Norman M. Dott, master of hypothalamic craniopharyngioma surgery: the decisive mentoring of Harvey Cushing and Percival Bailey at Peter Bent Brigham Hospital

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Norman McOmish Dott (1897–1973) developed surgical neurology in Edinburgh, Scotland, and was a scholar of worldwide renown. One of Dott’s most notable contributions to neurosurgery was his understanding of hypothalamic physiology, mostly acquired through the comprehensive study of patients with lesions involving this region of the diencephalon, particularly craniopharyngiomas (CPs). Recognition of symptoms caused by hypothalamic disturbances allowed him to predict the accurate anatomical relationships between CPs and the hypothalamus, despite the rudimentary radiological methods available during the 1930s. His sophisticated knowledge permitted Dott to perform radical removals of CPs originating within the third ventricle floor with acceptable success. Between 1934 and 1937, he operated on 4 CP cases originating in the hypothalamus, achieving a satisfactory postoperative outcome in 3 of the 4 patients. Aware of the strong attachment of hypothalamic CPs to the infundibulo-tuberal area, Dott used a double transbasal and transventricular approach to these lesions, a strategy providing an optimal view and control of the tumor boundaries. The decisive mentorship of several legendary figures of physiology and neurosurgery greatly influenced Dott’s surgical evolution. The experimental pituitary gland work he performed with Sir Edward Sharpey-Schäfer at the beginning of his career stirred Dott’s curiosity about the issue of hypothalamus-pituitary relationships. As a result, he decided to move to Peter Bent Brigham Hospital (Boston, Massachusetts) in 1923, to train in neurosurgery and neuropathology under the guidance of the leaders in these fields, Harvey Williams Cushing (1869–1939) and Percival Sylvester Bailey (1892–1973). They inspired the young Dott and shared with him their clinical and pathological expertise, in addition to their surgical strategies for best approaching and removing these challenging tumors. In time, Dott would come to surpass his mentors. This paper aims to credit Norman M. Dott for his decisive, modern contributions to hypothalamic CP surgery.

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rochiasmatic area, followed by a second transcortical-transventricular procedure to remove the upper portion of the lesion within the third ventricle. Such a combination of basal and upper approaches to complex intra-extraventricular CPs remains the standard method for removal of these lesions today.

Considering Dott lacked accurate neuroradiological methods of diagnosis, surgical microscopes, hormonal replacement therapies, and antibiotics, his record of hypothalamic CP removal should be regarded as a remarkable accomplishment.

During his fellowship in Boston (1923–1924), Harvey Cushing kindled Dott’s enthusiasm for pituitary tumors and the study of pituitary and hypothalamic disturbances. Dott also had the good fortune to meet Percival Sylvester Bailey (1892–1973), who taught him the essential concepts of hypothalamic dysfunction necessary to understand the sort of symptoms observed in patients with CPs. Dott witnessed firsthand the disheartening results that followed Cushing’s early attempts to remove CPs involving the hypothalamus. The fundamental lesson Dott learned from Cushing and Bailey was that the patients’ severe morbidity or death almost inevitably followed any surgical injury to the hypothalamus.

This study reviews Dott’s innovative surgical techniques for the treatment of hypothalamic CPs. In particular, our work analyzes the knowledge Dott acquired at Peter Bent Brigham Hospital that significantly contributed to his success with this specific topographical CP variant, judged as the most “baffling” type of brain tumor by Harvey Cushing. We have systematically examined the information related to the treatment of CPs at Brigham Hospital stored in the Manuscripts and Archives Department at Sterling Memorial Library, Yale University, New Haven, Connecticut, for the two periods Norman Dott spent as a visiting neurosurgical fellow at Cushing’s department: first, from November 1923 to June 1924, and later, in the summer of 1929. In addition, an extensive review was performed of the Cushing-Dott correspondence kept at Yale, as well as the published literature on the subjects of CPs and the hypothalamus by Harvey Cushing, Percival Bailey, and Norman M. Dott. Our major objective was to draw attention to the pathological concepts and surgical lessons about CPs that Dott learned from Cushing and Bailey, which allowed him to achieve a radical removal of hypothalamic tumors. These essential lessons remain valid for neurosurgeons even today.

Intellectual Background: From Engineer Apprentice to Committed Pituitary Gland Researcher

Norman M. Dott was born in Colinton, on the southern outskirts of Edinburgh, Scotland, on August 26, 1897. Raised in a family promoting the enjoyment of culture and rational thinking, Dott aspired to become an engineer, but on August 29, 1913, he suffered a motorcycle accident, a stroke of fate that altered the tenor of his life. He suffered a compound fracture of his left femur and tibia, requiring complex surgery and from which he endured a painful limp for the rest of his life. His own disability along with the impression that other sick and injured patients made on him, prompted a desire to study medicine at the University of Edinburgh, from which he graduated in December 1919. From 1920 to 1921, Dott was trained in general surgery under Dr. John Wheeler Dowden at the Royal Infirmary (Fig. 2A). In 1923, he obtained the Fellowship of the Royal College of Surgeons of Edinburgh (FRCSE).

In 1908, Sir Edward Albert Sharpey-Schäfer (1850–1935), chair of physiology at the University of Edinburgh and discoverer of the active principle of the posterior pituitary gland, was invited to deliver a lecture on the physiology of the pituitary gland at Johns Hopkins University in Baltimore, Maryland. Stunned by the lecture, a young Harvey Cushing immediately embarked upon his important series of experimental hypophysectomies in dogs, and shortly afterward he began to treat clinical cases of pituitary disease. Nearly a decade later, in 1917, Sharpey-Schäfer offered Dott the opportunity to join his laboratory of physiology as a researcher (Fig. 2B). During his training in general surgery, Dott became actively engaged in experiments on gastric secretions and on thyroid and pituitary physiology. Therefore, Professor Sharpey-Schäfer
should be regarded as an influential figure that helped awaken an interest in pituitary tumors in his fellows Cushing and Dott.\textsuperscript{13,16,17,19,31}

Dott began his studies on the pituitary gland by assessing the physiological effects of its ablation in dogs and cats (Fig. 2C1 and C2).\textsuperscript{33} Impressed by his talent, Sir Walter Fletcher, Secretary of the Medical Research Council, arranged a Rockefeller fellowship for Dott to travel to Boston for further training with Harvey Cushing.\textsuperscript{6,61} The experience he lived while working at Brigham Hospital was a crucial period in his life, a time that, in his own words, “sealed [his] destiny” to devote himself to neurological surgery.\textsuperscript{29,31,32,41}

**Neurosurgical Instruction at Peter Bent Brigham Hospital: Forging His Indelible Friendship With Harvey Cushing**

The Rockefeller fellowship gave Dott the opportunity to become Cushing’s junior associate in surgery from November 1923 to June 1924.\textsuperscript{6,29,61} As Dott grew enthusiastic about Cushing’s activities, the latter discovered the former’s talents. Thus began an enduring personal friendship based on mutual respect and admiration, as evidenced by the collection of 67 letters between them housed in the Manuscript and Archives Department at the Sterling Memorial Library, Yale University.\textsuperscript{22,23} These letters, characterized by increasing affection and familiarity, covered a wide range of subjects, from technical neurosurgical topics to Dott’s personal life.

During his apprenticeship, Dott learned a vast range of neurosurgical principles and techniques that would prove extremely valuable for his own career.\textsuperscript{24,41} Dott was imbued with Cushing’s philosophy to perform a thorough, thoughtful study of the chronological sequence of symptoms, to determine an accurate preoperative topographical diagnosis of intracranial tumors. Cushing insisted on the paramount importance of perimetry for the assessment of visual disturbances associated with pituitary tumors, in addition to the careful interpretation of cranial radiography studies.\textsuperscript{64} Dott also learned from his mentor the imperative need to perform a meticulous postmortem examination of the brain specimens, with the aim of checking for possible diagnostic mistakes or operative errors. Finally, Dott observed the enormous importance Cushing placed on experimental research as a fundamental tool to answer clinical questions. To Dott, Harvey Cushing represented “The embodiment of an ideal, the combined experimental investigator and clinical surgeon” (Dott to Cushing, April 27, 1924)\textsuperscript{23}
Dott became fascinated by pituitary tumors, and his interest was certainly noticed by Cushing, who assigned him the monumental task of reviewing all his pituitary adenomas, a work that Dott performed in collaboration with Percival Bailey.34,35,38 Upon Dott’s return to Edinburgh, Cushing encouraged Dott to continue working in the field of pituitary surgery as he had full confidence in Dott’s abilities (Fig. 3A). Dott’s respect for Cushing’s knowledge about the pituitary gland is noticeable in the content of their correspondence over the following years. For example, Dott wrote a letter on May 15, 1926, in which he asked Cushing for advice about what to say regarding pituitary diseases to the congress of the British Medical Association. Dott wrote, “As my experience on pituitary diseases has been acquired entirely under your [Cushing’s] direction, I shall, of course, speak from this point of view.”22 He also sent Cushing reprints of the article “Diseases of the pituitary body” he published in 1927 to obtain Cushing’s verdict on his statements about the functional role played by the hypothalamus, a controversial topic at the time.22,28 Dott likewise consulted Cushing on his surgical pituitary cases. For instance, in a letter written on July 30, 1927, Dott reported his experience with a macroadenoma to Cushing:22

I operated on the enormous pituitary adenoma which I spoke to you about... The patient made an excellent primary recovery but suddenly developed spasmodic respiration and died in a few minutes, some fifteen hours later. Do you think it is unwise for me to attempt such cases where the risk is obviously very great at my present stage? I feel very unwilling to deny these people such chance as lies in operation and feel that it is humanly and scientifically the right thing to do. ...I should be very glad of your advice on this subject.

Dott’s second stay in Boston, from mid-July to mid-August 1929, was instigated by Cushing himself, who thought Dott needed more time with him to polish and further improve on the progress he was making in Edinburgh. Dott finally agreed to come to Boston, but only for 1 month, apparently due to his limited finances.29,61 Three years later, appreciative of Dott’s interest in the issue of pituitary-hypothalamic physiology, Cushing sent him a copy of his recently published book chapter “The pituitary body and hypothalamus” in January 1933.15 When Dott wrote back to thank Cushing for such a “splendid New Year’s gift,” he informed Cushing about his latest experiences with CPs and how he had dealt with a recent case (Fig. 3B):22

On the whole I have had fairly good luck with my pituitaries... I have been particularly fortunate with the craniopharyngiomas. We did our seventh complete extirpation of a large cystic one on a child of ten a few weeks ago with good result... (Norman Dott to Harvey Cushing, January 5, 1933)

Cushing rejoiced at Dott’s success and was proud to have played a part in it.22

In the Midst of the Storm: The Bailey-Cushing Conflict on the Hierarchy of Hypothalamus-Hypophyseal Relationships

The original ideas Dott had on the physiological role played by the pituitary gland were mostly influenced by Sharpoy-Schäfer’s and Cushing’s concepts.38 Schäfer’s and Cushing’s view supported the vital role of the pituitary gland as the organ in control of body homeostasis and metabolism, a concept derived from their consistent observation that hypophysectomized animals died after a process of progressive weakening and corporal emaciation, a clinical condition Cushing defined as “cachexia hypophyseopriva.”11,16,55,62 Dott had interpreted the results of his own experimental model of hypopituitarism in the same terms, by concluding that depression of metabolism was so severe after total pituitary removal that it usually led to the death of the animals (Fig. 2C1 and C2).53

When Dott arrived at Brigham Hospital in 1923, Percival Bailey was working as an assistant resident under Cushing.22 Without even realizing it, Dott found himself caught up in the battle between Cushing and Bailey regarding the origin of diabetes insipidus (DI), adiposity, and somnolence produced by pituitary tumors. Bailey had proved that minute injuries to the hypothalamus, even while sparing the pituitary gland, were sufficient to cause DI, somnolence, and adiposity in dogs.4,24 Moreover, he found that extensive lesions of the tuber cinereum were incompatible with life.4 Consequently, he defended the hypothalamic origin of both DI and the adipose-genital syndrome (Fröhlich’s).

Cushing vigorously criticized Bailey by claiming, erroneously, that he was “unqualified” to attribute these symptoms to a lesion of the diencephalon. Contrary to Bailey’s postulations, Cushing considered that the polyuria and adiposity observed in some dogs after hypophysectomy could be interpreted as being similar to the DI and Fröhlich’s syndrome observed in patients with large pituitary tumors.16–19,49 He also dismissed the results obtained by other experimental physiologists showing that experimental DI could be caused by a lesion limited to the hypothalamus without injuring the pituitary gland.1,2,8,9 Cushing believed that these symptoms were due to the insufficient secretion of the substance produced by the posterior pituitary lobe (“pitressin”), owing to the obstruction pituitary tumors caused on its release, which he presumed occurred via an upward pathway through the pituitary stalk into the third ventricle.16,49

Nonetheless, Cushing confessed his puzzlement at the contradictory results observed after hypophysectomy procedures in animals and human patients, as he had never observed the syndrome of cachexia hypophyseopriva among patients who underwent operations for pituitary tumors other than CPs.15,16,55 He missed the damage inflicted to the tuber cinereum by the subtotal method of hypophysectomy used in his laboratory. Such an unnoticed injury was more easily caused in dogs due to the peculiar close anatomical relationship between the gland and the third ventricle in these animals, which lack the intervening dural barrier of the sellar diaphragm present in humans.49 Cushing did not accept the possible solution to the riddle, Erdheim’s suggestion that polyuria and dystrophia adiposogenitalis (Fröhlich’s syndrome) observed in the group of hypophyseal duct tumors (CPs) could be due to the gross anatomical distortion to the tuber cinereum induced by these tumors.15,36,37,49,57

Working together in the analysis of symptoms present in Cushing’s patients with pituitary adenoma, Dott and...
Bailey confirmed Erdheim’s observations and found that DI and somnolence only occurred in those lesions that had grown beyond the sella turcica and encroached upon the region of the hypothalamus. Accordingly, in their co-authored manuscript on Cushing’s series of pituitary adenomas, they related the DI observed in some patients to a hypothalamic lesion. When Cushing reviewed the paper, he disagreed with such a concept and sent a letter to Dott on May 13, 1925, in which he requested that he remove any assumption against his theory supporting the pituitary origin of DI, with the following words:23

“...the discussion of diabetes insipidus and the possible lesions of the hypothalamus have so far as I can see, very little to do with the subject with which you are dealing.”

In spite of the admiration Dott felt for Cushing, he eventually sided with Bailey. In the speech he delivered to the British Medical Association on July 23, 1926, in Nottingham, he recognized the uncertainty about the origin of DI, but at the same time expressed, “...I am convinced that diabetes insipidus and the possible lesions of the hypothalamus have so far as I can see, very little to do with the subject with which you are dealing.”

Bailey’s Categorization of “Hypothalamic Cranioopharyngiomas”: Awakening Dott’s Awareness of a Forbidding Type of Lesion

Percival Bailey presented Dott with critical information regarding the topography and pathology of CPs (Fig. 4). Prior to Dott’s arrival at Brigham Hospital, Bailey had examined the brain specimens from Cushing’s patients with CP who had died either from complications of the procedure or from tumor progression.2,4,7 From this valuable material, Bailey learned that CPs occupying the region of the third ventricle usually showed histological evidence of tumor invasion to the hypothalamic “centers” that formed the diencephalon. As a general rule, in these CP cases, a sharp anatomical discrimination of the tumor boundaries from the adjacent brain tissue forming the infundibulum and the tuber cinereum could not be made. Bailey categorized this type of CP as true “tumors of the hypothalamus.”23 He acknowledged that such an intimate relation between the tumor and the surrounding hypothalamus was the critical factor that explained the high mortality and morbidity observed following surgical attempts to radically remove these lesions.23
Bailey’s topographical concepts about CPs convinced Dott that an accurate preoperative diagnosis of CP extension for each case was essential, to plan the optimal surgical approach for maximizing the likelihood of a radical excision while minimizing the risks of hypothalamic injury. For a correct diagnosis of CP topography, Dott learned from Bailey the importance of a thorough assessment of symptom chronology. For example, the development of aphasic-genital dystrophy, followed by hypersonnia, hyper/hypothermia, and/or emotional disturbances, usually occurred when the tumor gradually encroached upon the base of the brain. Topographical diagnosis of CPs should include a campimetric examination of visual defects and the identification of abnormal dense shadows found on skull radiographs, present in approximately 80% of tumors of this kind.\\n\\n**Immersion in the “Baffling Problem of Neurosurgery”: Cushing’s Strategies for Removal of “Hidden” Interpeduncular CPs**\\n
Harvey Cushing started pituitary surgery circa 1910 at John Hopkins Hospital by attempting the removal of pituitary tumors using the sublabial transphenoidal approach, a route that proved inadequate to safely remove tumors extending above the sella turcica. More challenging for Cushing was the approach to the group of “interpeduncular” cystic lesions, also known at first as “suprasellar cysts,” which did not originate within the sella and could therefore not be identified preoperatively on skull radiographs. Most of these lesions corresponded to solid-cystic CPs developed at the base of the brain, within the infundibulo-tuberal region.\\n
Cushing taught Dott the subfrontal method to approach the optic chiasm, his preferred route for the excision of CPs. This method allowed an easy identification of cystic lesions lodged beneath the optic apparatus, which could be pricked to evacuate the cyst content and achieve an adequate decompression of the optic chiasm. Nevertheless, once the drained cyst collapsed, the retrochiasmatic position of the solid, calcified portion of the lesion represented an insurmountable obstacle for Cushing, due to the fact that the optic apparatus itself hindered a proper view of the tumor and its attachments. Strong adherence of the tumor capsule to the hypothalamus precluded the use of “blind,” forceful surgical maneuvers to dislodge the tumor, as these were invariably followed by severe symptoms of hypothalamic failure, including malignant hyperthermia, leading to death in a few days. Discouraging experiences of catastrophic hypothalamic failure after apparently straightforward procedures compelled Cushing to express his belief that CPs represented “the most forbidding of the intracranial tumors.” Novel surgical strategies to achieve a safe dissection of the cleavage plane between the tumor and the hypothalamus were needed.\\n
Dott had the privilege of witnessing Cushing’s original strategies to overcome the huge difficulties posed by CPs involving the hypothalamus. According to our extensive review of the Brain Tumor Registry, a total of 11 patients with CPs were admitted to Brigham Hospital during the periods that Dott spent there. Some of these cases corresponded to intraventricular CPs hidden from surgical view beneath the optic chiasm. The methods devised by Cushing to manage these cases provided Dott with useful lessons and insights for coping with his own hypothalamic CPs.\\n
On January 7, 1924, Cushing operated on a blind 19-year-old girl who presented with a large calcified suprasellar cyst, as evidenced by the radiography studies (Patient M.P., surgery no. 20411). A right-side subfrontal approach to the optic chiasm region revealed a mass bulging beneath the lamina terminalis. Given the impossibility of accessing the tumor through the interoptic space,
he decided to open the lamina terminalis with the aim of emptying the cyst. Cushing’s own words regarding the case were, “It is the first time that I have ever carried out this measure… the fluid from the dilated ventricles may… escape by normal channels.” Dott witnessed how the patient improved after surgery and was discharged in good condition 3 weeks after the operation.

A similar infeasibility to remove a tumor hidden behind the optic chiasm occurred in another case (A.M., surgery no. 20814) assessed by Dott in February 1924. Cushing employed a subfrontal approach to the lesion, but no trace of the tumor could be found, and he envisioned for the first time splitting the optic chiasm as a potential solution. In his own words, “The only thing that could have been done in the way of improving the field of operation in this case would have been to split the chiasm in an antero-posterior direction.” However, he restrained himself from splitting the chiasm because campimetry studies had not shown visual deficits, and eventually he used a transcallosal route.

Another case of a CP hidden behind the optic chiasm occurred in a 46-year-old man treated by Cushing in November 1928 (Patient K.K.S., surgery no. 32358). In this patient, a ventriculography examination showed the presence of a mass in the third ventricle region. After exposing the optic chiasm through the standard subfrontal approach, Cushing presumed the presence of a craniopharyngeal pouch cyst hidden behind a chiasm of normal appearance. Then he reasoned to himself, “There was nothing to be seen to the outer side of the optic nerves… Realizing that this man’s vision was practically gone in one eye, I thought that it was advisable to split the chiasm....” By working through the chiasm, Cushing attempted to separate the lesion from the third ventricle, but because of the tumor’s profuse bleeding, he was able to remove only a small portion of it (Fig. 5A and B). Although Dott did not attend this procedure, he met the patient during the summer of 1929 when he was readmitted for clinical assessment. At that time Cushing was writing his work about “The chiasmal syndrome,” which included this case. Certainly, he must have talked with Dott about the strategy he followed to approach this lesion. After the patient’s death 13 months later, the brain autopsy proved the presence of a CP occupying the third ventricle.

Cushing would soon rebound from the previous disappointment. On June 25, 1929, he decided to transect the optic chiasm in a 15-year-old girl with a recurrent CP, to attempt a radical removal of the tumor (patient B.L.E., surgery no. 34286; Fig. 5C). On this occasion, the CP was removed successfully. Dott met the patient during her recovery and witnessed how she was discharged in excellent condition (Fig. 5D).

Through Cushing’s experiences, Dott learned the valuable technique of chiasm splitting to reach the intra–third ventricle extension of CPs hidden behind the optic chiasm. The transection of the chiasm could counteract the lack of proper illumination, and it was particularly advantageous to identify, under direct view, the cleavage plane of the mass and its degree of adhesion to the adjacent hypothalamus. The most valuable lesson Norman Dott took from Harvey Cushing was the need to preserve hypothalamus integrity at all costs. This conviction gave Dott the confidence to establish his own method of staged subfrontal and transventricular techniques for a safer excision of the lower infundibulo-tuberal and upper intraventricular cystic components of hypothalamic CPs.
Growth Pattern Classification of Hypophyseal Epidermoid Tumors (CPs)

It is remarkable that Norman Dott decided to use the word “craniopharyngioma” only in the letters he sent to Cushing, the author who precisely introduced this term in the late 1920s. Even so, Dott did choose to refer to CPs in his scientific publications using the terms “cystic pituitary epidermoid tumor” or “hypophyseal epidermoid tumor.” By using such terminology, Dott assumed Erdheim’s embryological theory for the origin of CPs: from cell remnants of the squamous epithelium that forms the hypophyseal duct, the embryological epithelial channel through which Rathke’s pouch migrates to join the diencephalic vesicle.

In accordance with Erdheim’s theory and Bailey’s pathological findings, Dott classified hypophyseal epidermoid tumors into 3 major groups, depending on their original development site along the hypophyseal-hypothalamic axis: the sellar, suprasellar, and hypothalamic topographical categories, each one associated with a characteristic growth pattern (Fig. 6A).

Sellar CPs originate in the substance of the anterior lobe of the hypophysis, within the boundaries of the sella turcica, causing a syndrome of pituitary insufficiency. Suprasellar CPs develop from the pars tuberalis, the tongue of adenohypophyseal glandular tissue that envelops the pituitary stalk and infundibulum. These lesions, confined to a subchiasmatic-suprasellar position, usually cause visual symptoms resulting from anatomical distortion of the neighboring optic chiasm at an early stage of tumor development. Lastly, the category of hypothalamic CPs grow within the substance of the third ventricle floor (TVF) itself, within the area of the infundibulum and tuber cinereum (Fig. 6B1 and B2). These lesions usually expand within the third ventricle. Consequently, they cause early symptoms of hypothalamic derangement in addition to acute hydrocephalus, due to the obstruction of the foramina of Monro (Fig. 6C1–C3).

Although simple, this topographical classification was useful to preoperatively predict a rather accurate location of CPs and to plan the surgical approach accordingly. Dott claimed that a correct preoperative distinction between tumors originating below or above the diaphragma sellae was possible with the clinical and radiological information available at the time. He warned that the different relationship between the tumor and the leptomeninges observed for the intrasellar and suprasellar CP categories would lead to a different sequence of anatomical distortions around the tumor, which, in turn, would result in a different cluster of symptoms. Fröhlich’s syndrome, DI, and somnolence were all symptoms occurring early in patients with hypothalamic tumors developing within the TVF as well as for suprasellar lesions extending into the third ventricle, whereas they did not occur in patients with intrasellar tumors until the lesion had invaded the hypothalamic region. Such a significant correlation between the type of syndrome (pituitary, infundibulo-tuberal, or hypothalamic) observed in the patient and the anatomical structures involved by the tumor has recently been confirmed by our group in a historical cohort of CPs.

Despite the obvious interest in CPs that Dott showed throughout his career, he published few works focused on these tumors. To the best of our knowledge, his first account consisted of a brief presentation of his CP cases in a...
For the treatment of these cases, Dott employed the transvenricular approach he had learned from Cushing.

He claimed that, contrary to the disheartening results of the surgery of hypothalamic CPs reported by other colleagues, he had been able to achieve the successful complete removal of the tumor in 8 (57%) of these 14 cases. The remaining 6 cases corresponded to 2 patients whose tumors were considered too advanced for surgery, and 4 patients who died after incomplete removal.

His following article on pituitary tumors, written in collaboration with the pathologist J. H. Biggart, defended the thesis that, contrary to other suprasellar lesions such as adenomas or meningiomas, the “epidermoid tumors” (CPs) could occupy the third ventricle and that tumors of this subgroup “have to be approached through a transvenricular route.” This was the first time that the intraventricular position of CPs was acknowledged in the medical literature. The third and last work on CPs published by Dott was his masterwork chapter “Surgical aspects of the hypothalamus,” in which he addressed in detail 47 ,48,50,51,56,58,59,60 all cases.

Therefore, Dott’s contribution to the surgery of hypothalamic CPs is worth mentioning.

### Clinical Impairment by CPs: Surgical Insights into the Workings of the Hypothalamus

Dott has bequeathed to us a comprehensive knowledge of the hypothalamus through the avenue of brain surgery.
It was in 1927 that Dott first claimed that a number of symptoms originally attributed to the pituitary gland—including adiposity, DI, and somnolence—were actually due to disturbances of the hypothalamic region. 28 He also localized the heat- and water-regulating centers in the tuber cinereum. 28 For that reason, he warned that the involvement of the hypothalamus should be included in any consideration of pituitary tumors, particularly in patients with hyperthermia, rapidly developing adiposity or unnatural emaciation, vasomotor disturbances, psychological changes, DI, or glycosuria. 28

Dott’s work culminated with the publication of his chapter on hypothalamic surgery included in the masterpiece *The Hypothalamus: Morphological, Functional, Clinical and Surgical Aspects*, at the age of 41 (Fig. 7). 34 This volume assembles an extensive and superbly illustrated account of the William Ramsay Henderson Trust Lectures on the hypothalamus delivered at the Anatomy Theater of Edinburgh in October 1936 by 4 outstanding neuroscientists: Sir Wilfred Edward Le Gros Clark, Professor of Anatomy at Oxford; John Beattie, Director of Research at the Royal College of Surgeons, London; George Riddoch, an eminent neurologist from the National Square Hospital in London; and Norman Dott. This book can be considered the founding work on the clinical and surgical science on the hypothalamus. 34 Reproduced from Dott 1938, 34 with permission from Susan Fraser Hider.

It was now identified as a brain center which orchestrated the inner body, but also for the stability of the psychic status of the individual. In addition, he confirmed the association of sleep disturbances with lesions developing at the level of the hypothalamus, even in the absence of signs of intracranial hypertension. Visual hallucinations occurring after surgery in Cases 746 and 996 were interpreted by Dott as waking dreams, a type of sleep disturbance (Table 1). Finally, he emphasized the characteristic psychic disturbances observed in patients with CPs encroaching upon the hypothalamus. These included personality changes, emotional volatility, with either euphoric state or apathy, and impairment of memory retention (alterations present after surgery in Cases 746 and 996 were interpreted by Dott as waking dreams, a type of sleep disturbance (Table 1). Finally, he emphasized the characteristic psychic disturbances observed in patients with CPs encroaching upon the hypothalamus. These included personality changes, emotional volatility, with either euphoric state or apathy, and impairment of memory retention (alterations present in Cases 746, 1105, and 1395). 34,14,34,39 In addition, he confirmed the association of sleep disturbances with lesions developing at the level of the hypothalamus, even in the absence of signs of intracranial hypertension. Visual hallucinations occurring after surgery in Cases 746 and 996 were interpreted by Dott as waking dreams, a type of sleep disturbance (Table 1). Finally, he emphasized the characteristic psychic disturbances observed in patients with CPs encroaching upon the hypothalamus. These included personality changes, emotional volatility, with either euphoric state or apathy, and impairment of memory retention (alterations present in Cases 746, 1105, and 1395; Table 1). The hypothalamus was now identified as a brain center which orchestrated critical functions, not only for the proper homeostasis of the inner body, but also for the stability of the psychic status of the individual.

**Surgery on Hypothalamic CPs**

Dott’s successful removal of hypothalamic CPs was a product of his thoughtful understanding of the CP-brain relationships, and, of no less importance, from his careful surgical handling of brain tissue. It can be said that Dott not only fulfilled but also exceeded the expectations Cushing had of him. In a letter Cushing sent to Bailey on August 15, 1929, he expressed the pride and high esteem he felt for Dott with the following words: “He is a fine lad and has matured in just the way I hoped he would. I shall expect great things of him. It’s a poor pupil that does not surpass his master, as Leonardo wisely said.” 31

Certainly, witnessing the numerous troublesome experiences that Cushing endured during his attempts of CP...
removal indelibly influenced Dott’s own surgical procedures. Training with Cushing taught Dott that CPs involving the hypothalamus were not easily reachable from under the frontal lobe. Instead, he argued that these lesions should be approached in the same way as true intraventricular tumors, a notion that represented progress over Cushing’s less precise concept of a general suprasellar topography for CPs.\textsuperscript{5,34,56} Indeed, in the revision of third ventricle tumors operated on by Cushing that Fulton and Bailey coauthored, they deliberately excluded CPs, despite their awareness that these lesions represented, “possibly the best examples of the hypothalamic syndrome.”\textsuperscript{39}

Norman Dott definitely advanced hypothalamic tumor surgery by realizing that any undue surgical manipulations of the CP attachment to the infundibulo-tuberal region of the hypothalamus had devastating effects on patient outcome.\textsuperscript{52-54,56} Therefore, he warned against radical dissection of the basal portion of the tumor, the area usually showing the strongest adherence to the hypothalamus.\textsuperscript{56} Acute hemorrhage or edema in the hypothalamus, undoubtedly the result of operative trauma, led to the death of his patient no. 996 (Table 1).\textsuperscript{34} Dott reasoned that had he just removed the free upper half of the tumor and left in place the lower adherent portion, “…doubtless the fatality would have been avoided and the patient might have done well enough for many years.”\textsuperscript{34}

Such a tragic experience made Dott think that the proper way to deal with CPs involving the hypothalamus was with a double-staged procedure: one to explore and bulk out the lower portion of the lesion attached to the hypothalamus, and a second to remove its upper portion lodged within the third ventricle (Table 1).\textsuperscript{34} In his chapter, “Surgical aspects of the hypothalamus,” Dott recommended using the subfrontal route to attack the basal portion of the CP adhered to the infundibulo-tuberal area, while leaving the upper, intraventricular cystic dome of the tumor for a second round through a frontal-transventricular approach (Fig. 8).

To avoid the injury associated with a forced lifting of the frontal lobe in patients with hydrocephalus, Dott employed the same method used by Cushing, consisting of tapping the anterior horn of the right lateral ventricle and aspirating the cystic content of the tumor to release tension and collapse the lobe. Then, if a flattened, compressed-forward optic chiasm was found, which prevented a direct view of the tumor, Dott’s choice was to sacrifice and lift one of the optic nerves, usually the one most impaired, to widen the view and provide an expanded space for a safe dissection of the cleavage plane between the CP and the hypothalamus (Fig. 8B2). This technique clearly represented a modification of Cushing’s midline division of the optic chiasm, the method he envisaged for removing inaccessible “interpeduncular cysts” (intraventricular CPs).\textsuperscript{12,20} Even so, Cushing was the first surgeon who, to improve the access to a retrochiasmatic CP, proceeded to divide the right optic nerve of the patient, on December 12, 1913 (Case “Lavestein,” surgical no. 663), and he might have informed Dott about this alternative method.\textsuperscript{20} Dott proceeded to sever one of the optic nerves in 2 of the 4 hypothalamic CP cases he operated on, both patients already presenting with very poor vision before the procedure (Cases 746 and 1105, Table 1; Fig. 8B2–B5). Certainly such a technical nuance contributed to Dott’s accurate judgment as to the degree of tumor adherence to the TVF and the chances for a safe CP radical removal while avoiding any undue injury to the hypothalamus.\textsuperscript{54,60} All the concepts upheld by Norman Dott’s work regarding the optimal surgical strategies for the removal of hypothalamic or infundibulo-tuberal CPs remain useful and valid today.\textsuperscript{54,63,65}

Conclusions

Norman M. Dott should be credited for the surgical methods he employed to safely and efficiently remove hypothalamic CPs. Between 1934 and 1937 he operated on 4 cases of third ventricle CPs developed from the infundibulo-tuberal area of the hypothalamus, with a satisfactory postoperative outcome in 3 out of the 4 patients. This series of procedures represents a notable accomplishment, especially when considering the enormous limitations of the available diagnostic methods at the time, as well as the crudeness of the existing surgical techniques. Dott’s acceptable success with hypothalamic CPs was directly related to his thorough scientific background and the vast surgical training he received at Peter Bent Brigham Hospital, under the tutelage of Harvey Cushing and Percival Bailey. From the observations of the cases treated by Cushing during his two stays at the Brigham, Dott realized that the group of CPs originating in the TVF had an intimate relationship with the hypothalamus. He devised a 2-stage surgical approach for removing hypothalamic CPs: first a basal, subfrontal, or perionial approach to attack the basal portion of the tumor attached to the infundibulo-tuberal area; then a subsequent transventricular approach to remove the upper cystic component inside the third ventricle. He was aware of the high risk of hypothalamic trauma during surgical maneuvers for CP dissection and recommended leaving behind the portion of the tumor strongly attached to the TVF to avoid fatality. Dott’s surgical methods addressing hypothalamic CPs represent not only a notable progress in the battle against one of the most serious pathologies facing contemporary neurosurgeons but also one of his major legacies to the field of pituitary surgery.

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FIG. 8. Dott’s 2-stage approach to hypothalamic CPs. A1: Diagram of a sagittal section of surgical case no. 1105 (Table 1), showing the tumor before surgery. Note this large solid-cystic lesion grows from the tuberal area and occupies the third ventricle, causing obstructive hydrocephalus. A2: Midsagittal illustrative scheme showing the upper cystic remnant after the first procedure of CP removal through a subfrontal (SF) approach, in which the lower pole of the tumor attached to the tuber cinereum has been excised. A3: Diagram after the second operation through a frontal-transventricular (FTV) approach showing the third ventricle free of tumor. B1–B5: Surgical steps for removal of the infundibulo-tuberal portion of the lesion. B1: Exposure of the optic chiasm. Note the chiasm is pushed forward and the optic nerves are shortened. B2: The right optic nerve has been severed to give access to the lesion hidden from view behind the chiasm. B3: Dissection of the tumor from the optic chiasm and TVF. B4: The chiasm is retracted backward and the tumor is pulled out with forceps. B5: The tuberal part of the cyst has been cut away from the upper cystic component. C1–C5: Surgical steps for removal of the intraventricular cystic component of the lesion through a transfrontal-transventricular route. C1: The right lateral ventricle is approached by excising a conical section of the frontal lobe. The sketch of the surgical avenue is shown in the inset. C2–4: After sectioning both columns of the fornix, the third ventricle cavity is widely exposed, and the cyst wall is grasped and pulled out with forceps. C5: The white shining walls of the ventricle can be seen at the end of the procedure. Reproduced from Dott 1938, with permission from Susan Fraser Hider.
in contacting the Dott family. We would like to particularly thank Susan Fraser Hider, Jackeline Tidder, and Katherine McQuade, Dott’s grandchildren, for their kind permission to reproduce the letter written by Norman M. Dott on January 5, 1933, as well as the images from his surgical procedures displayed in the book The Hypothalamus: Morphological, Functional, Clinical and Surgical Aspects. Finally, we wish to express our gratitude to George Hamilton for his critical review of the language and style of the paper.

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