palmer & Company in London and exported to the United States for animal research soon after the First World War, the latter to Johns Hopkins

after agreement that the Baltimore institution would publish Clarke’s stereotaxic atlas [14].

Another of Horsley’s students, Aubrey Mussen also contemplated translation of Horsley-Clarke stereotaxis to humans. Mussen purchased one of the original Horsley-Clarke apparatus second-hand for £100 while working at the National Hospital in London from 1905 to 1906 and returned to McGill University with it, subsequently publishing results from studies of the hypoglossal nuclei that Horsley traversed with his deep cerebellar lesions [15]. Mussen designed further stereotactic instruments with Clarke, including a “cyclotome,” a probe used to make disk-shaped incisions along its axis and a “spherotome” used to cut spherical volumes bearing much resemblance to António Egas Moniz’ leucotome [10]. Mussen designed and had commissioned a modification of the Horsley-Clarke apparatus for use in humans in 1914 on his return to London. It was completed around 1918, again in brass, and most likely again by Palmer & Company (▶ *Figure 8-4*). In the frame, electrode holders slid along horizontal graduated bars or vertical corner

■ **Figure 8-2**

Clarke and Horsley's 1905 primate stereotaxic apparatus, showing also Clarke's 1920 equatorial modification (top left), (courtesy of the Wellcome Library, London)

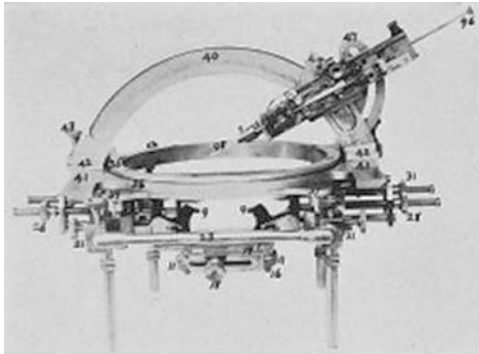


Plate XXX.

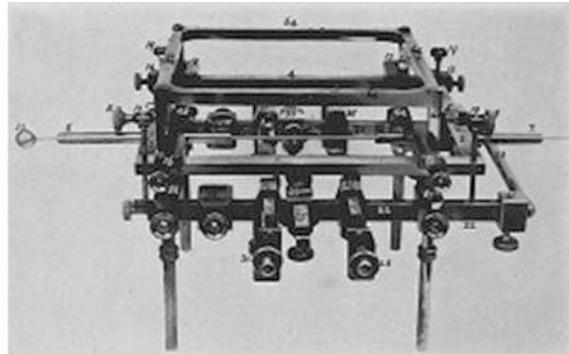


Plate XXXII.

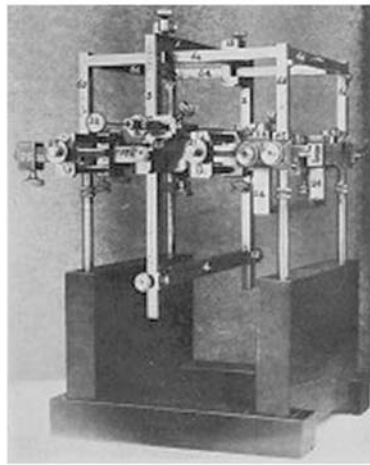


Plate XXXI.

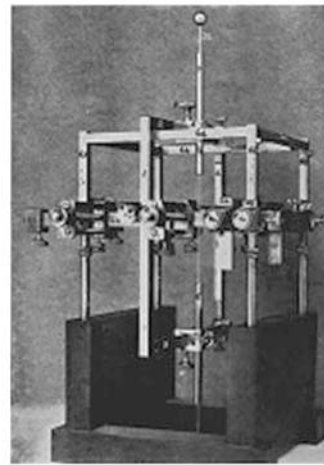


Plate XXXIII

posts enabling orthogonal approaches to intracranial structures in anteroposterior and lateral directions. The apparatus required a human brain atlas and Mussen envisaged its use to thermocoagulate tumors using “Galvanic current...through a 5 mm trephine in the skull and puncturing the dura without exposing the brain at all” [17]. In the two decades that followed, Mussen neither completed the human atlas nor convinced neurosurgical colleagues to take up use of his frame [18]. He wrapped the unused British made apparatus in newspaper dating from the 1940s and placed it in his loft [19].

After Horsley's original experiments, Sachs, Wilson and Barrington all had loan of the original Horsley-Clarke frame. Sachs and Mussen utilized Clarke's second and third frames respectively for animal experiments in North America throughout the 1920s [20,21], as did others during the following decade. However, at least two key challenges remained in translating experimental animal stereotaxis into a clinical tool. Firstly there was great variability between human skull landmarks and cerebral structures and secondly humans could not be sacrificed as animals were to enable confirmatory histology of accurate targeting - and thus experimental validity. Three decades on from

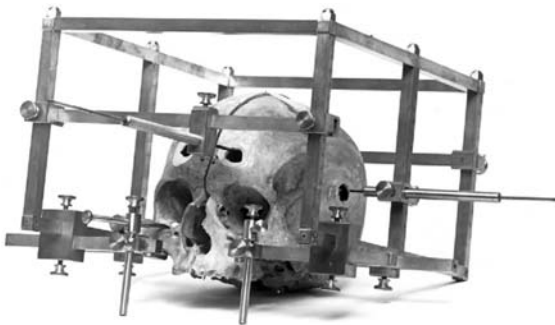
■ **Figure 8-3**

The senior author with one of the original Horsley-Clarke frames in 2000



■ **Figure 8-4**

Mussen's circa 1918 human stereotactic instrument (after Picard et al. [16])



Horsley and Clarke's work, Spiegel and Wycis devised an apparatus for stereotactic neurosurgery in humans, publishing their achievement in 1947 [22]. The North Americans established "stereotactic" as the preferred term, fusing Greek with the Latin word "tactis," the pluperfect passive form of the verb "tangere" meaning "to touch." Their

major advances were firstly to create a frame tailored to the individual skull by means of a plaster skull cap and secondly to align their so-called "stereoenkephalotome" not just to skull but to brain landmarks like the calcified pineal gland and foramen of Monro by means of intraoperative pneumoencephalography.

Post-War Innovation

With two World Wars, British stereotactic surgery remained fallow for the half century after Horsley's discovery, the discipline only reaching the clinic once word had spread of Spiegel and Wycis' invention. At first, primary applications were for treating psychiatric disorders and later clinical usage diffused to movement disorders in the 1950s and chronic pain soon after.

Ahead of the rest, an English crusader and two Scottish pioneers emerged, each a clinical polymath but with an academic focus. In London, Geoffrey Knight developed stereotactic subcaudate tractotomy for psychiatric disorders, treating hundreds of patients while his eminent contemporary Sir Wylie McKissock continued freehand approaches. In Edinburgh, John Gillingham established stereotactic surgery for multiple clinical indications, designing his own stereotactic frame. In turn, his talented associate Ted Hitchcock was inspired first at Edinburgh and then in Birmingham to pioneer stereotactic approaches to the high cervical spinal cord and brainstem.

Francis John Gillingham (b.1916; ▶ *Figure 8-5*) trained in St. Bartholomew's Hospital in London before entering the neurosurgical faculty at Edinburgh in 1950. Gillingham spent 12 years as first assistant to Norman McOmish Dott, one of the great triumvirate alongside Sir Hugh Cairns in Oxford and Sir Geoffrey Jefferson in Manchester, the Cushing apostles who definitively established neurosurgery as a specialty in Great Britain [24–26]. Gillingham was a brilliant and pioneering aneurysm surgeon

■ **Figure 8-5**

Francis John Gillingham (left) preparing for a stereotactic thalamotomy in 1968 (after Housepian 2004 [23])



like his mentor Dott [27,28]. A passionate educator, he also introduced the concept of subspecialty fellowships to British neurosurgical training [29], but stereotactic surgery received his greatest contributions.

The Parisian neurosurgeon Gerard Guiot introduced Gillingham to stereotactic surgery. They had become friends after Guiot visited Edinburgh to learn aneurysmal surgery from Dott and Gillingham. Guiot's 1953 telegram to Gillingham read "I have something interesting to show you – come over." Four days were spent performing freehand pallidotomies to treat parkinsonism under local anesthesia using a subfrontal approach to the anterior perforated substance interrupting the ansa lenticularis as described by Fenelon and Thiebaut following the seminal discoveries of Cooper [30–32]. Gillingham returned to Edinburgh to treat two patients in 1955 and 1957, reporting improvements in tremor, rigidity and quality of life. Wishing to reduce risks from the demanding subfrontal approach, he adapted Guiot's stereotactic method [33]. In 1960 he published results from stereotactic "thermal electrocoagulation lesions of the globus pallidus, internal

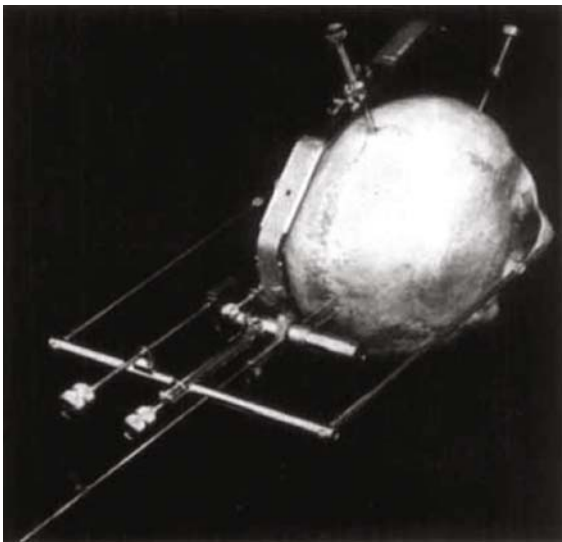
capsule and thalamus either separately or in combination" in a further 58 patients operated upon from 1957 to 1959 [34]. In addition to globus pallidus and internal capsule, he began targeting the ventrolateral thalamus for refractory tremor based on work by Hassler [35]. "Of these (60) patients 53, or 88%, had tremor and/or rigidity abolished or significantly reduced without complications" [34].

From his early clinical results, Gillingham drew several conclusions. On targeting he wrote that "The best type of lesion. . . would seem to be the double one, made at the same time in the ventro-lateral nucleus of the thalamus and in the globus pallidus 16mm from the mid-line, both lesions bordering on the internal capsule. . . . Bilateral lesions in the treatment of bilateral Parkinsonism, provided they are small and strategically placed, would seem to be eminently practicable. . . usually with an interval of 3–6 months between the two operations." On his modification of Guiot's stereotactic apparatus he felt "that the merits of this method lie in the relatively short operative procedure and in its accuracy and simplicity. Its principles are based

on the fact that the globus pallidus and thalamus bear a reasonably constant anatomical relationship to the anterior and posterior commissures, the intercommissural line, and the mid-sagittal plane of the head... The method used has evolved progressively, and is unique, in allowing the creation of lesions in the globus pallidus, internal capsule, or thalamus with one electrode track at different depths” [34].

In their stereotactic apparatus design, Guiot and Gillingham favored operative principles to prioritize patient comfort, not restricting their movements by clamping their head, and to reduce laborious calculations. Guiot planned a parasagittal approach using intraoperative encephalography to delineate the midline and intercommissural point. Gillingham favored an occipitoparietal entry to avoid striate arteries and horizontal patient positioning to reduce putative brain shift. Thus the Guiot-Gillingham stereotactic apparatus was devised (▶ *Figure 8-6*). Radioopaque midline markers were used for the procedure and a 1 mm steel ball placed in each 5 mm lesion for subsequent charting. Over the

■ **Figure 8-6**
The Guiot-Gillingham stereotactic apparatus using a posterior rather than a coronal approach (after Gillingham et al. [34])



post-operative weeks, the ball was seen to fall through the necrotic lesion on skull radiographs, elegantly providing an estimate of lesion size. The frame's conception preceded Hassler's targeting of the thalamus for tremor and hence Gillingham attributed to serendipity that his posterior approach enabled multiple targets to be lesioned in a single pass [36].

Despite impressive clinical outcomes, Gillingham noted some inaccuracy to his lesions in the context of Brierley and Beck's demonstration that relationships between basal ganglia structures and commissural landmarks were highly variable [37,38]. David Whitteridge, his neurophysiologist colleague at Edinburgh, had demonstrated to him in 1961 how microelectrode recording could distinguish between grey and white matter and thus delineate the lateral geniculate nuclei in the cat [39]. He immediately saw its utility for distinguishing functionally between deep brain structures and, with his colleague Michael Gaze, developed the technique for humans as did Guiot [40]. Fundamental physiological insights were gained in the quest to improve lesion accuracy and clinical efficacy, including spontaneous rhythmical discharge in the thalamus found to be synchronous with tremor [41]. Using microelectrode recording, target localization could be done accurately with a margin of error less than 1 mm.

Gillingham evolved the Guiot-Gillingham apparatus throughout the 1960s and 1970s. He added a phantom to allow an oblique track to more medial brain targets for epilepsy and psychiatric disorders, then an inferior extension to the posterior limb of the frame for targeting the cerebellum, brain stem and cervical spine in chronic pain and dystonias [42]. In 1977 he added a motor to automatically drive an electrode in at a slow and measured rate for microelectrode recording. Stereotactic surgery for deep hematomas and tumor biopsies was also performed [43]. Ten year follow-up in the post levodopa era of a second 60 patient parkinsonian cohort of Gillingham's operated upon between

1965 and 1967 showed decline in efficacy for bradykinesia, but consistent relief of tremor and rigidity [44]. Gillingham remained engaged in academic neurosurgery well into his ninth decade [45].

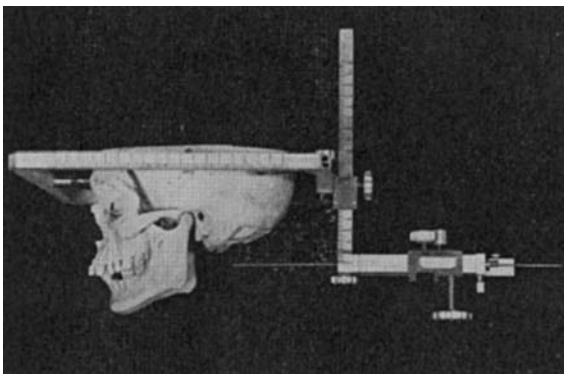
As Gillingham was Dott's protégé, so Ted Hitchcock was Gillingham's. Edward Robert Hitchcock (1929–1993) studied medicine at Birmingham then neurosurgery at Oxford before joining the Edinburgh staff at the then recently opened Western General Hospital in 1965. While there, he received unique exposure to Gillingham's stereotactic surgery which attracted international renown [23]. Hitchcock's developed an interest in chronic pain and in particular the concept of percutaneous high spinal stereotactic commissural myelotomy. This procedure aimed to divide the decussating spinothalamic tracts through a targeted lesion and reduce the risks of respiratory paralysis conferred by open cordotomy. It was aimed at chronic cancer pain. It required access below the plane of a versatile frame, thus he invented his own target-centered arc system secured on a hollow square aluminum base ring secured to the skull by three-point fixation (▶ *Figure 8-7*). Vertical and horizontal bars determined probe length and laterality. The system was first used both for surgery and for microelectrode recording in the spinal cord by

percutaneous approach using portable radiographs [46–48]. Hitchcock reported initial results of good or complete pain relief in 13 out of 19 patients at follow-up ranging from 1 week to 4 years [49]. A stereotactic pontine approach to spinothalamic tractotomy and to the trigeminal nucleus for anesthesia dolorosa was also applied [50–54], as were approaches to the thalamus and dentate nucleus to treat dystonia and in particular the spasticity of cerebral palsy [55]. The rationale behind the stereotactic pontine spinothalamic approach was to provide good analgesia with minimal risks to respiration, micturition and upward gaze [54]. Hitchcock wrote of his apparatus in the early 1970s that “the design and construction make this one of the most accurate, adaptable and simplest of modern stereotactic instruments” [56].

Hitchcock became Professor of Neurosurgery at Birmingham in 1978, succeeding Brodie Hughes (1913–1989) who was also an established stereotactic surgeon [57,58]. Hitchcock put his stereotactic frame to many further clinical uses including biopsy of supratentorial, infratentorial and high spinal tumors and intraventricular masses [59–61], foreign body removal [62], real-time clipping of otherwise inoperable arteriovenous malformations [56], image-guided craniotomies [63], and in the 1980s in the planning and treatment stages of radiosurgery [64]. These many varied clinical indications in brain and spine earned him the nickname “Columbus of the brain” in the local clinical neuroscience community. At the Midland Hospital for Neurology and Neurosurgery, he used his stereotactic expertise to establish a programme at first for adrenal medullary and then in the late 1980s for fetal mesencephalic transplantation in Parkinson's disease, performing the procedure on 55 patients [65–68].

Neurosurgery for psychiatric disorders in Great Britain echoed its popularization in the United States following Freeman and Watts' simplification of Moniz' procedure in the 1940s [69,70]. Its foremost British proponent was the

■ **Figure 8-7**
Hitchcock's stereotactic apparatus for brainstem and cervical spine surgery (after Hitchcock [46])



London neurosurgeon Sir Wylie McKissock (1906–1994), founder of the neurosurgical department at Atkinson Morley's Hospital in Wimbledon [71]. McKissock favored a freehand approach to the frontal lobe from above [72]. He described the rostral leucotomy in 1951 as a rejoinder to Freeman and Watt's transorbital "ice-pick" leucotomy which he considered to contravene "established aseptic surgical principles" [73,74]. McKissock's immense South England practice and his reputation for extraordinary surgical speed inculcated a peripatetic service visiting other hospitals in his car with his surgical instrument set in the boot, drawing parallels with Freeman [75,76]. It is suggested that McKissock alone may have performed one quarter of the 10,365 procedures performed in the United Kingdom from 1942 to 1954 [77].

Geoffrey Cureton Knight (1906–1994) of Hammersmith and Brook Hospitals in London and Woolwich saw more readily than McKissock the merits of stereotactic over freehand approaches in reducing the morbidity and mortality of neurosurgery for psychiatric disorders [74,78]. After his freehand experience [79], Knight created the procedure of stereotactic subcaudate tractotomy in 1961 using a modified stereotactic device that his London colleague the Scottish neurosurgeon Ian Reay McCaul (1916–1989) reported in 1959 [58,80]. His first few hundred orbital under-cuttings led him to conclude that lesions extending posteriorly under the caudate were most efficacious and that the last 2 cm was key [81,82]. Knight used bony landmarks on lateral radiographs, and later air encephalography to guide him. In addition, he employed brachytherapy as an ablative tool, implanting radioactive Yttrium (Y^{90}) to create flat lesion approximately 20 by 20 by 7 mm (▶ *Figure 8-8*) [83–85].

The treatment proved effective and endured four decades amid decline in use of other psychosurgical treatments. The group described treatment of 1,300 patients with "non-schizophrenic affective disorders," 40–60% going on to live normal or near normal lives with a reduction in

▶ **Figure 8-8**

Anteroposterior radiograph of Geoffrey Knight's stereotactic subcaudate tractotomy showing yttrium seeds in situ for brachytherapy (after Knight [83])



suicide rates from 15 to 1% [86,87]. Long-term outcomes were published by the psychiatrist Bridges and the London neurosurgeon John Bartlett, Knight's successor from 1972. Following the retirement of Knight, the unit was named the Geoffrey Knight Unit for Affective Disorders to emphasize Knight's appreciation of the fundamental importance of psychiatric evaluation both in diagnosis and in full consideration of medical treatments prior to offering surgery. In 1996 the unit moved to the Maudsley Hospital and Y^{90} production ceased. Bartlett adapted a Leksell frame arc compatible with modern neuroimaging using concepts that underlay the McCaul device. Radiofrequency lesioning replaced radioisotope implantation [88,89].

It is a tribute to Knight that McKissock's colleague at Atkinson Morley's Hospital, Alan Richardson (1926–1998), adopted a stereotactic approach for his psychiatric procedures [72]. Together with his psychiatrist colleague Desmond Kelly, he combined Knight's subcaudate tractotomy with a cingulotomy to invent the procedure of limbic leucotomy in the early

1970s [90,91]. It is interesting to note that cingulectomy for psychiatric disorders was first performed in 1948 in Oxford by Sir Hugh Cairns, albeit freehand [92]. Both Knight's subcaudate tractotomy and Richardson's limbic leucotomy continue to be performed in carefully selected cases refractory to medical treatment worldwide including in Great Britain and elsewhere [93–95].

Stereotactic neurosurgery was embraced by Dott's unit in Edinburgh and, at Oxford after Cairns, Pennybacker appointed Watkins to establish a service, but other regions were also keen to commence it. In Manchester, Jefferson's successor Richard Johnson appointed John Dutton to undertake a high volume of ablations for parkinsonism and other stereotactic procedures throughout the 1960s using a Leksell frame. Soon after, John Gleave (1925–2006) established a stereotactic service in Cambridge also using a Leksell frame, treating parkinsonism with cryosurgery and developing a side-cutting stereotactic biopsy cannula [96,97]. Other British neurosurgeons like McCaul made and modified stereotactic frames. Of particular note was the frame of Alfred Michael Bennett (1920–1996) and his use of a sphere inserted into a burr hole to aid targeting [98,99]. Bennett's apparatus were popular locally, used by Sid Watkins and later David Thomas in London amongst others [100,101]. Most designs were less radical and therefore perhaps less memorable than those of Gillingham and Hitchcock.

Stereotactic Atlases

Horsley and Clarke produced the first stereotaxic atlas, a monkey version appearing in their 1908 publication. Later publications were by Clarke at first for the cat in collaboration with the British ophthalmic surgeon E. Erskine Henderson in 1912 and later by Clarke alone for the monkey in 1920 [10,102,103]. Both atlases comprised brain slices 2 mm thick. The latter atlas showed sections of monkey brain at calibrated intervals

with a scale giving slice thickness and height from the base of the apparatus. Sections were registered by a Cartesian coordinate system to the skull landmarks of inferior orbital rim and both external auditory canals to which the frame was fixed. Zero axes were the plane between these structures axially, the mid-sagittal plane and the coronal plane between both external auditory meatus orthogonal to both other planes.

The human brain atlases produced outside Great Britain, in particular by Spiegel and Wycis, Schaltenbrand and Bailey and Talairach transformed stereotactic functional neurosurgery. Schaltenbrand detailed anatomical nuclei with an emphasis on the thalamus and adjacent deep brain structures now used in deep brain stimulation for movement disorders and Talairach revealed vasculature relevant to epilepsy surgery [104–106]. The British neurosurgeon Sid Watkins also made rigorous contributions.

Eric Sidney Watkins (b.1932) was given the task of starting stereotactic neurosurgery at the Radcliffe Infirmary in Oxford in the 1950s by Joe Pennybacker. Dissatisfied with the variability of basal ganglia structures with respect to the frequently uncalcified and thus radiolucent pineal gland using the Spiegel and Wycis atlases, he used the Schaltenbrand and Talairach atlases that appeared shortly after. Initially globus pallidus and ansa lenticularis were targeted for Parkinsonian rigidity, tremor and dystonia then later the lateral thalamus in the 1960s. The desire to create his own atlas arose in the early 1960s from a wish to commence thalamotomy for pain and a concern at the adequacy of available atlases to accurately enable targeting based upon anatomy alone in the absence of subjective or physiological guidance. Encouragement came from London neurosurgical colleagues John Andrew and Valentine Logue who were also keen to begin such therapies.

Another atlas that became available was created by Brierley and Beck who sectioned 40 brains in 3–5 mm slices, relating them in a proportional hypothesis for thalamic nuclear determination to

anterior and posterior thalamic limits and the midthalamic point and describing great individual variations [38]. Watkins found the atlas to be limited clinically as the use of simultaneous positive and air ventriculography using air in the ambient cisterns to outline the pulvinar nuclei and thus the thalamic limits was not consistently reproducible.

In the 1960s at the National Hospital for Nervous and Mental Diseases together with Watkins then at the Royal London Hospital, John Andrew produced a greatly enlarged atlas with drawings defining in detail deep brain nuclei including the thalamus and its relations [107]. The atlas was based upon 38 formalin fixed brains. It measured the position of the thalamic centromedian nucleus using 1 mm coronal slices with reference planes between the posteroinferior margin of the foramen of Monro and posterior commissure and the midpoint between the ventricular surfaces of the anterior and posterior commissures. Its utility lies in the presentation of statistical data in a graphic form together with stereotactic coordinates superimposed on simple line drawings of the thalamus.

In 1978 at the London Hospital, Fari Afshar detailed brain stem and cerebellar nuclei, again under Sid Watkins' supervision [108]. The impetus for the Afshar atlas came from an interest in attempting to ameliorate spasticity in cerebral palsy by ablation of the cerebellar dentate nucleus. Approximately 30 brains were prepared using positive-contrast ventriculography with skull and brain mounted in a stereotactic frame in order to accurately correlate structures with coordinates. Again, formalin fixation of 1 mm slices was performed. Modified Mulligan stain was used and each section magnified, with drawings made using a camera lucida. Reference plains were the fourth ventricular floor and fastigium and the mid-sagittal plane. As before, variability profiles were quantified and standard deviations presented.

Both Watkins atlases are resources used today to help ratify localization and indeed the

Afshar atlas continues to augment heated debates regarding the targeting of the novel functional neurosurgical treatment of deep brain stimulation of the pedunculopontine region for Parkinson's disease [109,110].

Watkins has commented upon the major difficulties in measurement due to distortion related to fixation and shrinkage, past atlases suffering from approximately 10% shrinkage. To reduce shrinkage to 2–5%, he utilized Corsellis' technique – a ten day formalin suspension after removing brain and skull en bloc minus the frontal and facial bones [111]. To appease undertakers' concern at cosmetic consequences, each cadaver's scalp was replaced over a plaster of Paris prosthesis fixed to a broom handle on a nail inserted into the cervical canal. However, cremation of the augmented cadavers became suboptimal, precipitating a strike among undertakers serving the London Hospital by the time Afshar's posterior fossa atlas had reached its completion [112].

Computed Tomography

By the late 1970s, British stereotactic functional surgery was a decade on from its first successes, having declined with the advent of neuropsychopharmacology. Levodopa was introduced to relieve Parkinson's disease [113], chlorpromazine and monoamine oxidase inhibitors to ameliorate schizophrenia and depression respectively, and the case series showing good relief after lesional surgery for chronic pain paled against a background of new analgesics and peripheral neuro-modulatory therapies. Stereotactic approaches to tumors had been established but most neurosurgeons did not train in stereotactic neurosurgery. Hitchcock continued psychiatric procedures for medically refractory depression, obsessive-compulsive disorders and anxiety alongside Bartlett and Richardson, but the developing subspecialty sought advances in other domains. Enter the British engineer.

Sir Godfrey Newbold Hounsfield (1919–2004; ▶ *Figure 8-9*) joined EMI in Hayes, Middlesex in 1951, having been first a mechanic first of radios then later radars in the Royal Air Force and obtained a diploma from Faraday House Electrical Engineering College in London. At EMI he worked first on radars and guided weapons, then the first all-transistor computers. During a weekend ramble in 1967 he conceived what later became the first EMI-scanner and the technique of computed tomography (CT), which he recounted as “a realization that you could determine what was in a box by taking readings at all angles through it.”

Recording multiple pictures from a rotating X-ray source, a series of slices could be photographed and a three-dimensional image reconstructed from the slices. After initial successful experiments with a cylindrical phantom containing radio-opaque objects in his Hayes laboratory using X-rays, Hounsfield forged a collaboration

with James Ambrose, radiologist at Atkinson Morley’s Hospital, to translate the device’s utility to humans. McKissock gave the endeavor his blessing [75]. Hounsfield set to work on bullock’s heads obtained from a kosher slaughterhouse in East London to obviate the traumatic intracranial hemorrhage seen after conventional slaughter [114]. Ambrose interpreted the early scans and suggested the use of sodium iohalamate contrast to highlight tumors [115]. His early interpretations and predictions formed the basis of contemporary diagnostic neuroradiology [116,117]. The first patient was scanned in 1971, revealing a cyst [118].

In 1979 Hounsfield was awarded the Nobel Prize for Physiology or Medicine together with Allan Cormack, the Cape Town physicist whose mathematical theories Hounsfield had realized [119].

The advent of CT breathed new life into stereotactic surgery in Britain. Several neurosurgeons began to experiment with CT compatible apparatus, both imported, usually Leksell, and those of Gillingham and Hitchcock [36,120]. Magnetic resonance imaging (MRI) followed shortly after, again with frames being modified as required. After a quiescent decade, the late 1980s augured for a renaissance. Alongside emerging limitations of drug therapies for movement disorders resurrecting clinical indications for functional neurosurgery, great advances came from increasing computer power enabling the fusion of more spatially robust CT information with the greater soft tissue detail of MRI and comparison to computerized brain atlas images. In Britain, the current generation of senior stereotactic neurosurgeons were gaining their clinical training and conducting their first research, some in classical stereotactic methods abroad, some by subspecialty fellowships in Britain thanks to Gillingham’s enduring influence upon neurosurgical programmes, and others by animal experiments true to Horsley’s hybrid scientist-surgeon mould. The stage was set for two decades of rapid advances in British stereotactic neurosurgery.

■ *Figure 8-9*

Sir Godfrey Hounsfield at the controls of the EMI scanner in Atkinson Morley’s Hospital in London (after Petrik et al. [114])



Radiosurgery

Lars Leksell's brilliance showed not only in his frame design [121], employing the novel arc-quadrant principle, but also in his insight that focused radiation could be used as the tool. Many intersecting radiation beams focused towards a target would result in a high cumulative radiation dose, with radiation intensity declining rapidly with distance from the "isocenter." Thus, a deep brain structure could be lesioned non-invasively by focused radiation. The technology of "radiosurgery" could be applied to acoustic neuromas, arteriovenous malformations and other discrete pathologies [122].

Britain acquired one of the first gamma knives in 1985 at the same time as Argentina just 3 years on from the Falklands War. David Forster achieved incredible feats in leading the campaign to fund the device on the British National Health Service, building the infrastructure over 2 years to host it and ultimately purchasing the first custom-made unit in 1985. The National Centre for Stereotactic Radiosurgery was refurbished in 1991 and its cobalt sources renewed. The unit receives approximately one half to two thirds of all radiosurgery referrals from all over the United Kingdom. Approximately 500 cases a year are performed, a third of cases treated being arteriovenous malformations, with small to medium sized acoustic neuroma treatment having increased from 10% to one third over the period 1994–2001 and approximately 100 meningiomas and other skull base or recurrent tumors treated per year. Other indications treated have included trigeminal neuralgia, pituitary tumors and metastases, although the latter two indications are treated in smaller proportions than outside the United Kingdom, reflecting more conservative referral patterns [123]. For similar reasons, few epilepsy and functional cases have been performed.

Several neurosurgical centers use linear accelerators to perform radiosurgery, each performing up to 40 cases per year. A gamma knife was also

acquired by the Cromwell Hospital in London in 1998, run privately by Christer Lindquist. It has treated 1,000 patients since installation and has recently been refurbished.

Functional Surgery

European factors driving British stereotactic surgery included Benabid's application of thalamic deep brain stimulation to Parkinson's disease in 1987 and Laitinen's reapplication of Leksell's pallidotomy in 1992 [124,125].

Functional neurosurgery was resurrected at the Radcliffe Infirmary in Oxford four decades after Watkins' departure under the headship of Mr. Christopher Adams [126]. We had already established with Alan Crossman in Manchester by the early 1990s at the same time as DeLong's team across the Atlantic that lesions made to the subthalamic nucleus in primates reversed the motor symptoms of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) induced parkinsonism [127–129]. At Oxford and Charing Cross Hospital in London, we undertook stereotactic surgery of this target and others [130–135]. At the same time we continued non-human primate research into establishing the pedunculopontine nucleus as a potential target for gait freezing and postural instability [136–139]. The former target is now the target of choice for Parkinson's disease surgery and initial clinical results of the latter show great promise [140–143]. Other translational research at the University of Oxford and Imperial College London included invasive deep brain electrophysiological insights into tremor and dystonia [144–146], use of single photon emission tomography (SPET) [147], magnetoencephalography (MEG) [148], and diffusion tensor imaging (DTI)[149,150] to study deep brain stimulation and research into deep brain stimulation for pain and blood pressure control and brainstem control of exercise [151,152]. We have used deep brain stimulation to treat 70 patients

with dystonia [153], 60 with chronic pain [154], and we perform one fifth of Britain's movement disorders surgery.

In Bristol, Professor Steven Gill has continued the Great British tradition of innovation, creating a stereotactic frame convenient for radiosurgery under Professor David Thomas' supervision in London [155,156], and performing several clinical firsts including glial-cell derived neurotrophic factor infusion and pedunculopontine nucleus stimulation for Parkinson's disease [157–160]. With Mr. Nikunj Patel, he continues to drive the field forward.

After the retirement last decade of Mr. John Miles in Liverpool whose tremendous pain practice still left time for several innovations [161–163], Professor David Thomas also recently

retired as the Gough-Cooper Professor of Neurosurgery at the National Hospital of Neurology and Neurosurgery at Queen Square. He had devoted three decades to the improvement of stereotactic surgical techniques with and without frames [164–168]. Britain welcomed Professor Marwan Hariz at Queen Square as the first Edmond J. Safra Chair of Functional Neurosurgery, "solving" the functional neurosurgery service there [169], and establishing a biennial international workshop like its host, unsurpassed for its conviviality and candour (► *Figure 8-10*).

Almost all of the 34 hospitals conducting neurosurgery in Great Britain and Northern Ireland have consultants able to offer stereotactic surgery a century on from Horsley's first experiments. A third of these hospitals have

► Figure 8-10

The faculty of the International Workshop on Functional Neurosurgery for Movement Disorders and Mental Illness & Commemoration of the 150th Anniversary of the Birth of Sir Victor Horsley, London, 2007 (courtesy of Professor Marwan Hariz). Back Row from left to Right: Lazaro Alvarez La Habana, Peter Brown, Gun Marie Hariz, Paul Krack, Pierre Pollak, Bart Nuttin, Roger Melvill, Steven Gill, Patricia Limousin-Dowsey, Niall Quinn, John Rothwell, Veerle Visser-Vandewalle, Roger Lemon, Rees Cosgrove, Andres Lozano, Laura Cif, Ludvic Zrinzo, Marjan Jahanshahi, Stephen Tisch, Hans Speelman, Philippe Coubes, Pat Forsdick. Front Row Left to Right: Takaomi Taira, Jean-Luc Houeto, Alim-Louis Benabid, Tipu Aziz, Boulos-Paul Bejjani Byblos, Alan Crockard, Marwan Hariz, Carmelo Sturiale



subspecialty trained stereotactic surgeons offering functional procedures, the majority of them affiliated to universities and conducting clinical or translational research. Far from being the reserve of the eccentric scientist-surgeons looked upon with suspicion by the rest of the neurosurgical fraternity, stereotactic surgery has become an established clinical subspecialty and academic discipline in its own right.

The Society of British Neurological Surgeons formed in 1929 has recently begun devoting specific sections to stereotactic and functional neurosurgery at its meetings. A further society with a focus upon pain that welcomes stereotactic neurosurgeons, the Neuromodulation Society of the United Kingdom and Ireland (NSUKI) was founded in 2001. Such factors prove good indicators of the definitive establishment of the subspecialty in the United Kingdom.

Phil Gildenberg has commented that there are four central tenets of the field of stereotactic surgery [170]. The need to be innovative – that a better way to do something may be more apparent to the most junior member of the team rather than the most senior. That stereotactic surgeons work as a community not in isolation. That stereotactic surgery is, to a large extent, a basic science. Although not appealing to the neurosurgeon interested only in a better way to cut, it is exciting to one appreciating the associated basic science. Finally, there is awed appreciation for the insight and courage of the true pioneers in the field. The British school exemplifies such values. It is hoped that its practitioners will continue to uphold tradition as we look to the future with excitement.

Acknowledgments

We thank Mr. John Bartlett for helpful comments, Professor David G. T. Thomas, Professor Anthony J. Strong, Professor John D. Pickard, Mr. Robert Macfarlane and Mr. Colin Watts for advice on historical sources and Professor Marwan I. Hariz

for helpful comments and advice on [Figure 8-10](#). The authors receive financial support for research from the UK Medical Research Council, Normal Collisson Foundation, Charles Wolfson Charitable Trust and Oxford Partnership Comprehensive Biomedical Research Centre.

References

1. Dittmar C. *Ueber die Lage des sogenannten Gefaesszentrums in der Medulla oblongata*. *Bersaechs Ges Wiss Leipzig (Math Phys)* 1873;**25**:449-69.
2. Zernov DN. *Encephalometer: device for estimation of parts of brain in human*. *Proc Soc Physicomed Moscow Univ* 1889;**2**:70-80.
3. Paget S. *Sir Victor Horsley: a study of his life and work*. New York: Harcourt, Brace and Howe; 1920.
4. Northfield WC. *Sir Victor Horsley, his contributions to neurological surgery*. *Surg Neurol* 1973;**1**:131-4.
5. Davis RA. *Victorian physician-scholar and pioneer physiologist (Robert Henry Clarke)*. *Surg Gynecol Obstet* 1964;**119**:1333-40.
6. Sachs E. *Victor Horsley*. *J Neurosurg* 1958;**15**:240-4.
7. Schurr PH, Merrington WR. *The Horsley-Clarke stereotaxic apparatus*. *Br J Surg* 1978;**65**:33-6.
8. Clarke RH, Horsley V. *On a method of investigating the deep ganglia and tracts of the central nervous system (cerebellum)*. *Br Med J* 1906;**2**:1799-800.
9. Horsley V, Clarke RH. *The structure and functions of the cerebellum examined by a new method*. *Brain* 1908;**31**:45-124.
10. Clarke RH. *Part I: Investigation of the central nervous system, methods and instruments*. Baltimore, MD: Johns Hopkins; 1920.
11. Sachs E. *On the structure and functional relations of the optic thalamus*. *Brain* 1909;**32**:95-186.
12. Wilson SAK. *An experimental research into the anatomy and physiology of the corpus striatum*. *Brain* 1914;**36**:427-92.
13. Barrington FJF. *The effect of lesions of the hind- and mid-brain on micturition in the cat*. *Q J Exp Physiol* 1925;**15**:81-102.
14. Fodstad H, Hariz M, Ljunggren B. *History of Clarke's stereotactic instrument*. *Stereotact Funct Neurosurg* 1991;**57**:130-40.
15. Mussen AT. *Notes on the movements of the tongue from stimulation of the twelfth nucleus, root and nerve*. *Brain* 1909;**32**:206.
16. Picard C, Olivier A, Bertrand G. *The first human stereotaxic apparatus. The contribution of Aubrey Mussen to the field of stereotaxis*. *J Neurosurg* 1983;**59**:673-6.
17. Bertrand G. *Stereotactic surgery at McGill: the early years*. *Neurosurgery* 2004;**54**:1244-51; discussion 1251-2.

18. Jensen RL, Stone JL, Hayne R. *Use of the Horsley-Clarke stereotactic frame in humans*. Stereotact Funct Neurosurg 1995;**65**:194-7.
19. Gildenberg PL. *The history of stereotactic neurosurgery*. Neurosurg Clin N Am 1990;**1**:765-80.
20. Sachs E, Fincher EF. *Anatomical and physiological observations on lesions in the cerebellar nuclei in Macacus rhesus (preliminary report)*. Brain 1926;**50**:350-6.
21. Mussen AT. *Experimental investigations on the cerebellum*. Brain 1927;**50**:313-49.
22. Spiegel EA, Wycis HT, Marks M, Lee AJ. *Stereotaxic apparatus for operations on human brain*. Science 1947;**106**:349-50.
23. Housepian EM. *Stereotactic surgery: the early years*. Neurosurgery 2004;**55**:1210-4.
24. Fraenkel GJ. *Hugh Cairns: first Nuffield professor of surgery*, University of Oxford. Oxford: Oxford University Press; 1991.
25. Rush C, Shaw JF. *With sharp compassion: Norman Dott Freeman surgeon of Edinburgh*. Aberdeen: Aberdeen University Press; 1990.
26. Schurr PH, *Royal Society of Medicine (Great Britain). So that was life: a biography of Sir Geoffrey Jefferson, Kt CBE FRS MS FRCS (1886–1961): master of the neurosciences and man of letters*. London: Royal Society of Medicine Press; 1997.
27. Todd NV, Howie JE, Miller JD. *Norman Dott's contribution to aneurysm surgery*. J Neurol Neurosurg Psychiatry 1990;**53**:455-8.
28. Gillingham J. *Proceedings: twenty-five years' experience with middle cerebral aneurysms*. J Neurol Neurosurg Psychiatry 1975;**38**:405.
29. Gillingham FJ. *Surgical training in the EEC – the training of a specialist*. Acta Neurochir (Wien) 1982;**61**:17-24.
30. Cooper IS. *Ligation of the anterior choroidal artery for involuntary movements: parkinsonism*. Psychiatr Q 1953;**27**:317-9.
31. Fenelon F, Thiebaut F. *Resultats du traitement neurochirurgical du syndrome parkinsonien par intervention direct sur les voies etrapyramidales immediatement sous-striopallidales (anse lenticulaire)*. Rev Neurol (Paris) 1950;**83**:437-40.
32. Guiot G, Brion S. *Traitement des mouvements anormaux par la coagulation pallidale; technique et resultats*. Rev Neurol (Paris) 1953;**89**:578-80.
33. Guiot G. *Le traitement des syndromes parkinsoniens par la destruction du pallidum interne*. Neurochirurgia (Stuttg) 1958;**1**:94-8.
34. Gillingham FJ, Watson WS, Donaldson AA, Naughton JA. *The surgical treatment of parkinsonism*. Br Med J 1960;**2**:1395-402.
35. Hassler R, Riechert T. *Indikationen und lokalisationen: methode de gezielten hirnoperationen*. Nervenarzt 1954;**25**:441-7.
36. Gillingham J. *The Guiot-Gillingham Apparatus*. In: Gildenberg PL, Tasker RR, editors. Textbook of stereotactic and functional neurosurgery. New York: McGraw Hill; 1998. p. 139-44.
37. Gillingham J. Introduction to the scientific sessions. Accidents in stereotaxy – side-effects or bonus? Acta Neurochir (Wien) 1974;Suppl 21:5–12.
38. Brierley JB, Beck E. *The significance in human stereotactic brain surgery of individual variation in the diencephalon and globus pallidus*. J Neurol Neurosurg Psychiatry 1959;**22**:287-98.
39. Gillingham FJ. *Neurosurgery*. Br J Surg 1966;**53**:833-6.
40. Guiot G, Hardy J, Albe-Fessard D. *Delimitation precise des structures sous-corticales et identification de noyaux thalamiques chez l'homme par l'electrophysiologie stereotaxique*. Neurochirurgia (Stuttg) 1962;**5**:1-18.
41. Gaze RM, Gillingham FJ, Kalyanaraman S, Porter RW, Donaldson AA, Donaldson IM. *Microelectrode recordings from the human thalamus*. Brain 1964;**87**:691-706.
42. Gillingham FJ, Campbell D. *Surgical interruption of the conduction pathways for the control of intractable epilepsy*. Acta Neurochir Suppl (Wien) 1980;**30**:67-74.
43. Kalyanaraman S, Gillingham FJ. *Stereotaxic biopsy*. J Neurosurg 1964;**21**:854-8.
44. Kelly PJ, Gillingham FJ. *The long-term results of stereotaxic surgery and L-dopa therapy in patients with Parkinson's disease. A 10-year follow-up study*. J Neurosurg 1980;**53**:332-7.
45. Gillingham J. *Forty-five years of stereotactic surgery for Parkinson's disease: a review*. Stereotact Funct Neurosurg 2000;**74**:95-8.
46. Hitchcock E, Lewin M. *Stereotactic recording from the spinal cord of man*. Br Med J 1969;**4**:44-5.
47. Hitchcock E. *Stereotaxic spinal surgery. A preliminary report*. J Neurosurg 1969;**31**:386-92.
48. Hitchcock E. *An apparatus for stereotactic spinal surgery*. Lancet 1969;**1**:705-6.
49. Hitchcock E. *Stereotactic myelotomy*. Proc R Soc Med 1974;**67**:771-2.
50. Hitchcock E. *Stereotactic trigeminal tractotomy*. Farmatsiia 1970;**19**:131-5.
51. Hitchcock E, Kim MC, Sotelo M. *Further experience in stereotactic pontine tractotomy*. Appl Neurophysiol 1985;**48**:242-6.
52. Hitchcock E, Teixeira MJ. *Pontine stereotactic surgery and facial nociception*. Neurol Res 1987;**9**:113-7.
53. Hitchcock E, Sotelo MG, Kim MC. *Analgesic levels and technical method in stereotactic pontine spinothalamic tractotomy*. Acta Neurochir (Wien) 1985;**77**:29-36.
54. Hitchcock ER. *Stereotaxic pontine spinothalamic tractotomy*. J Neurosurg 1973;**39**:746-52.
55. Gornall P, Hitchcock E, Kirkland IS. *Stereotaxic neurosurgery in the management of cerebral palsy*. Dev Med Child Neurol 1975;**17**:279-86.

56. Shieff C. *The Hitchcock apparatus*. In: Gildenberg PL, Tasker RR, editors. *Textbook of stereotactic and functional neurosurgery*. New York: McGraw Hill; 1998. p. 101-4.
57. Hughes B. *Involuntary movements following stereotactic operations for parkinsonism with special reference to Hemi-Chorea (Ballismus)*. *J Neurol Neurosurg Psychiatry* 1965;**28**:291-303.
58. Lyle I, Taylor S. *Lives of the fellows of the Royal College of Surgeons of England: 1983–1990*. London: Royal College of Surgeons of England; 1995.
59. Hitchcock ER, Issa AM, Sotelo MG. *Stereotactic excision of deeply seated intracranial mass lesions*. *Br J Neurosurg* 1989;**3**:313-20.
60. Hitchcock E, Kenny BG. *Stereotaxy of third ventricular masses*. *Acta Neurochir Suppl (Wien)* 1989;**46**:82-5.
61. Hitchcock E, Morris CS. *Immunocytochemical techniques in stereotactic biopsy*. *Stereotact Funct Neurosurg* 1989;**53**:21-8.
62. Hitchcock E, Cowie R. *Stereotactic removal of intracranial foreign bodies: review and case report*. *Injury* 1983;**14**:471-5.
63. Hitchcock E. *Open stereotactic surgery*. *Acta Neurochir Suppl (Wien)* 1991;**52**:9-12.
64. Hitchcock E, Kitchen G, Dalton E, Pope B. *Stereotactic LINAC radiosurgery*. *Br J Neurosurg* 1989;**3**:305-12.
65. Hitchcock E. *Stereotactic neural transplantation*. *Stereotact Funct Neurosurg* 1994;**62**:120-33.
66. Hitchcock ER, Kenny BG, Clough CG, Hughes RC, Henderson BT, Detta A. *Stereotactic implantation of foetal mesencephalon (STIM): the UK experience*. *Prog Brain Res* 1990;**82**:723-8.
67. Hitchcock ER, Clough CG, Hughes RC, Kenny BG. *Transplantation in Parkinson's disease: stereotactic implantation of adrenal medulla and foetal mesencephalon*. *Acta Neurochir Suppl (Wien)* 1989;**46**:48-50.
68. Kudoh C, Detta A, Meyer C, Byrne P, Hitchcock E. *Bilateral intracaudate cogafting of fetal ventral mesencephalon and striatum in advanced Parkinson's disease*. *Transplant Proc* 1999;**31**:3397-402.
69. Freeman W, Watts JW. *Psychosurgery in the treatment of mental disorders and intractable pain*. 2nd ed. Springfield, IL: C. C. Thomas; 1950.
70. Moniz E. *Tentatives Opératoires dans le Traitement de Certaines Psychoses*. Paris: Masson; 1936.
71. Richardson AE. *Sir Wylie McKissock*. *Surg Neurol* 1988;**30**:173-4.
72. Kitchen N. *Neurosurgery for affective disorders at Atkinson Morley's Hospital 1948–1994*. *Acta Neurochir Suppl* 1995;**64**:64-8.
73. McKissock W. *Rostral leucotomy*. *Lancet* 1951;**2**:91-4.
74. McKissock W. *Discussion on psychosurgery*. *Proc R Soc Med* 1959;**52**:206-9.
75. Bell BA. *Wylie McKissock – reminiscences of a commanding figure in British neurosurgery*. *Br J Neurosurg* 1996;**10**:9-18.
76. El-Hai J. *The lobotomist: a maverick medical genius and his tragic quest to rid the world of mental illness*. Hoboken, NJ: Wiley; 2005.
77. Tooth J, Newton M. *Leucotomy in England and Wales 1942–1954: report on public health and medical subjects no. 104*. London: Her Majesty's Stationery Office; 1961.
78. Knight GC. *Discussion on psychosurgery*. *Proc R Soc Med* 1959;**52**:209-10.
79. Knight GC, Tredgold RF. *Orbital leucotomy; a review of 52 cases*. *Lancet* 1955;**268**:981-6.
80. McCaul IR. *Stereotaxic surgery and involuntary movement*. *Proc R Soc Med* 1961;**54**:378-80.
81. Knight G. *The orbital cortex as an objective in the surgical treatment of mental illness. The results of 450 cases of open operation and the development of the stereotactic approach*. *Br J Surg* 1964;**51**:114-24.
82. Knight G. *Stereotactic tractotomy in the surgical treatment of mental illness*. *J Neurol Neurosurg Psychiatry* 1965;**28**:304-10.
83. Knight GC. *Bi-frontal stereotactic tractotomy: an atraumatic operation of value in the treatment of intractable psychoneurosis*. *Br J Psychiatry* 1969;**115**:257-66.
84. Knight G. *Neurosurgical aspects of psychosurgery*. *Proc R Soc Med* 1972;**65**:1099-104.
85. Knight G. *Further observations from an experience of 660 cases of stereotactic tractotomy*. *Postgrad Med J* 1973;**49**:845-54.
86. Bridges PK, Bartlett JR, Hale AS, Poynton AM, Malizia AL, Hodgkiss AD. *Psychosurgery: stereotactic subcaudate tractotomy. An indispensable treatment*. *Br J Psychiatry* 1994;**165**:599-611; discussion 612-3.
87. Hodgkiss AD, Malizia AL, Bartlett JR, Bridges PK. *Outcome after the psychosurgical operation of stereotactic subcaudate tractotomy, 1979–1991*. *J Neuropsychiatry Clin Neurosci* 1995;**7**:230-4.
88. Malhi GS, Bartlett JR. *A new lesion for the psychosurgical operation of stereotactic subcaudate tractotomy (SST)*. *Br J Neurosurg* 1998;**12**:335-9.
89. Malhi GS, Bartlett JR. *Depression: a role for neurosurgery?* *Br J Neurosurg* 2000;**14**:415-22; discussion 423.
90. Kelly D, Richardson A, Mitchell-Heggs N. *Stereotactic limbic leucotomy: neurophysiological aspects and operative technique*. *Br J Psychiatry* 1973;**123**:133-40.
91. Kelly D, Richardson A, Mitchell-Heggs N, Greenup J, Chen C, Hafner RJ. *Stereotactic limbic leucotomy: a preliminary report on forty patients*. *Br J Psychiatry* 1973;**123**:141-8.
92. Williams LM. *Arousal dissociates amygdala and hippocampal fear responses: evidence from simultaneous fMRI and skin conductance recording*. *Neuroimage* 2001;**14**:1070-9.
93. Christmas D, Matthews K, Eljamel MS. *Neurosurgery for mental disorder*. *Br J Psychiatry* 2004;**185**:173-4; author reply 174.
94. Feldman RP, Alterman RL, Goodrich JT. *Contemporary psychosurgery and a look to the future*. *J Neurosurg* 2001;**95**:944-56.

95. Kopell BH, Machado AG, Rezaei AR. *Not your father's lobotomy: psychiatric surgery revisited*. Clin Neurosurg 2005;**52**:315-30.
96. Marks PV, Wild AM, Gleave JR. *The 'Cambridge' stereotactic biopsy instrument*. Br J Neurosurg 1990;**4**:127-8.
97. Wild AM, Xuereb JH, Marks PV, Gleave JR. *Computerized tomographic stereotaxy in the management of 200 consecutive intracranial mass lesions. Analysis of indications, benefits and outcome*. Br J Neurosurg 1990;**4**:407-15.
98. Bennett. A stereotaxic apparatus for use in cerebral surgery. Br J Radiol 1960;**33**:343-51.
99. Blandy JP, Greig CM, Gillam SJ, Williams DI. *Lives of the fellows of the Royal College of Surgeons of England: 1997-2002: vol. 9 with a cumulated index to vol. 1-8*. London: Royal College of Surgeons of England; 2005.
100. Eljamel MS, Forster A, Tulley M, Matthews K. *Staged functional neurosurgery using image fusion: electronic atlas and microelectrode recording at Dundee*. Stereotact Funct Neurosurg 1999;**73**:140-2.
101. Pell MF, Thomas DG. *The initial experience with the Cosman-Roberts-Wells stereotactic system*. Br J Neurosurg 1991;**5**:123-8.
102. Clarke RH. *Part II: Atlas of the frontal sections of the cranium and brain of the rhesus monkey*. Baltimore, MD: Johns Hopkins; 1920.
103. Clarke RH, Henderson EE. *Atlas of photographs of sections of the frozen cranium and brain of the cat (Felis Domestica)*. J Psychol Neurol 1912;**18**:391-409.
104. Spiegel EA, Wycis HT, Baird HW. *Studies in stereoencephalotomy. I. Topical relationships of subcortical structures to the posterior commissure*. Confin Neurol 1952;**12**:121-33.
105. Schaltenbrand G, Bailey P. *Introduction to stereotaxis with an atlas of the human brain*. Stuttgart: Thieme; 1959.
106. Talairach J, David M, Tournoux P, Corredor H, Krasina T. *Atlas d'Anatomie Stereotaxique*. Paris: Masson; 1957.
107. Andrew J, Watkins ES. *Stereotactic surgery. A stereotaxic atlas of the human thalamus*. Baltimore, MD: Williams & Wilkins; 1969.
108. Afshar F, Watkins ES, Yap JC. *Stereotaxic atlas of the human brainstem and cerebellar nuclei: a variability study*. New York: Raven Press; 1978.
109. Mazzone P, Insola A, Lozano A, Galati S, Scarnati E, Peppe A, Stanzione P, Stefani A. *Peripeduncular and pedunculopontine nuclei: a dispute on a clinically relevant target*. Neuroreport 2007;**18**:1407-8.
110. Zrinzo L, Zrinzo LV, Hariz M. *The pedunculopontine and peripeduncular nuclei: a tale of two structures*. Brain 2007;**130**:e73; author reply e74.
111. Corsellis JA. *Individual variation in the size of the tentorial opening*. J Neurol Neurosurg Psychiatry 1958;**21**:279-83.
112. Watkins ES. *On making stereotactic atlases*. In: Gildenberg PL, Tasker RR, editors. Textbook of stereotactic and functional neurosurgery. New York: McGraw Hill; 1998. p. 235-6.
113. Cotzias GC, Van WM, Schiffer LM. *Aromatic amino acids and modification of parkinsonism*. N Engl J Med 1967;**276**:374-9.
114. Petrik V, Apok V, Britton JA, Bell BA, Papadopoulos MC. *Godfrey Hounsfield and the dawn of computed tomography*. Neurosurgery 2006;**58**:780-7; discussion 780-7.
115. Ambrose J, Gooding MR, Richardson AE. *The Lancet - saturday 11 october 1975. Sodium iothalamate as an aid to diagnosis of intracranial lesions by computerised transverse axial scanning*. Lancet 1975;**2**:669-74.
116. Ambrose J. *CT scanning: a backward look*. Semin Roentgenol 1977;**12**:7-11.
117. Ambrose J, Hounsfield G. *Computerized transverse axial tomography*. Br J Radiol 1973;**46**:148-9.
118. Hounsfield GN. *Historical notes on computerized axial tomography*. J Can Assoc Radiol 1976;**27**:135-42.
119. Hounsfield GN. *Computed medical imaging*. Science 1980;**210**:22-8.
120. Hitchcock E. *Stereotactic-computerized tomography interface device*. Appl Neurophysiol 1987;**50**:63-7.
121. Leksell L. *A stereotaxic apparatus for intracerebral surgery*. Acta Chir Scand 1949;**99**:229-33.
122. Leksell L. *The stereotaxic method and radiosurgery of the brain*. Acta Chir Scand 1951;**102**:316-9.
123. Rowe JG, Radatz MW, Walton L, Kemeny AA. *Changing utilization of stereotactic radiosurgery in the UK: the Sheffield experience*. Br J Neurosurg 2002;**16**:477-82.
124. Benabid AL, Pollak P, Louveau A, Henry S, de Rougemont J. *Combined (thalamotomy and stimulation) stereotactic surgery of the VIM thalamic nucleus for bilateral Parkinson disease*. Appl Neurophysiol 1987;**50**:344-6.
125. Laitinen LV, Bergenheim AT, Hariz MI. *Leksell's posterovenral pallidotomy in the treatment of Parkinson's disease*. J Neurosurg 1992;**76**:53-61.
126. Aziz TZ, Adams CB. *Neurosurgery at the radcliffe infirmary, Oxford: a history*. Neurosurgery 1995;**37**:505-10.
127. Bergman H, Wichmann T, DeLong MR. *Reversal of experimental parkinsonism by lesions of the subthalamic nucleus*. Science 1990;**249**:1436-8.
128. Aziz TZ, Peggs D, Sambrook MA, Crossman AR. *Lesion of the subthalamic nucleus for the alleviation of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced parkinsonism in the primate*. Mov Disord 1991;**6**:288-92.
129. Aziz TZ, Peggs D, Agarwal E, Sambrook MA, Crossman AR. *Subthalamic nucleotomy alleviates parkinsonism in the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-exposed primate*. Br J Neurosurg 1992;**6**:575-82.

130. Parkin S, Nandi D, Giladi N, Joint C, Gregory R, Bain P, Scott R, Aziz TZ. *Lesioning the subthalamic nucleus in the treatment of Parkinson's disease*. Stereotact Funct Neurosurg 2002;**77**:68-72.
131. Parkin SG, Gregory RP, Scott R, Bain P, Silburn P, Hall B, Boyle R, Joint C, Aziz TZ. *Unilateral and bilateral pallidotomy for idiopathic Parkinson's disease: a case series of 115 patients*. Mov Disord 2002;**17**:682-92.
132. Liu X, Rowe J, Nandi D, Hayward G, Parkin S, Stein J, Aziz T. *Localisation of the subthalamic nucleus using radionics image Fusion? and Stereoplan? combined with field potential recording: a technical note*. Stereotact Funct Neurosurg 2001;**76**:63-73.
133. Aziz TZ, Nandi D, Parkin S, Liu X, Giladi N, Bain P, Gregory RG, Joint C, Scott RB, Stein JF. *Targeting the subthalamic nucleus*. Stereotact Funct Neurosurg 2002;**77**:87-90.
134. Aziz T, Torrens M. *CT-guided thalamotomy in the treatment of movement disorders*. Br J Neurosurg 1989;**3**:333-6.
135. Pereira EA, Green AL, Nandi D, Aziz TZ. *Deep brain stimulation: indications and evidence*. Expert Rev Med Devices 2007;**4**:591-603.
136. Munro-Davies LE, Winter J, Aziz TZ, Stein JF. *The role of the pedunculopontine region in basal-ganglia mechanisms of akinesia*. Exp Brain Res 1999;**129**:511-7.
137. Nandi D, Aziz TZ, Giladi N, Winter J, Stein JF. *Reversal of akinesia in experimental parkinsonism by GABA antagonist microinjections in the pedunculopontine nucleus*. Brain 2002;**125**:2418-30.
138. Jenkinson N, Nandi D, Miall RC, Stein JF, Aziz TZ. *Pedunculopontine nucleus stimulation improves akinesia in a parkinsonian monkey*. NeuroReport 2004;**15**:2621-4.
139. Nandi D, Jenkinson E, Miall C, Stein JF, Aziz TZ. *Pedunculopontine nucleus*. J Neurosurg 2004;**100**:978-9; author reply 979.
140. Kleiner-Fisman G, Herzog J, Fisman DN, Tamma F, Lyons KE, Pahwa R, Lang AE, Deuschl G. *Subthalamic nucleus deep brain stimulation: summary and meta-analysis of outcomes*. Mov Disord 2006;**21** Suppl 14: S290-304.
141. Stefani A, Lozano AM, Peppe A, Stanzione P, Galati S, Tropepi D, Pierantozzi M, Brusa L, Scarnati E, Mazzone P. *Bilateral deep brain stimulation of the pedunculopontine and subthalamic nuclei in severe Parkinson's disease*. Brain 2007;**130**(6):1596-1607.
142. Schupbach WM, Chastan N, Welter ML, Houeto JL, Mesnage V, Bonnet AM, Czernecki V, Maltete D, Hartmann A, Mallet L, Pidoux B, Dormont D, Navarro S, Cornu P, Mallet A, Agid Y. *Stimulation of the subthalamic nucleus in Parkinson's disease: a 5 year follow up*. J Neurol Neurosurg Psychiatry 2005;**76**:1640-4.
143. Rodriguez-Oroz MC, Obeso JA, Lang AE, Houeto JL, Pollak P, Rehnrona S, Kulisevsky J, Albanese A, Volkmann J, Hariz MI, Quinn NP, Speelman JD, Guridi J, Zamarbide I, Gironell A, Molet J, Pascual-Sedano B, Pidoux B, Bonnet AM, Agid Y, Xie J, Benabid AL, Lozano AM, Saint-Cyr J, Romito L, Contarino MF, Scerrati M, Fraix V, Van Blercom N. *Bilateral deep brain stimulation in Parkinson's disease: a multicentre study with 4 years follow-up*. Brain 2005; **128**:2240-9.
144. Liu X, Miall RC, Aziz TZ, Palace JA, Stein JF. *Distal versus proximal arm tremor in multiple sclerosis assessed by visually guided tracking tasks*. J Neurol Neurosurg Psychiatry 1999;**66**:43-7.
145. Liu X, Yianni J, Wang S, Bain PG, Stein JF, Aziz TZ. *Different mechanisms may generate sustained hypertonic and rhythmic bursting muscle activity in idiopathic dystonia*. Exp Neurol 2006;**198**:204-13.
146. Wang S, Liu X, Yianni J, Green AL, Joint C, Stein JF, Bain PG, Gregory R, Aziz TZ. *Use of surface electromyography to assess and select patients with idiopathic dystonia for bilateral pallidal stimulation*. J Neurosurg 2006;**105**:21-5.
147. Pereira EA, Green AL, Bradley KM, Soper N, Moir L, Stein JF, Aziz TZ. *Regional cerebral perfusion differences between periventricular grey, thalamic and dual target deep brain stimulation for chronic neuropathic pain*. Stereotact Funct Neurosurg 2007;**85**:175-83.
148. Kringelbach ML, Jenkinson N, Green AL, Owen SL, Hansen PC, Cornelissen PL, Holliday IE, Stein J, Aziz TZ. *Deep brain stimulation for chronic pain investigated with magnetoencephalography*. Neuroreport 2007;**18**:223-8.
149. Muthusamy KA, Aravamuthan BR, Kringelbach ML, Jenkinson N, Voets NL, Johansen-Berg H, Stein JF, Aziz TZ. *Connectivity of the human pedunculopontine nucleus region and diffusion tensor imaging in surgical targeting*. J Neurosurg 2007;**107**:814-20.
150. Aravamuthan BR, Muthusamy KA, Stein JF, Aziz TZ, Johansen-Berg H. *Topography of cortical and subcortical connections of the human pedunculopontine and subthalamic nuclei*. Neuroimage 2007;**37**:694-705.
151. Green AL, Wang S, Owen SL, Paterson DJ, Stein JF, Aziz TZ. *Controlling the heart via the brain: a potential new therapy for orthostatic hypotension*. Neurosurgery 2006;**58**:1176-83; discussion 1176-83.
152. Green AL, Wang S, Owen SL, Xie K, Bittar RG, Stein JF, Paterson DJ, Aziz TZ. *Stimulating the human midbrain to reveal the link between pain and blood pressure*. Pain 2006;**124**:349-59.
153. Yianni J, Bain P, Giladi N, Auca M, Gregory R, Joint C, Nandi D, Stein J, Scott R, Aziz T. *Globus pallidus internus deep brain stimulation for dystonic conditions: a prospective audit*. Mov Disord 2003;**18**:436-42.
154. Owen SL, Green AL, Nandi DD, Bittar RG, Wang S, Aziz TZ. *Deep brain stimulation for neuropathic pain*. Acta Neurochir Suppl 2007;**97**:111-16.
155. Kitchen ND, Thomas DG. *Minimally invasive stereotaxy: clinical use of the Gill-Thomas-Cosman (GTC)*

- repeat stereotactic localiser. *Minim Invasive Neurosurg* 1994;**37**:61-3.
156. Sofat A, Kratimenos G, Thomas DG. *Early experience with the Gill Thomas locator for computed tomography-directed stereotactic biopsy of intracranial lesions*. *Neurosurgery* 1992;**31**:972-4.
157. Gill SS, Patel NK, Hotton GR, O'Sullivan K, McCarter R, Bunnage M, Brooks DJ, Svendsen CN, Heywood P. *Direct brain infusion of glial cell line-derived neurotrophic factor in Parkinson disease*. *Nat Med* 2003;**9**:589-95.
158. Love S, Plaha P, Patel NK, Hotton GR, Brooks DJ, Gill SS. *Glial cell line-derived neurotrophic factor induces neuronal sprouting in human brain*. *Nat Med* 2005;**11**:703-4.
159. Patel NK, Bunnage M, Plaha P, Svendsen CN, Heywood P, Gill SS. *Intraputamenal infusion of glial cell line-derived neurotrophic factor in PD: a two-year outcome study*. *Ann Neurol* 2005;**57**:298-302.
160. Plaha P, Gill SS. *Bilateral deep brain stimulation of the pedunculopontine nucleus for Parkinson's disease*. *Neuroreport* 2005;**16**:1883-7.
161. Page RD, Miles JB. *Validation of CT targeting for functional stereotaxis with postoperative magnetic resonance imaging*. *Br J Neurosurg* 1994;**8**:461-7.
162. Dervin JE, Miles J. *A simple system for image directed stereotaxis*. *Br J Neurosurg* 1989;**3**:569-74.
163. Dervin JE, Miles JB. *Development of an analogue method to link stereotactic surgery to computed tomography*. *Neurochirurgia (Stuttg)* 1984;**27**:162-5.
164. Dorward NL, Alberti O, Palmer JD, Kitchen ND, Thomas DG. *Accuracy of true frameless stereotaxy: in vivo measurement and laboratory phantom studies. Technical note*. *J Neurosurg* 1999;**90**:160-8.
165. Thomas DG, Kitchen ND. *Stereotactic techniques for brain biopsies*. *Arch Dis Child* 1993;**69**:621-2.
166. Kitchen ND, Lemieux L, Thomas DG. *Accuracy in frame-based and frameless stereotaxy*. *Stereotact Funct Neurosurg* 1993;**61**:195-206.
167. Thomas DG, Nouby RM. *Experience in 300 cases of CT-directed stereotactic surgery for lesion biopsy and aspiration of haematoma*. *Br J Neurosurg* 1989;**3**:321-5.
168. Thomas DG, Anderson RE, du Boulay GH. *CT-guided stereotactic neurosurgery: experience in 24 cases with a new stereotactic system*. *J Neurol Neurosurg Psychiatry* 1984;**47**:9-16.
169. Powell M, Kitchen N. *The development of neurosurgery at the National Hospital for Neurology and Neurosurgery, Queen Square, London, England*. *Neurosurgery* 2007;**61**:1077-90; discussion 1090.
170. Gildenberg PL. *Stereotactic surgery: the early years (comment)*. *Neurosurgery* 2004;**55**:1214.