

Dr. Harvey Cushing's attempts to cure migraine based on theories of pathophysiology

Historical vignette

KATHERINE LATIMER, B.S.,¹ COURTNEY PENDLETON, B.S.,¹ JASON ROSENBERG, M.D.,² AARON A. COHEN-GADOL, M.D., M.Sc.,³ AND ALFREDO QUIÑONES-HINOJOSA, M.D.¹

Departments of ¹Neurosurgery and Oncology, and ²Neurology, The Johns Hopkins School of Medicine, Baltimore, Maryland; and ³Goodman Campbell Brain and Spine & Indiana University Department of Neurosurgery, Indianapolis, Indiana

A multitude of theories characterized medical thought on migraine in the early 20th century. Newly discovered historical case files revealed Dr. Harvey Cushing's previously unpublished early attempts at surgical cure of migraine. Following institutional review board approval, and through the courtesy of the Alan Mason Chesney Archives, the authors reviewed the microfilm surgical records for The Johns Hopkins Hospital from 1896 to 1912. Patients undergoing surgical intervention by Dr. Harvey Cushing for the treatment of migraine were selected for further review. All 4 patients in the series were women and ranged in age from 29 to 41 years old. The women were admitted and observed in the hospital until a migraine occurred. Surgeries were performed while the women were in the midst of an attack. Cushing used surgical strategies including decompression, temporal artery ligation, and removal of the spine of the second vertebra. In each case, the patients' headaches eventually returned following surgery. Cushing relied on a combination of contemporary theories on migraine including humeral science, vasospastic theory, organic cause, and increased intracranial pressure. His unpublished efforts foreshadowed future surgical efforts at curing migraines. (DOI: 10.3171/2011.5.JNS101855)

KEY WORDS • Harvey Cushing • migraine • headache • history • pain

Of all the common and much-dreaded nervous diseases we recognize, none are less perfectly understood than migraine; nor is there any other nervous disorder which is so disastrous to the physician's ability for effectual treatment.

J. M. AIKIN¹

This sentiment, published in a *Journal of the American Medical Association* article written by Dr. J. M. Aikin in 1902,¹ reflects the therapeutic conundrum that a diagnosis of migraine presented to physicians at the turn of the 20th century. During this period, doctors were armed with a multiplicity of noncurative therapies including electricity, hydrotherapy,¹² and drugs such as phenacetin⁹ and "morphia" (morphine).¹¹ Surgical treatments were also developed for headaches and were frequently directed at the nose and throat.¹² While definitive treatment remained elusive, newly discovered historical case files reveal that surgical management was also attempted by Dr. Harvey Cushing, the man widely regarded as the father of modern neurosurgery, in the early 1900s.⁶ Knowledge of these neurosurgical forays into treating headache has been lacking due to the fact that the results of Cushing's unsuccessful procedures were never published.

Medical literature in the late 19th and early 20th

century provided an array of explanations for migraines and headaches in general, blending newly characterized physiology,¹¹ personal experiences,²⁰ and humoral science, that is, the philosophy that the body was composed of basic substances that needed to be in balance for states of health.¹² Vasodilatory theories were upheld¹³ as explanatory alongside theories stating that pain was due to ailments of the eyes,¹⁰ nose, and throat.¹⁴ Others posited that pelvic conditions were the source of at least 10% of migraines in women,¹⁷ or that increased "brain work" was to blame.¹⁵ Further, many physicians believed that toxin overload due to absorption from the intestines, coupled with poor filtration by the liver, was the main mechanism producing head pain.¹

Newly discovered historical case files reveal that surgical cure of migraine headache was also attempted by Dr. Harvey Cushing in the early 1900s.⁶ In this paper we report on 4 cases with a diagnosis of migraine treated by Cushing at The Johns Hopkins Hospital in the early 1900s. The surgical approaches employed by Cushing in these cases integrated the disparate theories of migraines and attempted to tailor surgical treatment according to contemporary theories of pathophysiology.

Case File Review

Following institutional review board approval, and

Abbreviation used in this paper: IHS = International Headache Society.

Cushing's attempts to cure migraine

through the courtesy of the Alan Mason Chesney Archives, the microfilm surgical records for The Johns Hopkins Hospital from 1896 to 1912 were reviewed. Patients undergoing surgical intervention by Dr. Harvey Cushing for the treatment of migraine headache were selected for further review.

While at The Johns Hopkins Hospital, Cushing operated on 4 women who presented with migraine. The mean age of the patients was 33 years old, ranging from 29 to 41 years. Each woman was admitted and observed in the hospital until a typical headache occurred. Operations were planned to commence in the midst of an attack in the hope that the surgery would reduce the pain. Summaries of the cases are provided below.

Case 1

On June 29, 1909, a 41-year-old woman presented with a history of left temporal headaches that had occurred every 2 to 6 weeks since she was 14 years old. She occasionally vomited, and felt that her temporal artery stood out "as if it would burst" during some attacks. She had found that a dark room and pressure applied to the temples, along with "morphea," lessened pain. Her prior treatments included glasses, hydrotherapy, electricity, Christian sciences, "pure mental science," and living in a sanitarium. She had her ovaries, Fallopian tubes, and a portion of her uterus removed after a physician diagnosed her with an ovarian condition that "was serious and probably accounted for headaches," but her headaches persisted, and she developed a hernia at the site of the incision. Upon physical examination, she was noted to be thin with sluggish pupils, a tortuous temporal artery, and prominent veins throughout her body and on her eyelids.

She was diagnosed with "migraine," and on July 12, while the patient was experiencing an attack, Dr. Cushing performed a "left sub-temporal decompression, ligation of the left temporal artery." His operative note describes the procedure:

An anomalous condition was found in the bone, there being found anteriorly two layers of skull resembling a laterally prolonged frontal sinus or very large diploetic cavity... On incising [the dura], there was found a considerable amount of cerebrospinal fluid. The cortex appeared edematous and swelling bulged into the defect in the dura. It was suggested by the operator that the condition might be cerebral oedema, possibly resembling aneural neurotic oedema. Operation consumed twenty-five minutes.

Postoperatively, her migraine headaches ceased, and she was left with only slight discomfort, believed to be typical following a neurosurgical procedure. She also gained weight after placement on a "forced diet." The patient was discharged with her condition recorded as "improved." Unfortunately, she sent a letter 2 months later reporting that her headaches had returned with a slightly different localization and that "three times the pain had got so hard we had to call a Dr but I only had a light opiate and was alright the next day."

Case 2

On January 16, 1910, a 32-year-old woman presented with a 10-year history of right-sided headaches occurring

every 2 weeks. Each attack lasted 3 days and confined her to bed. She had prodromal right-sided tightness and "weakness and burning" in her right eye. Her temporal artery became tense and prominent during the severe part of the headache. After trying many drugs, she relied on "morphia." During a migraine attack, a "special note" in the chart documents sensitivity over the suboccipital area "akin to cases of meningitis serosa," a "slower" pulse, and no external vessel dilation, although Dr. Crowe described dilation and tortuosity of vessels on ophthalmological exam.

Dr. Cushing performed a right-sided decompressive craniotomy (Fig. 1). His operative note reported:

Disclosing of possible organic basis for migraine: The entire temporal region was occupied by the same double layered bone that was observed in the case of [Case One]... there was a definite endostosis which must have been possibly 5 mm in thickness. This indented the dura and...was found subsequently to directly overlay the vessels...in the Sylvian fissure...A natural suggestion arose as to whether this direct pressure of its fairly sharp point might not have led to permanent spasms of the vessel...Thickening of the dura and cerebral oedema, possibly confined to the right side.

Postoperatively, the patient reportedly developed a CSF leak, the treatment of which was not specified. She was discharged with instructions for morning exercise, hot water, a careful diet with laxative foods, and avoidance of horseback riding. Fourteen days later she was readmitted with another migraine. At that time, Cushing avoided surgery; he administered chloroform until the woman was unconscious and then gave her "morphea." She was discharged on February 24, 1910.

The patient wrote to Dr. Cushing in July 1910 that her migraines persisted, but she lacked funds for further care since her husband had been "idle." Another letter arrived in May 1914 stating that her headaches were now much less frequent.

Case 3

In November 1910, a 29-year-old woman presented with a 3-year history of headache occurring once every 3 weeks and lasting 1 to 2 days. She experienced an aura over her left eye prior to the development of throbbing, constant pain behind the left eye. She typically vomited when she had attacks and reported that she had one deceased brother who had similar symptoms. Upon physical examination during a migraine, she was noted to have marked dilation of venules of her head and fullness of vessels of the fundus (Fig. 2).

Dr. Cushing performed a subtemporal decompression. He reported:

A very difficult decompression owing to the bleeding from the meningeal...combated for almost two hours...it finally was necessary to cut down and occlude the vessel near the foramen spinosum. The bone was thick and showed changes similar to those seen in the other cases i.e., large diploetic spaces and peculiarly brittle breaking on rongeur the bone...on opening the dura...the brain was wet and there was an abundance of CSF.

Postoperatively, the patient had another migraine before her discharge on December 10, 1910, but was record-

Jan 22nd,
Operation

Decompressive craniotomy (Right)
Spongy, brittle bone - a definite
sinus was opened into in the
posterior portion of the decompressive
opening - operation during an "attack"

Fig. 1. Cushing's note describing the surgical procedure in Case 2, which reads: "Decompressive craniotomy (Right) Spongy, brittle bone - a definite sinus was opened into in the posterior portion of the decompressive opening - Operation during an 'attack'."

ed as improved because she reported that her pain had decreased. No additional follow-up was available.

Case 4

In January 1912, a 30-year-old woman was admitted complaining of "sick headaches" since the age of 9, associated with a "heavy feeling of the head" and facial flushing. She stated that her pain began in the right suboccipital region and spread to the right side of her head or left suboccipital region. Typical attacks confined her to bed for a day at a time, but she stated that a low-level pain could persist for weeks. She had numerous prior treatments including electricity, counter irritation, and large doses of narcotics. Ice bags and aspirin provided the most relief; she took 50–60g aspirin daily until her stomach became upset. Upon physical examination, the patient was noted to have an unusually prominent and broad spine of the axis. Initially, Cushing decided not to operate; however, when the patient, desperate for a potential cure, returned in May of the same year, Cushing decided to remove the spine of the axis: "Superficial tissues seemed somewhat tense...possibly the consequence of old scarification...The bifid spine after all did not seem to show any abnormality. It was removed with rongeurs." The procedure had no effect on the patient's condition. When her headache returned, Cushing used phenacetin and aspirin for pain control, and administered nitroglycerin to reduce blood pressure.

Discussion

These cases provide a reference point for the variety of theories on migraine pathophysiology present at the turn of the 20th century, all of which Cushing relied on and regarded highly enough to test on the operative table. The cases also provide a historical comparison for the diagnosis of migraine. Historically, migraine was described similarly to the definition provided in Dr. Joseph Nagel's 1904 *Manual for Students and Practitioners* of "a peculiar form of severe paroxysm of unilateral headache associated with vasomotor disturbances and often accompanied by nausea and vomiting."¹⁶ Interestingly, the symptoms of Cushing's patients generally conform to the 5 modern diagnostic criteria developed by the

International Headache Society (IHS) (Table 1) except that the presence of photophobia or phonophobia was not typically elicited during the medical interview.

Historically, pathophysiology of headache relied heavily on humoral theories; even the 4th edition medical text of Cushing's mentor, William Osler, suggested a humor-based headache cure.¹² Cushing's headache cases contain clear traces of humoral theory, the notion that states of health were dictated by concentrations of 4 basic body substances or humors, which was popular in the 1600s and 1700s and evolved into the notion that general substances or toxins in the body were responsible for ailments.^{2,15,18} The term "sick" used in Case 4 classically referred to a bilious-natured headache caused by the buildup of bile, and became a synonym for migraine.^{2,15} Cushing's recommendation of a laxative diet for Case 2 was potentially based on theories that clearing products from the intestines could decrease headaches;¹¹ toxins absorbed from the intestines were believed to be capable of overwhelming the liver, escaping into the body, and causing pain.²

Cushing also considered the idea that "organic," or structural, causes were responsible for migraine. While it was not uniformly believed that structural causes for migraine existed,¹⁶ some textbooks during the era made efforts to classify distinct types of headache including congestive, neuralgic, anemic, or organic; migraine fell into the organic class, which was due to structural



Fig. 2. Photograph from Case 3 with accompanying note, which reads: "Photo taken morning of operation during a hemicrania attack, showing the dilatation of the venules of the lids."

TABLE 1: Symptoms of patients in Cases 1–4 according to IHS migraine criteria

Case No.	Criteria								
	A*	B†	C (need 2 listed below)				D (need 1 listed below)		E‡
			unilateral	pulsating	moderate/severe intensity	worse w/ activity	nausea or vomiting	photophobia/phonophobia	
1	yes	yes	yes	unknown	yes	yes	yes	yes	yes
2	?	yes	yes	yes	yes	yes	no	unknown	yes
3	yes	yes	yes	yes	yes	yes	yes	unknown	yes
4	no	no§	yes	no	yes	yes	yes¶	unknown	yes

* At least 5 attacks meeting criteria B–E.

† Attacks lasting 4–72 hours.

‡ No other reason for attacks.

§ Some attacks had pain that lasted 1 week.

¶ Nausea was implied.

factors.⁸ Cushing documented similarities between the thickness and layering of portions of the skull in 3 of his headache patients, although the cases were months or years apart. He also noted potential cerebral edema in Case 1. In Case 4, Cushing targeted the patient's abnormal physical examination finding of a prominent spine of the axis. Ultimately, however, Cushing was unable to devise a coherent theory for how these anatomical variations explained each patient's pain.

Cushing favored the theory that increased intracranial pressure could account for migraines. Trephining the skull to treat headache was practiced even in prehistoric times as evidenced by the skulls of Neolithic men found in Europe, Africa, Asia, and North and South America.^{13,19} The idea that opening the skull could relieve the pressure responsible for headaches was established in medical literature in the 1890s.⁷ In 3 of Cushing's 4 migraine patients, his operative procedure included some element of decompression. This is not surprising; Cushing described the symptoms of headache and nausea in his patients with brain tumors, and he routinely used decompression to successfully alleviate these symptoms.⁴ His efforts paralleled other efforts to cure migraine by decreasing intracranial pressure; Schuller proposed trepanation and craniotomy with third ventricle puncture in 1909¹² while others, such as Heinrich Irenaeus Quincke, performed lumbar puncture.¹²

Cushing also endorsed the competing idea that headaches were a problem of nerves or blood vessels rather than the result of gastrointestinal or other issues,^{2,20} suggesting the position of vessels below an aberrant growth of bone led to the migraines experienced in Case 2. Articles written as early as 1872 attributed pain to the stretching of nerve fibers within blood vessels.²⁰

Another pathophysiological explanation that is evident in Cushing's work is the vasomotor hypothesis. This explanation contained 2 core elements: vasospasm and vasodilation.¹⁸ Historically, Du Bois Reymond posited that arterial spasm from sympathetic stimulation was a possible cause of migraine.¹⁸ In fact, some of Cushing's contemporaries contributed the zigzag patterns of vision observed in migraine sufferers to vasospasm in the occipital region.² Mollendorff and contemporaries of Cushing

asserted that increased, violent pulses of blood flow toward the brain^{12,18} or hypertension⁷ were problematic in migraine. Literature from the 1880s stated that signs of vascular dilation were prominent during attacks.¹¹ These notions of vasospasm and vasodilation were combined by Latham into the theory that contraction of vessels of the brain led to diminished blood supply and sympathetic stimulation.¹⁸ When this stimulation ended, headache ensued.¹⁸ Cushing's reliance on these principles is noted in Case 1, in which temporal artery ligation was performed, and in Case 4, when Cushing used nitroglycerin to decrease blood pressure in an attempt to provide palliation. Additionally, each of Cushing's patients was observed for external signs of vascular involvement during migraines and had dilations or engorgements of vessels photographed and described.

Migraine theory has continued to evolve. In the 1930s, Harold G. Wolff and colleagues demonstrated the proportional relationship between dilation of extracranial arteries and the release of local pain-producing factors as a basis for explaining migraine.^{5,18} Vasoconstriction was believed to be prominent during aura in the patients who experienced this phenomenon; it was believed to conclude prior to onset of extracranial vasodilation.^{5,18} In the 1980s, Lauritzen and Olesen questioned the findings of Wolff and concluded that aura may be due to spreading depression, originally described in 1944 by Brazilian neurophysiologist Leao.^{3,5,18} At present, several gene mutations have also been identified that contribute to familial cases of migraine.³

Harvey Cushing's attempted neurosurgical cure of migraine has never been reported due to the fact that he did not publish his findings. Although he likely did not report the procedures because they failed to produce an effective cure, Cushing's cases provide a historical benchmark of the diagnosis of migraine and the diverse pathophysiological theories that described it during the early 20th century. Cushing considered humoral theory, organic cause, increased intracranial pressure, and the vasomotor hypothesis as plausible explanations. While the definition of migraine has remained similar, the cause continues to evolve and challenge modern day physicians as it did over a century ago.

Disclosure

Katherine Latimer is supported by the Bean Student Research Award from the American Osler Society. Courtney Pendleton is supported by a Howard Hughes Medical Institute (HHMI)-Ivy Research Training Grant. Alfredo Quiñones-Hinojosa is funded by a KO8 NIH grant and an HHMI grant. Figures provided courtesy of the Alan Mason Chesney Archives.

Author contributions to the study and manuscript preparation include the following. Conception and design: Quiñones-Hinojosa, Latimer, Pendleton. Acquisition of data: Latimer, Pendleton. Analysis and interpretation of data: Latimer, Pendleton. Drafting the article: Latimer. Critically revising the article: Quiñones-Hinojosa, Pendleton, Rosenberg, Cohen-Gadol. Reviewed submitted version of manuscript: all authors. Administrative/technical/material support: Quiñones-Hinojosa, Rosenberg.

References

1. Aikin JM: Etiology and treatment of migraine. **JAMA** **39**: 485–487, 1902
2. Brunton TL, Grant D, Allbutt TC, Campbell H, Tyson JW, Herschell G, et al: A discussion on headaches and their treatment. **BMJ** **2**:1241–1246, 1899
3. Charles A: Advances in the basic and clinical science of migraine. **Ann Neurol** **65**:491–498, 2009
4. Cushing H: **Intracranial Tumours. Notes Upon a Series of Two-Thousand Verified Cases with Surgical-Mortality Percentages Pertaining Thereto**. Springfield, IL: Charles C Thomas, 1932, pp 105–113
5. Diamond S, Franklin MA: **Headache Through the Ages**. West Islip, NY: Professional Communications, Inc., 2005
6. Greenblatt SH: The crucial decade: modern neurosurgery's definitive development in Harvey Cushing's early research and practice, 1900 to 1910. **J Neurosurg** **87**:964–971, 1997
7. Haig A: The treatment of headaches. **BMJ** **2**:1246–1247, 1899
8. Hamilton AM: **The Modern Treatment of Headaches**. Detroit: George S. Davis, 1888
9. Harris W: An address on the treatment of some of the severer forms of headache. **BMJ** **2**:297–298, 1908
10. Higgins C: On the relation of headaches to the condition of the eyes. **BMJ** **1**:104, 1887
11. Jewell JS: The nature and treatment of headaches. **J Nerv Ment Dis** **8**:64–79, 1881
12. Koehler PJ, Boes CJ: A history of non-drug treatment in headache, particularly migraine. **Brain** **133**:2489–2500, 2010
13. Magiorkinis E, Diamantis A, Mitsikostas DD, Androutsos G: Headaches in antiquity and during the early scientific era. **J Neurol** **256**:1215–1220, 2009
14. McKeown D: Headaches and other nervous symptoms in relation to post-nasal adenoids. **BMJ** **2**:894–895, 1900
15. McTavish JR: The headache in American medical practice in the 19th century: a historical overview. **Headache** **39**:287–298, 1999
16. Nagel JD: **Nervous and Mental Disease. A Manual for Students and Practitioners**. New York: Lea Brothers & Co., 1904, p 26
17. Perkins AE: The causes and symptoms of headaches. **Am J Nurs** **12**:26–29, 1911
18. Sacks OW: **Migraine**. Berkeley: University of California Press, 1992
19. Sangvichien S, Subhavan V: Skull trephining in prehistory. **J Sci Soc Thailand** **2**:142–147, 1976
20. Wilks S: On sick-headache. **BMJ** **1**:8–9, 1872

Manuscript submitted November 2, 2010.

Accepted May 17, 2011.

Please include this information when citing this paper: published online June 17, 2011; DOI: 10.3171/2011.5.JNS101855.

Address correspondence to: Alfredo Quiñones-Hinojosa, M.D., Brain Tumor Stem Cell Laboratory, Department of Neurosurgery and Oncology, 1550 Orleans Street, Cancer Research Building II Room 253, Baltimore, Maryland 21231. email: aquinon2@jhmi.edu.