

■ LITERATURE REVIEW

Role of the Extracranial Arteries in Migraine Headache: A Review

Elliot Shevel, B.D.S., M.B., B.Ch.; Egilius H. Spierings, M.D., Ph.D.

0886-9634/2202-132\$05.00/0, THE JOURNAL OF CRANIOMANDIBULAR PRACTICE, Copyright © 2004 by CHROMA, Inc.

Manuscript received June 2, 2003; revised manuscript received October 23, 2003; accepted January 7, 2004

Address for reprint requests:
Dr. Elliot Shevel
Johannesburg Branch
Headache Clinics International
Suite 256
P. Bag X2600
Houghton 2041
South Africa
E-mail: drshevel@headclin.com

ABSTRACT: The pain of the migraine headache is often so debilitating that it severely compromises quality of life. The vascular component of the trigeminovascular system has been implicated in the pain mechanism. There is, however, debate as to whether the pain originates in the intracranial or extracranial vasculature or in both. In this article, evidence is presented to suggest that the extracranial arteries are the source of the pain in some migraine sufferers.

Dr. Elliot Shevel studied at the University of the Witwatersrand in Johannesburg, South Africa, where he received a B.D.S. in 1967, a Dip. M.F.O.S. in 1972, and an M.B., B.Ch. in 1977. He is a practicing maxillofacial and oral surgeon and is founder and director of the Headache Clinic in Johannesburg.

Migraine is a common condition with a 1-year prevalence of approximately 18% in women, 6% in men, and 4% in children.¹ It has been shown that the intensity of the pain, combined with the concomitant neurological, gastrointestinal, and sensory symptoms, reduces the quality of life of migraine sufferers significantly.^{2,3} The quality of life of migraine sufferers is worse than that associated with other major conditions, such as arthritis and diabetes. It is comparable to the level of dysfunction seen with recent myocardial infarction or congestive heart failure.⁴ In order to develop more effective abortive and preventive treatment modalities for migraine headache, it is essential to have a clear understanding of the mechanisms involved.

The first recorded reference to the involvement of the extracranial vasculature in headache is attributed to Abu Qasim al-Zahrawi.⁵ This renowned Moorish physician, known in the West as Abulcasis or Abucalsis, treated headache by surgical ligation of the superficial temporal artery. Ambroise Pare (1510-1590), regarded by many as the father of modern surgery, divided his own superficial temporal artery to relieve his migraine headaches.⁶

Hare⁷ observed "headache . . . to diminish in intensity locally when the particular artery which supplies the affected region is pressed on." He found that compressing the occipital, superficial temporal, or angular artery relieved the headache over the distribution of the relevant

vessel. Similar findings stimulated interest in the role of the branches of the external carotid artery in vascular headache.⁸⁻¹⁰ Studies on the pulse waveform during migraine headache of the superficial temporal, occipital, supra-orbital, and posterior auricular arteries indicated that they were a major source of pain in migraine.¹¹⁻¹³ Graham and Wolff⁸ became the main protagonists of the then popular view that the pain of the migraine headache originates in the extracranial arteries (**Figure 1**).

The importance of the role of the extracranial vasculature was later challenged, and experimental evidence was produced to support the view that the pain of the migraine headache is predominantly of intracranial origin.¹⁴⁻¹⁷ Blau and Dexter¹⁷ set out to show that the pain of the migraine headache is intracranial in origin,¹⁵ and suggested that the following points favored an intracranial origin of the pain:

1. In temporal arteritis, when the superficial arteries are inflamed, headache is prominent but nausea, vomiting, and photophobia are absent. In meningitis, however, headache, nausea, vomiting, and photophobia are cardinal symptoms and signs. As the headache phase of migraine mimics meningitis, they make the tenuous conclusion that the pain in migraine is intracranial in origin.
2. Coughing, sneezing, and bending down potentiate the pain in most migraine sufferers due to raised intracranial pressure.
3. Jolting the head from side to side increases the pain in migraine.
4. Histamine headache simulates migraine.
5. Evidence from ocular and conjunctival vessels.

Blau and Dexter¹⁷ actually found that 43% of their

subjects experienced pain relief by digital compression of the superficial temporal arteries, or by compression of all the superficial terminal branches of the external carotid arteries by means of an inflated sphygmomanometer cuff. They state in their summary that "an extracranial factor is also present."

Ergotamine

The efficacy of ergotamine in terminating migraine headache¹⁸⁻²⁰ provided the opportunity to study changes in the pulsation amplitude of the superficial temporal and occipital arteries, before and after successful treatment. Graham and Wolff,⁸ using intravenous ergotamine, found that the "amplitude of pulsations declined with the diminishing intensity of the headache. When the amplitude of pulsations decreased slowly, headache likewise diminished slowly. When the amplitude dropped precipitously, the headache was ended promptly." They concluded that "the head pain of the migraine attack is produced by the distension of the cranial arteries and that termination of the headache by ergotamine tartrate is due to the capacity of this agent to constrict these cranial arteries and thus reduce the amplitude of their pulsations."

Although ergotamine causes vasoconstriction of the extracranial arteries, it does not affect cerebral blood flow,²¹ even when effective in abolishing migraine headache.²² The conclusion that the therapeutic effect of ergotamine depends on its ability to produce extracranial vasoconstriction led to experimentation with other vasoconstrictors: administration of ergonovine, caffeine, benzedrine, ephedrine, and pitressin all resulted in reduction of the migraine headache, commensurate with a reduction in the pulsation amplitude of the superficial temporal artery.¹⁰

Intracranial Pressure

Schumacher and Wolff²³ devised a method of rapidly increasing cerebrospinal fluid pressure by connecting the subarachnoid space with a column of sterile physiological saline. The column could be raised or lowered to increase or decrease the cerebrospinal fluid pressure respectively. In headache due to dilation of cranial arteries, pain reduction when the cerebrospinal fluid pressure is increased indicates the intracranial arteries to be the origin of the pain. On the other hand, no reduction in pain intensity indicates the pain to originate extracranially. Schumacher and Wolff²³ studied two groups of patients: one with migraine headache and the other with histamine-induced headache. In the eleven patients with histamine-induced headache, the pain was relieved within 15-90 seconds of raising the intracranial pressure. In seven of these, there was a constant relationship between

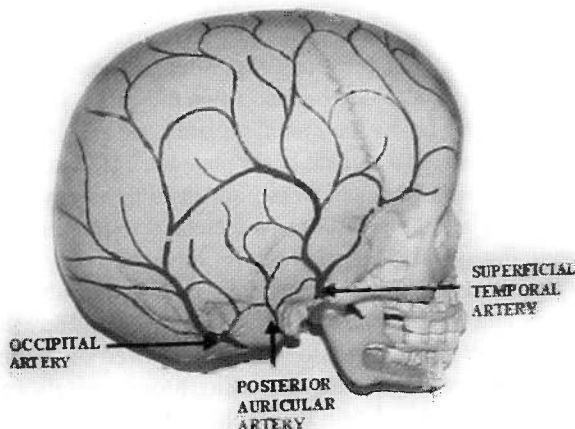


Figure 1
The superficial branches of the external carotid artery. There are extensive anastomoses between the branches, and between the left and right sides.

changing the cerebrospinal fluid pressure and the intensity of the headache. The subjects always experienced a recurrence of the pain following a rapid reduction of the pressure; the headache was relieved when the intracranial pressure was increased by an average of 350 mm H₂O.

In six out of seven subjects with migraine headache, however, no change in pain intensity occurred, even when the cerebrospinal fluid pressure was increased to as high as 700 to 1000 mm H₂O for up to 30 minutes. In one subject, there was reduction in headache intensity, but the authors suggested that this was possibly due to spontaneous resolution of the headache. Other patients had previously experienced spontaneous resolution of their headaches while waiting for the experiment to be carried out, but it is also possible that in this subject the pain was, indeed, intracranial.

They concluded that: 1. The pain of histamine-induced headache originates from the intracranial vessels; and 2. The pain of migraine headache is extracranial in origin.

Blau,¹⁵ in an attempt to refute Wolff's¹¹ extracranial hypothesis, quoted Von Storch,²⁴ who stated that histamine headache simulated migraine headache in 33 out of 37 migraine sufferers. He argued that this was evidence in support of the intracranial origin of the pain of the migraine headache. The fact that histamine also causes headache in nonmigraine sufferers was glossed over; furthermore, histamine headache is not migraine and is not accompanied by nausea and vomiting.

Pulsation Amplitude of the Branches of the External Carotid Artery

Graham and Wolff⁸ first demonstrated a positive correlation between the amplitude of pulsation of the branches of the external carotid artery and the intensity of the migraine headache. Further studies showed that the mean pulse amplitude of the frontal branch of the superficial temporal artery was twice that of normal controls.¹³ It was also shown that the temporal pulse diminished in amplitude by 12-84% in migraine sufferers as they stood up from lying down, while only minor changes (9-13%) took place in normal subjects.²⁵ Following exercise, the temporal artery on the affected side in migraine sufferers dilated more than on the headache-free side.²⁶ The luminal diameter of the frontal branch of the superficial temporal artery, measured with high resolution ultrasound, was significantly larger on the symptomatic side than on the non-symptomatic side, during but not between headaches.²⁷

Heyck¹⁴ was unable to repeat Graham and Wolff's⁸ experiments and in the light of this and other evidence, which will be discussed later, Blau¹⁵ concluded that "there is no relationship between the temporal artery pul-

sation and the presence or absence of headache." Others²⁵⁻²⁷ have, however, confirmed Graham and Wolff's⁸ findings. This also suggests that Heyck's¹⁴ failure was because of the considerable technical difficulty in obtaining reproducible pulse recordings from scalp vessels.

Ocular and Conjunctival Vessels

Blau¹⁵ stated that certain reactions of the ocular and conjunctival vessels during migraine headache were points in favor of an intracranial origin of the pain. The vessels of the optic fundus derive solely from the internal carotid artery, and if the pain were due to dilation of the intracranial vessels, the fundal vessels would, therefore, be expected to reflect this. The opposite is in fact true: the vessels of the optic fundus show no significant changes during migraine attacks; the conjunctival vessels, on the other hand, which arise from both internal and external carotid arteries, do dilate during migraine pain.

Blau¹⁵ also suggested that the conjunctival vasculature reflects the meningeal circulation but later in the same article, he retracted the statement.

Inflatable Head Cuff

Blau and Dexter¹⁷ used a specially designed sphygmomanometer cuff, fitted around the head and inflated to ten mm Hg above the patient's systolic blood pressure for 20 seconds, to occlude the extracranial arteries in 48 migraine sufferers. In 21 (43%) of these patients the headache decreased, in 12 (25%) there was no change, and in 15 (31%) the headache was made worse. They concluded that this was "evidence for an intracranial element in migraine." However, the fact that there was decreased pain in 43% of the patients indicates that in these patients, the pain originated in the extracranial and not the intracranial vessels.

Preliminary results of a similar study carried out at the Headache Clinic in Johannesburg, South Africa indicate that the best results are obtained when the cuff is inflated to ten mm Hg below the systolic blood pressure with the patient seated. In a sample of 35 patients, 71% had pain relief, in 6% the pain was worse, and in 23% there was no change. When the pressure was increased to ten mm Hg above the systolic blood pressure, however, only 47% experienced pain reduction, whereas in 18% the pain was worse, and 35% experienced no change. The difference may be due to the increased pressure exerted on potentially tender scalp tissue, including blood vessels and muscles; also, local pain threshold is decreased during migraine headache,¹² causing cutaneous allodynia.²⁸

There is no certainty, however, that patients who still have pain when the cuff is applied, are indeed experiencing pain from an intracranial source. The inflatable cuff

only compresses the extracranial arteries and not, for example, the internal maxillary artery, also a branch of the external carotid artery, and its branch, the middle meningeal artery. It remains a possibility that some of the patients without relief from the inflatable cuff are experiencing pain from these deeper branches of the external carotid artery, or may have pain related to nonvascular mechanisms.

Intracranial Vascular Tests

Blau and Dexter¹⁷ used three tests to determine whether the pain of the migraine headache was intracranial or extracranial in origin. The tests were: 1. Breath holding in mid-inspiration for 30 seconds; 2. head jolt: subjects rotated the head three times rapidly from side to side through 180°; and 3. coughing: patients were asked to give three vigorous coughs.

They concluded from the results of these tests that 49 of the 50 subjects studied had pain of intracranial origin. However, their assumption that the tests only affected the intracranial and not the extracranial vasculature, does not seem logical. They clearly did not take into account the fact that performing any of these maneuvers would also raise the extracranial intravascular pressure.

Cranial Blood Flow

A number of cerebral blood flow studies using the ¹³³Xe-inhalation method have shown blood flow to be reduced transiently during migraine aura, without change during the migraine headache.²⁹⁻³² Sakai,³³ on the other hand, also using the ¹³³Xe-inhalation method but looking at extracranial blood flow, found it to be increased during migraine headache.

Digital Arterial Compression

There are numerous references in the literature to the reduction of the pain of the migraine headache by digital compression of one or more of the extracranial branches of the external carotid artery.⁷⁻¹³ In one study of 63 migraine sufferers, digital compression of extracranial branches of the ipsilateral external carotid artery during migraine headache reduced or eliminated the pain in 23 (36%) of them.³⁴ A simple bedside test has been described, using the Valsalva maneuver and digital temporal artery compression, to differentiate between intracranial and extracranial pain in cases of vascular headache. With headache due to vascular dilation, the pain improves during the maneuver, to worsen again within 2-5 seconds thereafter, gradually settling down to its normal level in 15-30 seconds. This occurs with both intracranial and extracranial vascular pain due to the lowering of the blood pressure, resulting from the decreased venous

return caused by the Valsalva maneuver. In patients where the pain does not recur when the test is carried out while both superficial temporal arteries are occluded, it may be concluded that the pain originates in these vessels. Approximately 95% of patients studied appeared to have extracranial pain determined with this technique.³⁵

Regarding the above bedside test, Drummond and Lance³⁴ made the assumption that the pain is extracranial only in cases where occlusion of the ipsilateral artery eliminates the pain. There are, however, extensive anastomoses between the terminal branches of the external carotid arteries, within and between the sides of the head.³⁶ Due to these anastomoses, occlusion of only one superficial temporal artery may not reduce blood flow to the painful area sufficient to allow resolution of the pain.

Vascular Surgery

Successful treatment of migraine headache by means of surgical ligation of the terminal branches of the external carotid artery has been reported.³⁷⁻⁴⁰ Most reports describe ligation of the superficial temporal and occipital arteries but other branches have also been implicated. Dickerson⁴¹ reported that resection of the middle meningeal artery, a branch of the internal maxillary artery, abolished migraine headaches in some patients; in others, the intensity of the pain was reduced. Cook⁴² and Bouche⁴³ described the successful treatment of migraine headache by cryosurgical ablation of the superficial temporal, occipital, and sphenopalatine arteries.

Discussion

Clinical and experimental consideration suggests the pathogenesis of the migraine headache to be intimately linked to the trigeminal innervation of the cranial blood vessels.⁴⁴ Dilation of these blood vessels and the consequent stimulation of the surrounding trigeminal sensory nerve fibers represent key mechanisms in the generation of the pain of the migraine headache.⁴⁵ The exact mechanism of how the perivascular trigeminal nerve terminals are stimulated is not completely known, but evidence suggests that local transmitters, such as calcitonin gene-related peptide, are involved. Orthodromic conduction along the trigeminovascular nerve fibers transmits the nociceptive information centrally, via the trigeminal nucleus caudalis onto third-order neurons in the thalamus and, from thereon, to cortical structures where the pain is perceived.⁴⁶ There is, however, controversy as to whether the pain originates from the intracranial or the extracranial arteries. In this article, evidence is presented to support the view that in certain patients, the pain of the migraine headache originates in the extracranial arteries.

This is demonstrated by: a. the effect of ergotamine, b. changes in intracranial pressure, c. compression by means of an inflatable cuff or digital pressure, d. intracranial vascular tests, e. cranial blood flow studies, and f. surgical ablation.

References

- Silberstein SD, Lipton RB, Goadsby PJ: *Headache in clinical practice*. Oxford: Isis Medical Media, 1998.
- Dahlof CGH, Solomon GD: The burden of migraine to the individual sufferer: a review. *Eur J Neurol* 1998; 5:525-533.
- Osterhaus JT, Townsend RJ, Gandek B, Ware JE: Measuring the functional status and well-being of patients with migraine headache. *Headache* 1994; 34:337-343.
- Solomon GD, Skobieranda FG, Gragg LA: Quality of life and well-being of headache patients. Measurement by the medical outcomes study instrument. *Headache* 1993; 33:351-358.
- Abu Qasim al-Zahrawi: *Al-Tasrif*: Cordoba, Spain; pp 936-1013.
- Lance JW, Lambert GA, Goadsby PJ, Duckworth JW: Brainstem influences on the cephalic circulation: experimental data from cat and monkey of relevance to the mechanism of migraine. *Headache* 1983; 23:258-265.
- Hare F: Mechanism of the pain in migraine. *Med Pr* 1905; 1:583.
- Graham JR, Wolff HG: Mechanism of migraine headache and action of ergotamine tartrate. *Arch Neurol Psychiat* 1938; 39:737-763.
- Pickering GW: Experimental observations on headache. *Br Med J* 1939; 1:907-912.
- Sutherland AM, Wolff HG: Further analysis of the mechanism of headache in migraine, hypertension, and fever. *Arch Neurol Psychiat* 1940; 44:929-949.
- Wolff HG, Tunis MM: Analysis of cranial artery pressure pulse waves in patients with vascular headache of the migraine type. *Trans Assn Am Phys* 1952; 65:240-244.
- Wolff HG, Tunis MM, Goodell H: Evidence of tissue damage and changes in pain sensitivity in subjects with vascular headaches of the migraine type. *Arch Int Med* 1953; 92:332-341.
- Tunis MM, Wolff HG: Long-term observations on the reactivity of the cranial arteries in subjects with vascular headaches of the migraine type. *Arch Neurol Psychiat* 1953; 70: 551-557.
- Heyck H: *Neue Beiträge zur Klinik und Pathogenese des Migrane*. George Thieme Verlag, Stuttgart, Germany; 1956:29.
- Blau JN: Migraine: a vasomotor instability of the meningeal circulation. *Lancet* 1978; 2:1136-1139.
- Blau JN, Davis E: Small blood vessels in migraine. *Lancet* 1970; 2:740-742.
- Blau JN, Dexter SL: The site of pain origin during migraine attacks. *Cephalalgia* 1981; 1:143-147.
- Tzanck A: Le traitement des migraines par le tartrate d'ergotamine. *Bull et me'm Soc med d'hop de Paris* 1928; 52:1057-1061.
- Lennox WG, Von Storch TJC: Experience with ergotamine tartrate in 120 patients with migraine. *JAMA* 1935; 105:169-171.
- O'Sullivan ME: Termination of 1000 attacks of migraine with ergotamine tartrate. *JAMA* 1936; 107:1208-1212.
- Andersen AR, Tfelt-Hansen P, Lassen NA: The effect of ergotamine and dihydroergotamine on cerebral blood flow in man. *Stroke* 1987; 18:120-123.
- Hachinski VC, Norris JW, Cooper PW, Edmeads JG: Ergotamine tartrate and cerebral blood flow. *Canad J Neurol Sci* 1975; 2:333.
- Schumacher GA, Wolff HG: Experimental studies on headache: A. Contrast of histamine headache with the headache of migraine and that associated with hypertension. B. Contrast of vascular mechanisms in pre-headache and in headache phenomena of migraine. *Arch Neurol Psychiat* 1941; 45:199-214.
- Von Storch TJC: Relation of experimental histamine headache to migraine and nonmigraine headache. *Arch Neurol Psychiat* 1940; 44:316.
- Wennerholm M: Postural vascular reactions in cases of migraine and related vascular headaches. *Acta Med Scand* 1961; 169:131-139.
- Drummond PD, Lance JW: Extracranial vascular reactivity in migraine and tension headache. *Cephalalgia* 1981; 1:149-155.
- Iversen HK, Nielsen TH, Olesen J, Tfelt-Hansen P: Arterial responses during migraine headache. *Lancet* 1990; 336:837-839.
- Burstein R, Yarnitsky D, Goor-Aryeh I, Ransil BJ, Bajwa ZH: An association between migraine and cutaneous allodynia. *Ann Neurol* 2000; 47:614-624.
- Lauritzen M, Olesen J: Regional cerebral blood flow during migraine attacks by ¹³³Xenon inhalation and emission tomography. *Brain* 1984; 107:447-461.
- Olsen TS: Migraine with and without aura: the same disease due to cerebral vasospasm of different intensity. A hypothesis based on CBF studies during migraine. *Headache* 1990; 30:269-272.
- Benarczyk EM, Remler B, Weikart C, Nelson AD, Reed RC: Global cerebral blood flow, blood volume, and oxygen metabolism in patients with migraine headache. *Neurology* 1998; 50:1736-1740.
- Cutrer FM, O'Donnell A, Sanchez del Rio M: Functional neuroimaging: enhanced understanding of migraine pathophysiology. *Neurology* 2000; 55 (Suppl 2):S36-45.
- Sakai F, Meyer JS: Abnormal cerebrovascular activity in patients with migraine and cluster headache. *Headache* 1979; 19:257-266.
- Drummond PD, Lance JW: Extracranial vascular changes and the source of pain in migraine headache. *Ann Neurol* 1983; 13:32-37.
- Louis S: A bedside test for determining the sub-types of vascular headache. *Headache* 1981; 21:87-88.
- Marty F, Montandon D, Gurnener R, Zbrodowski A: Subcutaneous tissue in the scalp: anatomical, physiological, and clinical study. *Ann Plast Surg* 1986; 16:368-376.
- Murillo CA: Resection of the temporal neurovascular bundle for control of migraine headache. *Headache* 1968; 8:112-117.
- Hankmeier U: Therapy of pulsating temporal headache. Resection of the superficial temporal artery. *Fortschr Med* 1985; 103:822-824.
- Holland JT: Three cases of post traumatic vascular headache treated by surgery. *Proc Aust Assoc Neurol* 1976; 13:51-54.
- Florescu V, Florescu R: Value of resection of the superficial temporal vasculo nervous bundle in some cases of vascular headache. *Rev Chir Oncol Radiol O R L Ophthalmol Stomatol Otorinolaringol* 1975; 20:113-117.
- Dickerson DG: The surgical relief of the headache of migraine. *J Nerv Ment Dis* 1933; 77:42.
- Cook N: Cryosurgery of migraine. *Headache* 1973; 12:143-150.
- Bouche J, Freche C, Chaix G, Dervaux JL: Surgery by cryotherapy of the superficial temporal artery in temporo-parietal neuralgia. *Ann Otolaryngol Chir Cervicofac* 1974; 91:56-59.
- Goadsby PJ, Edvinsson L: The trigeminovascular system and migraine: studies characterizing cerebrovascular and neuropeptide changes seen in humans and cats. *Ann Neurol* 1993; 33:48-56.
- Davis KD, Dostrovsky JO: Activation of trigeminal brain-stem nociceptive neurons by dural artery stimulation. *Pain* 1986; 25:395-401.
- Sanchez del Rio M, Reuter U, Moskowitz MA: Central and peripheral mechanisms of migraine. *Funct Neurol* 2000; 15 (Suppl 3):157-162.

Dr. Egilius H. Spierings is a pharmacologist, neurologist, and headache specialist. He studied medicine and pharmacology at the Erasmus University Faculty of Medicine in Rotterdam, the Netherlands. He trained in neurology and neurosurgery at the University Hospital in Rotterdam, in psychiatry at the Reinier de Graaf Hospital in Delft, the Netherlands, and in headache management at the Headache Research Foundation in Boston. He is a consultant in neurology at Brigham and Women's Hospital and an associate clinical professor of neurology at Harvard Medical School.
