

Cervicogenic Headache: Anatomic Basis and Pathophysiologic Mechanisms

Nikolai Bogduk, MD, PhD

Address

Newcastle Bone and Joint Institute, University of Newcastle,
Royal Newcastle Hospital, Newcastle, NSW 2300, Australia.
E-mail: mgillam@mail.newcastle.edu.au

Current Pain and Headache Reports 2001, 5:382-386

Current Science Inc. ISSN 1531-3433

Copyright © 2001 by Current Science Inc.

Cervicogenic headache is pain perceived in the head but referred from a primary source in the cervical spine. The physiologic basis for this pain is convergence between trigeminal afferents and afferents from the upper three cervical spinal nerves. The possible sources of cervicogenic headache lie in the structures innervated by the C1 to C3 spinal nerves, and include the upper cervical synovial joints, the upper cervical muscles, the C2-3 disc, the vertebral and internal carotid arteries, and the dura mater of the upper spinal cord and posterior cranial fossa. Experiments in normal volunteers have established that the cervical muscles and joints can be sources of headache.

Introduction

Neurologists have strongly disputed what the defining clinical features of cervicogenic headache are. This entity, however, cannot be validly defined using conventional clinical criteria, such as those that apply to migraine or cluster headache. Cervicogenic headache shares too many features in common with other forms of headache for it to be defined in terms of the location of pain, its quality, periodicity, or associated features [1,2].

The singular defining criterion for cervicogenic headache is that it is pain perceived in the head but whose source lies in the cervical spine. The diagnosis of cervicogenic headache, therefore, relies on establishing a source of pain in the neck, using reliable and valid diagnostic techniques.

Physiologic Basis

The pathophysiology of cervicogenic headache has not been explicitly demonstrated. However, there is sufficient circumstantial evidence that the fundamental mechanism must be convergence. When primary afferents from two topographically separate regions of the body converge on

the same second-order neuron in the spinal cord, nociceptive activity along one of the afferents can be perceived as pain arising in the territory of the other afferent.

In the context of cervicogenic headache, the convergence must be between nerves that innervate the head and nerves that innervate the cervical spine. This is not simply a matter of convergence between trigeminal and cervical afferents, for the head is innervated not only by the trigeminal nerve but also by cervical nerves. The occiput and regions as far forward as the coronal suture are innervated by the greater occipital nerve, the lesser occipital nerve, and the greater auricular nerve. Consequently, cervicogenic headache perceived in the forehead or orbital region requires convergence between trigeminal and cervical afferents, whereas cervicogenic headache perceived in the occiput requires convergence between certain cervical and other cervical afferents.

Anatomic studies in laboratory animals have revealed that the central terminals of the upper three cervical nerves overlap extensively [3,4]. In particular, the C2 spinal nerve not only ramifies in the grey matter of the C2 spinal cord segment but also sends ascending collaterals to the C1 segment, and descending collaterals to the C3 segment. The C3 spinal nerves express an analogous pattern of ascending and descending collaterals. The terminals of the C1 spinal nerve, however, are restricted to their own segment. This overlapping distribution of terminals allows for convergence between afferents from C1 and C2, and C2 and C3. Additionally, the spinal tract of the trigeminal nerve descends past the C1 and C2 segments, to end opposite at least to the C3 segment and perhaps as far caudally as the C4 segment [5,6]. From the tract, terminals of trigeminal nociceptive afferents ramify in the grey matter of the C1 to C3 spinal cord segments. This pattern of distribution allows for convergence between trigeminal afferents and afferents from any of the upper three cervical spinal nerves, and perhaps even the fourth.

Physiologic studies in laboratory animals have explicitly demonstrated convergence between trigeminal and cervical afferents. Neurons in the spinal cord can be found that respond to electrical stimulation both of the trigeminal nerve and of the cervical nerves. An earlier study showed convergence between the trigeminal nerve and afferents in the C1 dorsal roots [7]. A more recent study showed convergence between afferents from the superior sagittal sinus and afferents in the greater occipital nerve [8].

Anatomic Basis

The overlap between terminals of the trigeminal nerve and those of the upper three cervical nerves provides the substrate for the possible sources of cervicogenic headache. Any structure innervated by any of the upper three cervical spinal nerves could be a source of headache if the central terminals of its nerve supply converged with trigeminal afferents, or with cervical afferents from the occiput. Consequently, the peripheral distribution of the C1 to C3 spinal nerves constitutes the anatomic basis for the differential diagnosis of cervicogenic headache.

C1

The C1 spinal nerve is peculiar, or at least unique, in that it lacks the same form and pattern of branching shared by other cervical nerves. Also, it has been misrepresented as lacking a sensory distribution. That mistake has arisen because of a misrepresentation of the fact that it often "lacks" a dorsal root ganglion. The correct observation is that in some 20% of cases the C1 spinal nerve lacks a dorsal root, but in those cases dorsal root ganglion cells can be found among the roots of the spinal accessory nerve [9]. The correct interpretation, therefore, is not that C1 lacks sensory fibers but that its sensory ganglion is sometimes ectopic.

An additional error has been the inference that because the C1 spinal nerve lacks a cutaneous distribution, it must not be sensory. Although this nerve is not normally distributed to skin, it is nonetheless sensory to deep somatic tissues in the suboccipital region. Through its dorsal ramus it innervates the short muscles of the suboccipital triangle [10]. Through its ventral ramus and the cervical plexus it contributes to the innervation of the prevertebral muscles, and to the sensory innervation of the sternocleidomastoid muscle and trapezius. Its ventral ramus passes behind and just below the atlanto-occipital joint, to which it furnishes articular branches [11]. Its recurrent meningeal branch (the C1 sinuvertebral nerve) joins those from C2 and C3 to supply the median atlantoaxial joint and its ligaments, as well as the dura mater of the upper cervical spinal cord [12]. Furthermore, the C1, C2, and C3 sinuvertebral nerves extend through the foramen magnum to innervate the dura mater over the clivus in the posterior cranial fossa [12].

Sensory fibers from the vertebral artery are found in the plexus of nerves that accompany the artery—the vertebral nerve [13]. From the vertebral artery in the posterior cranial fossa, sensory fibers have been traced to the dorsal root ganglion of C1 [14].

C2

The ventral ramus of the C2 spinal nerve joins the cervical plexus, through which it supplies the prevertebral muscles, and the sternocleidomastoid muscle and trapezius. As it passes behind the lateral atlantoaxial joint it furnishes articular branches to this joint [11,15].

The C2 dorsal ramus supplies the splenius capitis and the semispinalis capitis [10]. Its medial branch emerges

from the semispinalis capitis to become the greater occipital nerve, which supplies the skin over the occiput. In this regard, modern studies, involving blocking the C2 spinal nerve or sectioning its dorsal roots, have shown that the entire cutaneous distribution of C2 is represented in the greater occipital nerve [16•]. The C2 dermatome, therefore, coincides with the distribution of the greater occipital nerve. C2 is not represented in the cutaneous distribution of the greater auricular and transverse cervical nerves. These nerves contribute only to the C3 dermatome.

The sinuvertebral nerve of C2 joins those of C1 and C3 to supply the median atlantoaxial joint and the transverse ligament of the atlas, along with the membrana tectoria. It also supplies the spinal dura mater and the dura mater over the clivus [12]. Other meningeal branches from the lateral walls of the posterior cranial fossa, and from the inferior surface of the tentorium cerebelli, join the meningeal branches of the vagus, glossopharyngeal, and hypoglossal nerves, but leave these cranial nerves in the neck to join the cervical plexus, and ultimately terminate at the C2 segment and adjacent segments of the spinal cord.

Although it has not been explicitly demonstrated, it is possible, and seems reasonable, that sensory fibers from the vertebral artery and from the internal carotid artery reach the C2 spinal nerve, through the cervical plexus. Such an innervation is necessary to explain the perception of neck pain in patients with aneurysms of either the vertebral artery or the internal carotid artery.

C3

The ventral ramus of C3 joins the cervical plexus and innervates the prevertebral muscles. The dorsal ramus of C3 innervates various posterior neck muscles [10]. Its lateral branch is distributed to the splenius capitis and cervicis, and to the longissimus capitis. Its deep medial branch supplies semispinalis cervicis and multifidus. Its superficial medial branch, known as the third occipital nerve, supplies the semispinalis capitis and becomes cutaneous over the suboccipital region. Immediately after its origin the third occipital nerve curves around the lateral and posterior aspects of the C2-3 zygapophyseal joint. As it crosses this joint it is embedded in the fascia surrounding the joint capsule, and supplies articular branches to the joint [10].

The sinuvertebral nerve from C3, like those of C1 and C2, innervates the atlantoaxial ligaments and the dura mater of the spinal cord and clivus. However, this nerve also innervates the C2-3 intervertebral disc from its posterior aspect [17]. Other branches to the disc stem from the ventral ramus of C3. These include branches from the vertebral nerve at C3 and branches from the nerves to the prevertebral muscles [17].

Catchment area

Systematically listed, the structures that could possibly be a source of cervicogenic headache are summarized in Table 1. This list is comprehensive but theoretic. Not all the structures have been implicated by clinical studies.

Table 1. The possible sources of cervicogenic headache, listed according to innervation and type of structure

Structure	Innervation		
	C1	C2	C3
Joints	Atlanto-occipital	Median atlantoaxial Lateral atlantoaxial	C2-3 zygapophyseal C2-3 disc
Ligaments	Transverse atlantoaxial and alar; membrana tectoria		
Muscles	Suboccipital	Prevertebral; sternocleidomastoid, trapezius Semispinalis, splenius	Multifidus; semispinalis
Dura	Upper spinal cord; posterior cranial fossa		
Arteries	Vertebral; internal carotid		

However, several have been shown to produce headache when stimulated experimentally, and several have been shown to be sources of headache in clinical studies.

Normal Volunteers

In normal volunteers, several structures innervated by the upper three cervical nerves have been shown to be capable of producing referred pain in the head when experimentally stimulated with a noxious stimulus. These include the upper cervical muscles, and the upper cervical synovial joints.

Cyriax [18] first showed that stimulation of the suboccipital muscles with injections of hypertonic saline could produce referred pain in the head. The more cephalad the site of stimulation the closer to the forehead did the pain project. These findings were reinforced by extensive studies by Campbell and Parsons [19]. Systematically, these investigators stimulated the periosteum around the occipital condyles by dry needling, and stimulated the paramedian muscles of the neck, from suboccipital levels to C4-5, with injections of hypertonic saline. They found that suboccipital stimuli often produced referred pain in the orbital and frontal regions, but as the site of stimulation progressed caudally, the incidence of frontal referral decreased, and the site of referred pain receded to the occipital and suboccipital regions. Feinstein *et al.* [20] showed that stimulation of the paramedian muscles above the C1 vertebra produces frontal and orbital pain.

Dreyfuss *et al.* [21•] stimulated the atlanto-occipital and lateral atlantoaxial joints with intra-articular injections of contrast medium at sufficient pressure to distend their capsules until pain was evoked. The pain was perceived in the occipital and suboccipital regions. Dwyer *et al.* [22•] stimulated the C2-3 zygapophyseal joints in a similar manner, and found that pain was perceived in the occipital region. Stimulation of lower cervical zygapophyseal joints did not refer pain to the head. The observations of Dwyer *et al.* [22•] were confirmed by Fukui *et al.* [23], who used a

combination of intra-articular injections and electrical stimulation of the medial branches of the cervical dorsal rami to map the distribution of pain from the cervical zygapophyseal joints.

Other structures have not been studied in the same manner in normal volunteers. It remains speculative, but theoretically reasonable that stimulation of the vertebral artery, the internal carotid artery, the dura mater, the median atlantoaxial joint, and the atlantoaxial ligaments should also produce referred pain in the head.

Clinical Studies

Complementing the studies in normal volunteers are the results of clinical studies in patients with headache in which particular structures innervated by the upper three cervical nerves have been either stimulated to aggravate the headache or selectively anesthetized in order to relieve the headache. These studies used highly selective, target-specific techniques, and should be distinguished from studies that used unreliable or nonspecific techniques, such as palpation, to establish a cervical source of pain.

Two studies have reported that in some patients with headache, the pain can be reproduced by stimulation of the C2-3 intervertebral disc, but not lower discs [24,25]. This constitutes *prima facie* evidence that this disc could be a source of cervicogenic headache, but the problem arises of false-positive inferences. Patients with pain can suffer hyperalgesia, such that noxious stimulation of any structure in the painful, neurologic segment might reproduce or aggravate their pain. That observation in itself does not necessarily implicate the stimulated structure as the singular or primary source of pain.

More compelling are the results of studies in which headache has been relieved by anesthetizing certain cervical structures. In this regard, the criterion is complete relief of headache. Partial relief of pain is insufficient evidence that the anesthetized structure is the source of

pain, for it begs the question: if the structure really is the source of pain why does the pain not stop completely if and when the structure is anesthetized? Also, the responses to anesthetic blocks are far more compelling if the blocks have been performed with controls. Uncontrolled blocks do not exclude a false-positive, alias placebo, response.

Ehni and Benner [26] reported complete relief of headache in patients with osteoarthritis of the lateral atlantoaxial joints following periarticular local anesthetic blocks of those joints. Busch and Wilson [27] reported relief of headache in a small number of patients following intra-articular blocks of either the atlanto-occipital or the lateral atlantoaxial joints. Neither of these studies, however, used control blocks. Thus, their results provide only prima facie evidence that these joints might be sources of cervicogenic headache.

Others have used nerve blocks in the investigation of putative cervicogenic headache. They report complete relief of headache following anesthetization of either the C2 spinal nerve or the greater occipital nerve [28,29]. However, because control blocks were not used, the responses constitute only prima facie evidence of a cervical source. Moreover, nerve blocks are not specific in that they do not identify the actual source of pain. They show only that the pain is mediated by the nerve which is anesthetized.

The strongest evidence on the possible sources of cervicogenic headache comes from studies in which the C2-3 zygapophyseal joint has been anesthetized under controlled conditions. Lord *et al.* [30••] used highly selective blocks of the third occipital nerve in order to anesthetize the C2-3 zygapophyseal joint. They used comparative local anesthetic blocks, in which on separate occasions the nerve was anesthetized, under double-blind conditions, with local anesthetic agents with different durations of action. The criteria for a positive response were that complete relief of pain occurred on both occasions that the nerve was blocked and that the relief was longer lasting when the longer-acting agent was used. They found that among patients with headache following whiplash, the headache could be completely abolished in over 50% of cases if the C2-3 joint was anesthetized. In another study, Lord and Bogduk [31] reported that the C3-4 zygapophyseal joint could also be a source of cervicogenic headache, but far less commonly than the C2-3 joint.

Conclusions

Although many clinical studies fall short of the scientific rigor now required to identify a source of pain, the data from clinical studies are concordant with results of studies on normal volunteers. They show that various joints in the upper cervical spine can be sources of headache. The studies of normal volunteers have additionally implicated the upper cervical muscles, although no controlled studies have convincingly demonstrated if or how often muscles are the

primary source of cervicogenic headache. In all instances, however, the structures implicated as sources of headache are all ones innervated by the upper three cervical nerves.

These data provide a foundation for the differential diagnosis and investigation of putative cervicogenic headache. The definition of cervicogenic headache requires that a cervical source of pain be established. The experimental data indicate that the source will lie somewhere among the structures innervated by the upper three cervical nerves. The definitive diagnosis of cervicogenic headache, therefore, rests on determining which of these structures is the source. This cannot be done reliably and validly by history and clinical examination, nor by medical imaging. At present, controlled diagnostic blocks of putative sources of pain are the only secure means of determining that source.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:

- Of importance
 - Of major importance
1. Leone M, D'Amico D, Moschiano F, *et al.*: Possible identification of cervicogenic headache among patients with migraine: an analysis of 374 headaches. *Headache* 1995, 35:461-464.
 2. Leone M, D'Amico D, Grazzi L, *et al.*: Cervicogenic headache: a critical review of the current diagnostic criteria. *Pain* 1998, 78:1-5.
 3. Escolar J: The afferent connections of the 1st, 2nd, and 3rd cervical nerves in the cat: an analysis by Marchi and Rasdolsky methods. *J Comp Neurol* 1948, 89:79-92.
 4. Kerr FWL: Structural relation of the trigeminal spinal tract to upper cervical roots and the solitary nucleus in the cat. *Exp Neurol* 1961, 4:134-148.
 5. Humphrey T: The spinal tract of the trigeminal nerve in human embryos between 71/2 and 81/2 weeks of menstrual age and its relation to early fetal behaviour. *J Comp Neurol* 1952, 97:143-209.
 6. Torvik A: Afferent connections to the sensory trigeminal nuclei, the nucleus of the solitary tract and adjacent structures. *J Comp Neurol* 1956, 106:51-141.
 7. Kerr FWL: Trigeminal nerve volleys. *Arch Neurol* 1961, 5:171-178.
 8. Angus-Leppan H, Lambert GA, Michalick J: Convergence of occipital nerve and superior sagittal sinus input in the cervical spinal cord of the cat. *Cephalalgia* 1997, 17:625-630.
 9. Ouaknine G, Nathan H: Anastomotic connections between the eleventh nerve and the posterior root of the first cervical nerve in humans. *J Neurosurg* 1973, 38:189-197.
 10. Bogduk N: The clinical anatomy of the cervical dorsal rami. *Spine* 1982, 7:319-330.
 11. Lazorthes G, Gaubert J: L'innervation des articulations interapophysaire vertebrales. *Comptes Rendues de l'Association des Anatomistes* 1956, 488-494.
 12. Kimmel DL: Innervation of the spinal dura mater and dura mater of the posterior cranial fossa. *Neurology* 1960, 10:800-809.
 13. Bogduk N, Lambert G, Duckworth JW: The anatomy and physiology of the vertebral nerve in relation to cervical migraine. *Cephalalgia* 1981, 1:11-24.
 14. Kimmel DL: The cervical sympathetic rami and the vertebral plexus in the human foetus. *J Comp Neurol* 1959, 112:141-161.
 15. Bogduk N: The anatomy of occipital neuralgia. *Clin Exp Neurol* 1980, 17:167-184.

16. • Poletti CE: C2 and C3 pain dermatomes in man. *Cephalalgia* 1991, 11:155-159.
A striking demonstration that traditional wisdom about the C2 dermatome is wrong.
17. Bogduk N, Windsor M, Inglis A: The innervation of the cervical intervertebral discs. *Spine* 1988, 13:2-8.
18. Cyriax J: Rheumatic headache. *BMJ* 1938, 2:1367-1368.
19. Campbell DG, Parsons CM: Referred head pain and its concomitants. *J Nerv Ment Dis* 1944, 99:544-551.
20. Feinstein B, Langton JBK, Jameson RM, Schiller F: Experiments on referred pain from deep somatic tissues. *J Bone Joint Surg* 1954, 36A:981-997.
21. • Dreyfuss P, Michaelsen M, Fletcher D: Atlanto-occipital and lateral atlanto-axial joint pain patterns. *Spine* 1994, 19:1125-1131.
A seminal study of pain patterns from joints that are difficult to access, and frequently ignored in the investigation of headache.
22. • Dwyer A, Aprill C, Bogduk N: Cervical zygapophysial joint pain patterns I: a study in normal volunteers. *Spine* 1990, 15:453-457.
A seminal study of pain from the cervical zygapophyseal joint, establishing that these joints are potent sources of neck pain and of headache.
23. Fukui S, Ohseto K, Shiotani M, et al.: Referred pain distribution of the cervical zygapophyseal joints and cervical dorsal rami. *Pain* 1996, 68:79-83.
24. Schellhas KP, Smith MD, Gundry CR, Pollei SR: Cervical discogenic pain: prospective correlation of magnetic resonance imaging and discography in asymptomatic subjects and pain sufferers. *Spine* 1996, 21:300-312.
25. Grubb SA, Kelly CK: Cervical discography: clinical implications from 12 years of experience. *Spine* 2000, 25:1382-1389.
26. Ehni G, Benner B: Occipital neuralgia and the C1-2 arthrosis syndrome. *J Neurosurg* 1984, 61:961-965.
27. Busch E, Wilson PR: Atlanto-occipital and atlanto-axial injections in the treatment of headache and neck pain. *Reg Anesth* 1989, 14(supp 2):45.
28. Sjaastad O, Fredriksen TA, Stolt-Nielsen A: Cervicogenic headache, C2 rhizopathy, and occipital neuralgia: a connection? *Cephalalgia* 1986, 6:189-195.
29. Bovim G, Berg R, Dale LG: Cervicogenic headache: anaesthetic blockades of cervical nerves (C2-C5) and facet joint (C2/C3). *Pain* 1992, 49:315-320.
30. •• Lord S, Barnsley L, Wallis B, Bogduk N: Third occipital headache: a prevalence study. *J Neurol Neurosurg Psychiatry* 1994, 57:1187-1190.
The singular, controlled study of a cervical source of headache, which established the C2-3 zygapophyseal joint as the most common source of headache after whiplash.
31. Lord SM, Bogduk N: The cervical synovial joints as sources of post-traumatic headache. *J Musculoskeletal Pain* 1996, 4:81-94.