Online ISSN : 2314-8969
Print ISSN: 2314-8950
www.esj.journals.ekb.eg

The EGYPTIAN SPINE Journal

CLINICAL ARTICLE EgySpineJ 40:53-64, 2021 ODI: 10.21608/ESJ.2022.113702.1207

Cervical Discopathy in Idiopathic Trigeminal Neuralgia: More than a Coincidence?

Ülkü Türk Börü[1], MD., Cem Bölük[2], MD., Adnan Özdemir[3], MD., Hayri Demirbaş[1], MD., Mustafa Taşdemir[4], MD., Tuğçe Gezer[5], MD., Fatma Gülhan Şahbaz[6], MD., Ahmet Dumanlı[7], MD.

[1]Afyonkarahisar University of Health Sciences, Department of Neurology, Afyonkarahisar, Turkey
[2]Sanliurfa Education and Research Hospital, Department of Clinical Neurophysiology, Sanliurfa, Turkey
[3]Kırıkkale University School of Medicine, Department of Radiology, Kirikkale, Turkey
[4] Istanbul Medeniyet University, Department of Public Health, Istanbul, Turkey
[5]Sanliurfa Mehmet Akif Inan Education and Research Hospital, Sanliurfa, Turkey
[6]Afyonkarahisar State Hospital, Department of Neurology, Afyonkarahisar, Turkey
[7]Afyonkarahisar University of Health Sciences, Department of Thoracic Surgery, Afyonkarahisar, Turkey

ABSTRACT

Background Data: The most common cause of trigeminal neuralgia is neurovascular compression. However, several patients present with unknown etiology.

Purpose: This study aims to investigate the relationship between trigeminal neuralgia and cervical pathology in patients previously diagnosed with idiopathic trigeminal neuralgia.

Study Design: We designed an observational case-control study in our tertiary center.

Patients and Methods: A study group consisting of patients previously diagnosed with idiopathic trigeminal neuralgia and a control group consisting of patients with tension-type headaches were included in the study. A blinded neuroradiologist reevaluated cranial MRIs of trigeminal neuralgia patients. Once it was confirmed that no signs of neurovascular compression or any secondary causes were present, a cervical MRI was performed to evaluate cervical pathologies. Cranial and cervical MRIs of the controls were evaluated by the same neuroradiologist.

Results: Twenty patients who had prior diagnoses of idiopathic trigeminal neuralgia and 20 controls were investigated. The mean age of trigeminal neuralgia patients was 64.9 ± 12.6, and the mean age of the control group was 61.3 ± 9.1 ($p = 0.305$). The male/female ratio in trigeminal neuralgia patients was 2.3 and 1.8 in the control group ($p = 0.736$). While indentation on the trigeminal spinal tract above the C4 spinal level was observed in 12 out of 20 patients, none of the controls had any involvement in the same region ($p < 0.001$).

Address correspondence and reprint requests: Cem Bölük, MD.
Sanliurfa Education and Research Hospital, Department of Clinical Neurophysiology, Sanliurfa, Turkey - E-mail: cem_boluk@hotmail.com

Submitted: July 27th, 2021.
Accepted: Sept 19th, 2021.
Published: October 2021.

The article does not contain information about medical device(s)/drug(s).
No funds were received in support of this work.
The authors report no conflict of interest.

Conclusion: The results of this study suggest that extramedullary indentation on the trigeminal spinal tract caused by upper cervical discopathy may be one of the possible etiological factors in trigeminal neuralgia. (2021ESJ244)

Keywords: trigeminal neuralgia, etiology, cervical discopathy, spinal trigeminal nucleus, pain

INTRODUCTION

Trigeminal neuralgia (TN) is an extremely debilitating condition characterized by a unilateral sudden stabbing, shock-like, and electrocution-type paroxysmal pain in one or more divisions of the trigeminal nerve triggered by innocuous stimuli. Under the International Classification of Headache Disorders (ICHD-3) diagnostic criteria, TN is divided into classical, secondary, and idiopathic trigeminal neuralgia.[30] New diagnostic criteria are developed based on several clinical pieces of research.[4,16,30,33] Classical trigeminal neuralgia, caused by neurovascular compression, is the most common form of TN.[16,48] Secondary TN, which accounts for approximately 15% of cases, results from an external cause, such as a tumor or multiple sclerosis.[16,17,30] TN of unidentified etiology is labeled idiopathic. [30]

The trigeminal nerve, the largest cranial nerve with three main branches, provides sensory innervations of the teeth, intracranial structures, neck, face, and head. In addition, it has motor branches that innervate the masticatory muscles, including the masseter, lateral pterygoid, and temporalis muscles. The sensory root, which extends from the ganglion, enters the pons and terminates three major nuclear complexes within the brainstem.[31,45,54]

Clinical Rationale for the Study

It is well-known that vascular contact has not been observed in a wide range (4%–89%) of TN patients.[1,5,17,29,48] Similarly, a considerable number of patients in our clinic were diagnosed with idiopathic TN due to no etiological factors being present.

A recent new hypothesis suggests that pathological changes in the upper cervical region create a change in the trigeminal spinal tract that results in TN. It has been argued that TN can result from pathology in the subnucleus oralis because the distribution of the trigger zone in the facial area is in line with the subnucleus oralis.[49] Additionally, several case reports have identified that the lesion in the upper cervical region can cause TN.[52,55]

As far as we know, no studies have illustrated upper cervical discopathy resulting in TN. This study aims to investigate whether there is a relationship between TN and cervical discopathy.

PATIENTS AND METHODS

The study was designed as an observational case-control study. It was conducted on patients admitted to the outpatient neurology clinic of a university hospital between 2018 and 2019. Patients who had a prior diagnosis of idiopathic TN and a control group consisting of patients with tension-type headaches were included in the study. Both patient groups were examined by the same experienced neurologist, and radiological findings were evaluated by a blinded neuroradiologist.

Inclusion criteria were as follows: a prior diagnosis of "idiopathic TN" according to ICHD-3, 18 years of age and above, no pathological findings on cranial MRI, written consent given, and no systemic illnesses.

Evaluation of clinical characteristics: all patients' data, including age, gender, duration of disease, side and involved branches of TN, pain severity (Visual Analogue Scale (VAS)), pain frequency (per day), and medical treatment, were recorded.

Clinical symptoms of upper cervical discopathy such as neck pain, shoulder pain, chest pain, pain in the auricular area, and occipital area were evaluated and recorded.

Patients previously diagnosed with idiopathic TN were reexamined; their cranial MRIs were

reevaluated by a neuroradiologist. After confirming that no signs of neurovascular compression or any secondary causes were present, a cervical MRI was performed to evaluate cervical pathologies.

Evaluation of MRI findings: MRI images were taken using a 1.5 Tesla magnet. Cervical MRI evaluation was carried out using sagittal fast spin-echo T1 and T2 and axial T2 weighted images. Section thickness was 3 mm. During cervical MRI evaluation, the spinal trigeminal tract was determined using Afshar's stereotactic atlas.[2] Assuming that the spinal trigeminal nucleus extends to the level of C4 and continues in Lissauer's tract and the medulla spinalis, the levels of the lesions were divided into two: above C4 level and below C4 level.[44] The level at which indentation was most pronounced was considered the level of the lesion.

Three items related to disc degeneration were assessed (nucleus signal, prolapses, and bone marrow signal). The classification was done according to Frobin. Disc degeneration is divided into 12 categories (ABC…L); while category A contains a normal disc with no findings, category L contains a disc in the state of maximal degeneration. We divided Frobin's classification into mild, moderate, and severe (ABCD mild, EFGH moderately, IJKL as severe).[25]

This study was performed in line with the principles of the Declaration of Helsinki. Ethical approval was obtained from the local ethics committee (approval number: 2011-KAEK-2/2019/147).

Informed consent was obtained from all individual participants included in the study.

Statistical Analysis:

Statistical analysis was performed using SPSS software (version 21.0 SPSS Inc., Chicago, IL, USA) for Windows. Frequency distribution, percentage, mean, standard deviation, median, and range were calculated where appropriate. The Chi-square test (x2) was used for categorical variables, while the *t*-test was used for continuous variables under parametric conditions. Results were considered to be statistically significant at the level of $p < 0.05$.

RESULTS

Twenty patients with a prior diagnosis of idiopathic TN and a control group consisting of 20 patients with tension-type headaches were included in the study. The mean age of TN patients was 64.9 ± 12.6 years, and the mean age of the control group was 61.3 ± 9.1 years ($p = 0.305$). The male/female ratio in TN patients was 2.3 and 1.8 in the control group ($p = 0.736$).

All patients with TN had at least one of the additional following symptoms: ipsilateral neck pain, ear-auricular pain, periorbital pain, chest pain, or shoulder pain. The symptoms of the patients are illustrated in Table 1.

Table 1. Additional clinical symptoms of patients with TN.

Symptoms	Number of the patients
Ipsilateral nape/neck pain	17 (85%)
Ipsilateral ear/auricular pain	11 (55%)
Ipsilateral periorbital pain	6 (30%)
Ipsilateral chest pain	8 (40%)
Ipsilateral shoulder pain	9 (45%)

Characteristics of trigeminal neuralgia: nine patients had TN on the right side, and 11 had TN on the left side. Six patients had isolated maxillary branch involvement. Five patients had isolated mandibular branch involvement. Two patients had isolated ophthalmic branch involvement. Seven patients had both maxillary and mandibular branch involvement. Moreover, the mean pain severity VAS was 8.6 ± 1.7. The mean frequency of pain was found to be 124.7 ± 113.5 per day. All patients were being treated with carbamazepine (16), pregabalin (12), gabapentin (9), and duloxetine (5).

An extramedullary, ipsilateral trigeminal spinal tract indentation above the C4 level was seen in 12/20 patients, while no indentation was seen in the control group ($p < 0.001$). Five patients had an

involvement under the C4 level, and no signs of changes were seen in 3 patients in the extension of the trigeminal spinal tract area.

Patients with TN on the right side: seven of nine patients with TN had an ipsilateral indentation on the spinal trigeminal tract and its caudal extension. Five of seven patients had a lesion above the C4 level. Two of the seven patients had a lesion under the C4 level. Two patients had no involvement.

Patients with TN on the left side: nine out of 11 patients with TN on the left side had an ipsilateral indentation on the spinal trigeminal tract and its caudal extension. Seven patients had a lesion above C4 level, while two patients had a lesion under the C4 level. In addition, one patient had a contralateral indentation under C4 level. One patient had no signs of any lesions. The radiological findings are shown in (Table 2). MRI examples of patients are shown in Figures 1, 2, 3, and 4.

Cervical degenerative findings of the patients and controls: ten out of 20 patients with TN had severe disc degeneration findings. Eight of 20 patients had medium-degree disc degeneration findings, and two had mild-degree degenerative findings.

In the control group, eight had severe degenerative changes and 11 had medium and one had mild degenerative changes. No statistical difference was found between the two groups ($p = 0.598$). A comparison of the two groups is shown in Table 3. MRI examples of disc degeneration are shown in Figure 5.

Table 2. Radiological findings of TN patients.

Patient number	TN side	Involved Branch	Compression level of STT	Compression side
1	Right	Maxillary+mandibular	C2	Right
2	Right	Maxillary+mandibular	C3	Bilateral
3	Right	Maxillary+mandibular	C4	Right
4	Right	Maxillary	C4	Right
5	Right	Maxillary	C4	Right
6	Right	Mandibular	C5	Bilateral
7	Right	Maxillary+mandibular	C5	Bilateral
8	Right	Mandibular	-	-
9	Right	Mandibular	-	-
10	Left	Mandibular	C3	Bilateral
11	Left	Maxillary	C3	Left
12	Left	Maxillary	C3	Bilateral
13	Left	Mandibular	C3	Left
14	Left	Opthalmic	C4	Left
15	Left	Opthalmic	C4	Left
16	Left	Maxillary+mandibular	C4	Left
17	Left	Maxillary	C5	Left
18	Left	Maxillary	C5	Left
19	Left	Maxillary+mandibular	C6	Right
20	Left	Maxillary+mandibular	-	-

TN: trigeminal neuralgia, STT: spinal trigeminal tract.

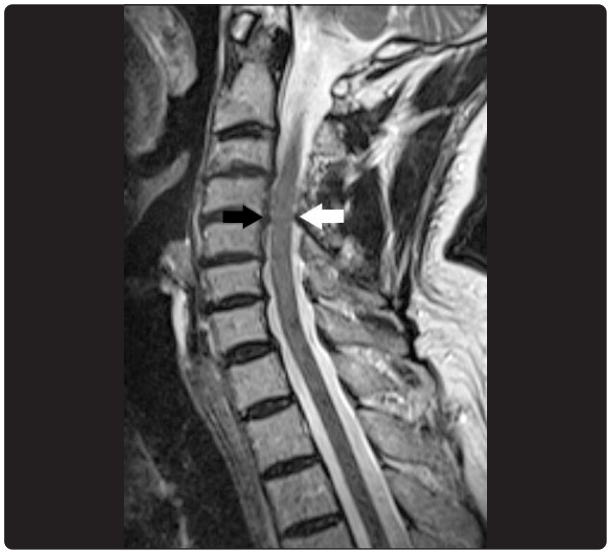

Figure 1. A 63-year-old male patient. Protruded disc at the level of C4-C5 (black arrow) and hypertrophy of ligamentum flavum (white arrow).

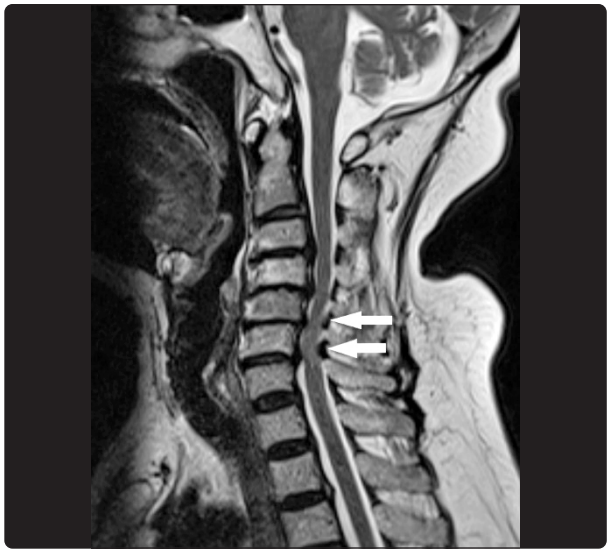

Figure 2. A 78-year-old female patient. Hypertrophy of ligamentum flavum and the compression of the medulla spinalis (white arrows).

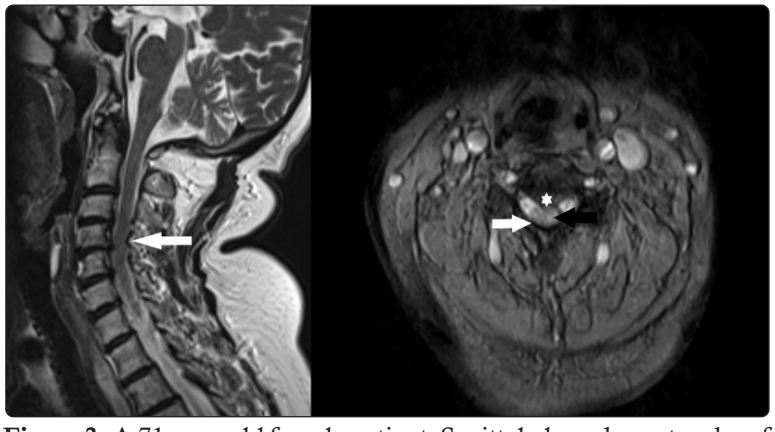

Figure 3. A 71-year-old female patient. Sagittal plane: hypertrophy of ligamentum flavum and compression of the medulla spinalis (white arrow). Axial plane: medulla spinalis (black arrow), protruded disc (*), hypertrophy of ligamentum flavum, and compression of the medulla spinalis (white arrow)

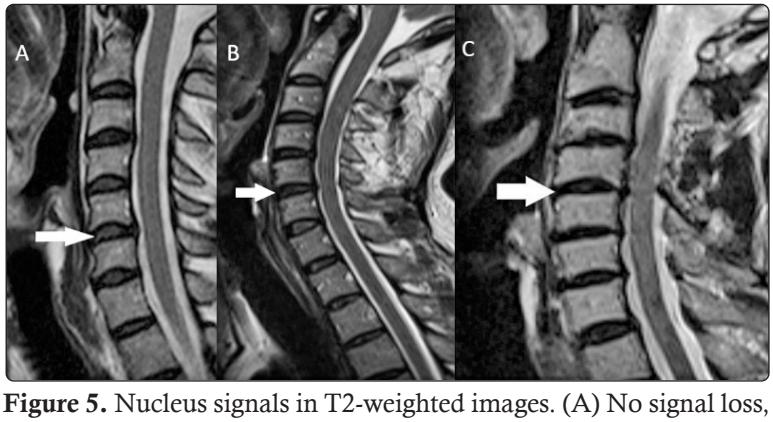

Figure 5. Nucleus signals in T2-weighted images. (A) No signal loss, (B) moderate signal loss, and (C) total loss.

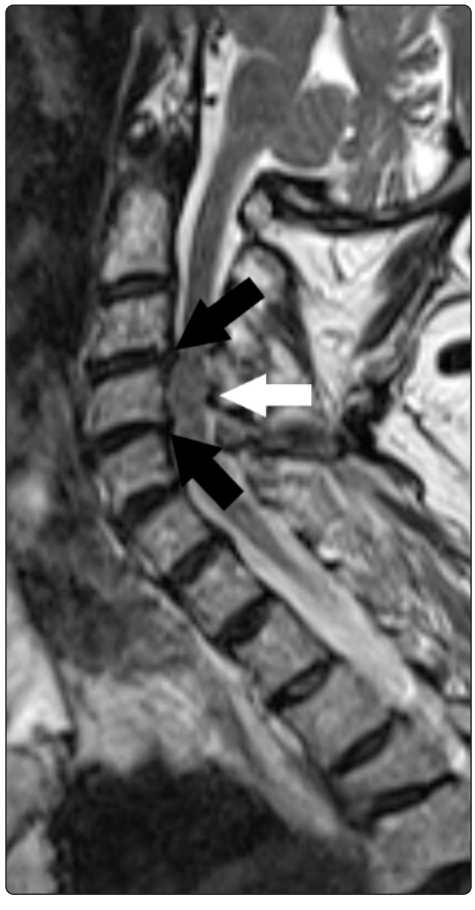

Figure 4. A 68-year-old female patient. Disc protrusions at the level of C3-C4 and C4-C5 (black arrows), hypertrophy of ligamentum flavum (white arrow)

Table 3. Comparison of the TN patients and controls.

Parameters	Patients with TN (n = 20)	Controls (n = 20)	p
Age (y)	64.9 ± 12.6	61.3 ± 9.1	0.305
Female/male ratio	2.3	1.8	0.736
Indentation to trigeminal spinal tractus	12	0	<0.001
Gliosis in medulla spinalis	9	0	0.001
Signal changes in nucleus	18	19	0.5
Signal changes in bone marrow	4	0	0.106

DISCUSSION

This study illustrates that two-thirds of patients who did not have intracranial findings on MRI and had a previous diagnosis of idiopathic TN have an ipsilateral extramedullary indentation on the spinal trigeminal tract. The severity of intervertebral disc degeneration is not directly associated with spinal trigeminal tract injury.

Compression caused by upper cervical discopathy can lead to TN in two different ways: either by direct indentation of the trigeminal spinal tract or by indirect anatomical, biochemical, or functional impairment of the trigeminocervical complex coming from the dorsal roots and dorsal horn. As far as we know, there is no research investigating the relationship between upper cervical discopathy and TN. However, there are some case reports which indicate that any pathology on the upper cervical region can cause TN.

One case reported that cervical discopathy on the level of C3-C4 resulted in trigeminal sensory neuropathy by affecting the spinal trigeminal tract. Surgical removal of the disk resulted in an immediate and complete resolution of TN-like symptoms in the patient.[7] Francois et al. demonstrated TN in 3 cases after posttraumatic cervical discopathy. Patients' symptoms of TN were reported to have disappeared after surgical decompression. It has been claimed that the cause of the pain may be due to compression of the spinal trigeminal tract. They argue that the spinal trigeminal nucleus can also extend to the lower cervical region.[23] Similarly, in our study, 25% of patients had an indentation on the Lissauer's tract, which is the continuation of the trigeminal spinal tract. In another paper, Samim et al. demonstrated 6 cases that had orofacial neuralgia associated with whiplash trauma. The pain of these patients has been described as typical TN. Two out of six patients had bulging between C2-C6 levels.[53]

Many studies are reporting that neuropathic pain develops due to spinal cord injuries. It has been reported that any pathology in the spinal cord may cause hyperexcitability in the dorsal horn.[26,60] This might occur through dysregulation of glutamate release, uptake, and receptor expression;[21,26,40,50,51] dendritic spine remodeling;[58,61] loss of local inhibitory (GABAergic) tone;[6,8,20,39,42,46] descending (particularly serotonergic) inhibitory input to spinal nociceptive circuitry;[28,34,40] or increased expression of calcium channel subunit.[11] Within a few months of spinal cord injury, NADPH-diphosphorase abnormality is seen in the nucleus cuneatus, nucleus gracilis, and spinal trigeminal tract of rats.[32] Neuropathic pain may be experienced by about 80% of individuals who sustain spinal cord injury.[22,56,57]

Some studies have pointed out the role of dorsal root ganglion in neuropathic pain. It is reported that chronic dorsal ganglia involvement can induce long-lasting N-methyl-D-aspartate receptor subunit 2B and neuronal nitric oxide synthase (nNOS) upregulation in the spinal dorsal horn. This upregulation may contribute to nociceptors activity-induced spinal plasticity and the development of central sensitization, and a close correlation between nNOS and neuropathic pain has been demonstrated.[14,43] After peripheral afferent fiber injury, a cascade of events within the dorsal root ganglion and upstream within the

dorsal horn of the spinal cord leads to a constitutive release of cytokines, production of abnormal ion channels, abnormal ion currents, early and late gene changes, and the development of chronic neuropathic pain.[37,38] It has been observed that compression with disc herniation may cause the spread of neuropathology from the dorsal part to the ventral area of the spinal cord.[41]

The studies that report cervical discopathies may also bring about neuropathic pain, suggesting that the cause of neuropathic pain may result from degenerative changes in the lamina I cell in the dorsal horn of the cervical disc. Ascending projection from the superficial dorsal horn of mammals is mainly sourced in the lamina I providing ascending trigeminal and spinothalamic tract projections that are key in sensations such as pain, itching, and temperature.[15,27,59] Animal studies show neuroplastic changes in various regions, including the primary synapses, spinal trigeminal tract, and the spinal dorsal horn, where the anatomical changes play a role in the production, modulation, and continuation of pain.[3,12,36]

It is well-known that the trigeminocervical complex plays the main role in many primary headaches. Kerr[35] was first to describe the trigeminocervical complex, which is formed by the association of the caudal trigeminal nucleus and the upper cervical segments. The pathogenic mechanism is hypothesized to involve the convergence of the upper cervical afferents from the C1, C2, and C3 spinal nerves and trigeminal afferents in the trigeminocervical nucleus of the upper cervical cord.[9,10] Functional convergence of the upper cervical and trigeminal sensory pathways seem to allow the bidirectional (afferent and efferent) referral of pain to the occipital, frontal, temporal, and/or orbital areas.[10] However, several previous studies have reported that lower cervical spine diseases (below C4) can also cause headache; to this end, it is not clear whether the middle-lower cervical roots also project into the trigeminocervical nucleus in humans.[9,19,24,47] The excitability of the second-order neurons within the trigeminal subnucleus caudalis has been shown to be responsible for pain perception and processing in migraine and TN.[18]

Our study shows that patients with upper cervical discopathy have a wide range of symptoms that can be mistaken for diseases such as ear, eye, or heart pathologies in clinical practice. Chen et al. also reported that various symptoms, including headache, perioral hyperesthesia, dizziness, and tinnitus, could be found in patients with upper cervical discopathy.[13]

Limitation of the study: the main limitation of this study is that it is not prospective. It does not observe the results of surgical procedures that may have been done to patients, such as cervical decompression, which is a major limitation. Second, such a small sample size might not be enough to prove our theory. Another limitation is that the MRI device used is a low-level Tesla. Additionally, a standard rather than specialized MRI protocol is used to investigate the cranial and cervical regions. It is very difficult to locate and explore the cervical region in a routine MRI scan because it is anatomically small in humans.

CONCLUSION

Cervical discopathy may be one cause of TN. Upper cervical discopathy may cause TN either by compressing the trigeminal spinal tract directly or by inducing biochemical changes coming from the dorsal roots to the ascendant pathways. Because it is seen in a significant number of all TN patients, the cervical region must be thoroughly investigated before diagnosing idiopathic trigeminal neuralgia. New clinical and experimental trials that focus on the upper cervical region are needed to shed light on this subject.

REFERENCES

1. Adams CB, Kaye AH, Teddy PJ: The treatment of trigeminal neuralgia by posterior fossa microsurgery. J Neurol Neurosurg Psychiatry 45(11):1020–1026, 1982, doi:10.1136/jnnp.45.11.1020
2. Afshar F, Watkins E, Yap JC: Sterotaxic atlas of the human brainstem and cerebellar nuclei; a variability study. New York: Raven Press, 1978, p 248
3. Amir R, Kocsis JD, Devor M: Multiple interacting sites of ectopic spike electrogenesis in primary sensory neurons. J Neurosci 9;25(10):2576–2585, 2005, doi:10.1523/JNEUROSCI.4118-04.2005
4. Antonini G, Di Pasquale A, Cruccu G, Truini A, Morino S, Saltelli G, et al: Magnetic resonance imaging contribution for diagnosing symptomatic neurovascular contact in classical trigeminal neuralgia: a blinded case-control study and meta-analysis. Pain 155(8):1464–1471, 2014, doi:10.1016/j.pain.2014.04.020
5. Apfelbaum RI: Surgery for tic douloureux. Clin Neurosurg 31:351–368, 1983, doi:10.1093/neurosurgery/31.cn_suppl_1.351
6. Arvidsson J, Pfaller K: Central projections of C4-C8 dorsal root ganglia in the rat studied by anterograde transport of WGA-HRP. J Comp Neurol 15;292(3):349–362, 1990, doi:10.1002/cne.902920303
7. Barakos JA, D'Amour PG, Dillon WP, Newton TH: Trigeminal sensory neuropathy caused by cervical disk herniation. AJNR Am J Neuroradiol 11(3):609, 1990
8. Berrocal YA, Almeida VW, Puentes R, Knott EP, Hechtman JF, Garland M, et al: Loss of central inhibition: implications for behavioral hypersensitivity after contusive spinal cord injury in rats. Pain Res Treat 178278, 2014, doi:10.1155/2014/178278
9. Biondi DM: Cervicogenic headache: a review of diagnostic and treatment strategies. J Am Osteopath Assoc 105(4 Suppl 2):16S–22S, 2005
10. Bogduk N, Govind J: Cervicogenic headache: an assessment of the evidence on clinical diagnosis, invasive tests, and treatment. Lancet Neurol 8(10):959–968, 2009, doi:10.1016/S1474-4422(09)70209-1
11. Boroujerdi A, Zeng J, Sharp K, Kim D, Steward O, Luo DZ: Calcium channel alpha-2-delta-1 protein upregulation in dorsal spinal cord mediates spinal cord injury-induced neuropathic pain states. Pain 152(3):649–655, 2011, doi:10.1016/j.pain.2010.12.014
12. Chaplan SR, Guo HQ, Lee DH, Luo L, Liu C, Kuei C, et al: Neuronal hyperpolarization-activated pacemaker channels drive neuropathic pain. J Neurosci 15;23(4):1169–1178, 2003, doi:10.1523/JNEUROSCI.23-04-01169.2003
13. Chen TY: The clinical presentation of uppermost cervical disc protrusion. Spine (Phila Pa 1976) 15;25(4):439–442, 2000, doi:10.1097/00007632-200002150-00008
14. Cízková D, Lukácová N, Marsala M, Marsala J: Neuropathic pain is associated with alterations of nitric oxide synthase immunoreactivity and catalytic activity in dorsal root ganglia and spinal dorsal horn. Brain Res Bull 58(2):161–171, 2002, doi:10.1016/s0361-9230(02)00761-x
15. Craig AD: How do you feel? Interoception: the sense of the physiological condition of the body. Nat Rev Neurosci 3(8):655–666, 2002, doi:10.1038/nrn894
16. Cruccu G, Finnerup NB, Jensen TS, Scholz J, Sindou M, Svensson P, et al: Trigeminal neuralgia: New classification and diagnostic grading for practice and research. Neurology 12;87(2):220–228, 2016, doi:10.1212/WNL.0000000000002840

17. Dandy WE: Concerning the cause of trigeminal neuralgia. Am J Surg 24:447–455, 1934
18. Davies AJ, North RA: Electrophysiological and morphological properties of neurons in the substantia gelatinosa of the mouse trigeminal subnucleus caudalis. Pain 146(1-2):214–221, 2009, doi:10.1016/j.pain.2009.07.038
19. Diener HC, Kaminski M, Stappert G, Stolke D, Schoch B: Lower cervical disc prolapse may cause cervicogenic headache: Prospective study in patients undergoing surgery. Cephalalgia 27:1050–1054, 2007, doi:10.1111/j.1468-2982.2007.01385.x
20. Drew GM, Siddall PJ, Duggan AW: Mechanical allodynia following contusion injury of the rat spinal cord is associated with loss of GABAergic inhibition in the dorsal horn. Pain 109(3):379–388, 2004, doi:10.1016/j.pain.2004.02.007
21. Falnikar A, Hala TJ, Poulsen DJ, Lepore AC: GLT1 overexpression reverses established neuropathic pain-related behavior and attenuates chronic dorsal horn neuron activation following cervical spinal cord injury. Glia 64(3):396–406, 2004, doi:10.1002/glia.22936
22. Finnerup NB, Norrbrink C, Trok K, Piehl F, Johannesen IL, Sørensen JC, et al: Phenotypes and predictors of pain following traumatic spinal cord injury: a prospective study. J Pain 15(1):40–48, 2014, doi:10.1016/j.jpain.2013.09.008
23. Francois EL, Clark NJ, Freedman BA: Facial numbness and paresthesias resolved with anterior cervical decompression and fusion: A report of 3 cases. JBJS Case Connect 9(3):e0294, 2019, doi:10.2106/JBJS.CC.18.00294
24. Fredriksen TA, Salvesen R, Stolt-Nielsen A, Sjaastad O: Cervicogenic headache: Long-term postoperative follow-up. Cephalalgia 19:897–900, 1999, doi:10.1046/j.1468-2982.1999.1910897.x
25. Frobin W, Brinckmann P, Kramer M, Hartwig E: Height of lumber discs measured from radiographs compared with degeneration and height classified from MR images. Eur Radiol 11:263–269, 2001, doi:10.1007/s003300000556
26. Gwak YS, Kang J, Leem JW, Hulsebosch CE: Spinal AMPA receptor inhibition attenuates mechanical allodynia and neuronal hyperexcitability following spinal cord injury in rats. J Neurosci Res 85(11):2352–2359, 2007, doi:10.1002/jnr.21379
27. Graff-Radford S, Gordon R, Ganal J, Tetradis S: Trigeminal neuralgia and facial pain imaging. Curr Pain Headache Rep 19(6):19, 2015, doi: 10.1007/s11916-015-0495-y
28. Hains BC, Johnson KM, Eaton MJ, Willis WD, Hulsebosch CE: Serotonergic neural precursor cell grafts attenuate bilateral hyperexcitability of dorsal horn neurons after spinal hemisection in rat. Neuroscience 116(4):1097–1110, 2003, doi: 10.1016/s0306-4522(02)00729-7
29. Hamlyn PJ, King TT: Neurovascular compression in trigeminal neuralgia: a clinical and anatomical study. J Neurosurg 76(6):948–954, 1992, doi:10.3171/jns.1992.76.6.0948
30. Headache Classification Committee of the International Headache Society (IHS): The International Classification of Headache Disorders, 3rd edition. Cephalalgia 38:1–211, 2018, doi:10.1177/0333102417738202
31. Henssen DJ, Kurt E, Kozicz T, van Dongen R, Bartels RH, van Cappellen van Walsum AM: New insights in trigeminal anatomy: A double orofacial tract for nociceptive input. Front Neuroanat 10:53, 2016, doi:10.3389/fnana.2016.00053
32. Hou W, Jia Y, Li Y, Wei Z, Wen X, Rao C, et al: NADPH diaphorase neuronal dystrophy in gracile nucleus, cuneatus nucleus and spinal trigeminal nucleus in aged rat. bioRxiv 12.21.885988, 2019, doi:10.1101/2019.12.21.885988

33. Jannetta PJ: Arterial compression of the trigeminal nerve at the pons in patients with trigeminal neuralgia. J Neurosurg 26:159–162, 1967, doi:10.3171/jns.1967.26.1part2.0159
34. Kalous A, Osborne PB, Keast JR: Spinal cord compression injury in adult rats initiates changes in dorsal horn remodeling that may correlate with development of neuropathic pain. J Comp Neurol 513(6):668–684, 2009
35. Kerr FW: The divisional organization of afferent fibres of the trigeminal nerve. Brain 86:721–732, 1963
36. Khan GM, Chen SR, Pan HL: Role of primary afferent nerves in allodynia caused by diabetic neuropathy in rats. Neuroscience 114:291–299, 2002, doi:10.1016/s0306-4522(02)00372-x
37. Kogelman LJA, Elgaard-Christensen R, Olesen J, Jansen-Olesen I, Hansen TF: Transcriptomic profiling of trigeminal nucleus caudalis and spinal cord dorsal horn. Brain Res 1692:23–33, 2018, doi:10.1016/j.brainres.2018.04.037
38. Krames ES: The role of the dorsal root ganglion in the development of neuropathic pain. Pain Med 15(10):1669–1685, 2014, doi:10.1111/pme.12413
39. Lee-Kubli CA, Ingves M, Henry KW, Shiao R, Collyer E, Tuszynski MH, et al: Analysis of the behavioral, cellular and molecular characteristics of pain in severe rodent spinal cord injury. Exp Neurol 278:91–104, 2016, doi:10.1016/j.expneurol.2016.01.009
40. Leem JW, Kim HK, Hulsebosch CE, Gwak YS: Ionotropic glutamate receptors contribute to maintained neuronal hyperexcitability following spinal cord injury in rats. Exp Neurol 224(1):321–324, 2010, doi:10.1016/j.expneurol.2010.02.012
41. Li Y, Jia Y, Hou W, Tan H: Novel morphological alteration and neural pathway of NADPH diaphorase positivity in the spinal cord with disc herniation of aged dog: A case report. Preprints 2020020280, 2020, doi:10.20944/preprints202002.0280.v1
42. Lu Y, Zheng J, Xiong L, Zimmermann M, Yang J: Spinal cord injury-induced attenuation of GABAergic inhibition in spinal dorsal horn circuits is associated with down-regulation of the chloride transporter KCC2 in rat. J Physiol 586(23):5701–5715, 2008, doi:10.1113/jphysiol.2008.152348
43. Ma ZL, Zhang W, Gu XP, Yang WS, Zeng YM: Effects of intrathecal injection of prednisolone acetate on expression of NR2B subunit and nNOS in spinal cord of rats after chronic compression of dorsal root ganglia. Ann Clin Lab Sci 37(4):349–355, 2007
44. Masdeu JC, Biller J: Localization in clinical neurology. Philadelphia: Lippincott Williams & Wilkins, 2011
45. Matsushita M, Okado N, Ikeda M, Hosoya Y: Descending projections from the spinal and mesencephalic nuclei of the trigeminal nerve to the spinal cord in the cat. A study with the horseradish peroxidase technique. J Comp Neurol 196(2):173–187, 1981, doi:10.1002/cne.901960202
46. Meisner JG, Marsh AD, Marsh DR: Loss of GABAergic interneurons in laminae I-III of the spinal cord dorsal horn contributes to reduced GABAergic tone and neuropathic pain after spinal cord injury. J Neurotrauma 27(4):729–737, 2010, doi:10.1089/neu.2009.1166
47. Michler RP, Bovim G, Sjaastad O: Disorders in the lower cervical spine. A cause of unilateral headache? A case report. Headache 31:550–551, 1991, doi:10.1111/j.1526-4610.1991.hed3108550.x
48. Miller J, Acar F, Hamilton B, Burchiel K: Preoperative visualization of neurovascular anatomy in trigeminal neuralgia. J Neurosurg 108(3):477–482, 2008, doi:10.3171/JNS/2008/108/3/0477
49. Peker S, Sirin A: Primary trigeminal neuralgia and the role of pars oralis of the spinal trigeminal nucleus. Med Hypotheses 100:15–18, 2017, doi:10.1016/j.mehy.2017.01.008

50. Putatunda R, Hala TJ, Chin J, Lepore AC: Chronic at-level thermal hyperalgesia following rat cervical contusion spinal cord injury is accompanied by neuronal and astrocyte activation and loss of the astrocyte glutamate transporter, GLT1, in superficial dorsal horn. Brain Res 1581:64–79, 2014, doi:10.1016/j.brainres.2014.05.003
51. Ruggiero DA, Ross CA, Reis DJ: Projections from the spinal trigeminal nucleus to the entire length of the spinal cord in the rat. Brain Res 225(2):225–233, 1981, doi:10.1016/0006-8993(81)90832-5
52. Saito N, Yamakawa K, Sasaki T, Saito I, Takakura K: Intramedullary cavernous angioma with trigeminal neuralgia: a case report and review of the literature. Neurosurgery 25:97–101, 1989
53. Samim, F, Epstein, JB: Orofacial neuralgia following whiplash-associated trauma: Case reports and literature review. SN Compr Clin Med 1(8):627–632, 2019
54. Shankland WE 2nd: The trigeminal nerve. Part I: An over-view. Cranio 18(4):238–248, 2000, doi:10.1080/08869634.2000.11746137
55. Shuhui G, Jiagang L, Siqing H, Haifeng C, Qingrong T, Bohao Z: Rare cervical intramedullary cavernous angioma with trigeminal neuralgia and cervical itch: Case report and review of the literature. Iran Red Crescent Med J 18:e25151, 2016, doi:10.5812/ircmj.25151
56. Siddall PJ, Loeser JD: Pain following spinal cord injury. Spinal Cord 39(2):63–73, 2001, doi:10.1038/sj.sc.3101116
57. Siddall PJ, McClelland JM, Rutkowski SB, Cousins MJ: A longitudinal study of the prevalence and characteristics of pain in the first 5 years following spinal cord injury. Pain 103(3):249–257, 2003, doi:10.1016/s0304-3959(02)00452-9
58. Tan AM, Stamboulian S, Chang YW, Zhao P, Hains AB, Waxman SG, et al: Neuropathic pain memory is maintained by Rac1-regulated dendritic spine remodeling after spinal cord injury. J Neurosci 28(49):13173–13183, 2008, doi:10.1523/JNEUROSCI.3142-08.2008
59. Wilcox SL, Gustin SM, Macey PM, Peck CC, Murray GM, Henderson LA: Anatomical changes at the level of the primary synapse in neuropathic pain: evidence from the spinal trigeminal nucleus. J Neurosci 35:2508–2515, 2015, doi:10.1523/JNEUROSCI.3756-14.2015
60. Zhang H, Xie W, Xie Y: Spinal cord injury triggers sensitization of wide dynamic range dorsal horn neurons in segments rostral to the injury. Brain Res 1055(1-2):103–110, 2005, doi:10.1016/j.brainres.2005.06.072
61. Zhao P, Hill M, Liu S, Chen L, Bangalore L, Waxman SG, et al: Dendritic spine remodeling following early and late Rac1 inhibition after spinal cord injury: evidence for a pain biomarker. J Neurophysiol 115(6):2893–2910, 2016, doi:10.1152/jn.01057.2015

LIST OF ABBREVIATIONS

GABAergic: Gamma-aminobutyric acid
MRI: Magnetic resonance imaging
NADPH-Diphosphorase: Nicotinamide adenine dinucleotide phosphate
nNOS: Neuronal nitric oxide synthase
ICHD: International Classification of Headache Disorders
TN: Trigeminal neuralgia
VAS: Visual Analogue Scale

الملخص العربي

اعتلال الغضروف العنقي في الام العصب الخامس مجهول السبب: أكثر من مجرد مصادفة؟

البيانات الخلفية: السبب الأكثر شيوعًا لألم العصب الخامس هو انضغاط الأوعية الدموية. ومع ذلك ، فإن العديد من المرضى يعانون من مسببات غير معروفة.

الغرض: تهدف هذه الدراسة إلى التحقق من العلاقة بين ألم العصب الخامس وأمراض الغضروف العنقي في المرضى الذين سبق تشخيصهم بألم العصب الخامس مجهول السبب.

تصميم الدراسة: لقد قمنا بتصميم دراسة مراقبة الحالة والمراقبة في مركز التعليم العالي لدينا.

المرضى والطرق: تم تضمين مجموعة الدراسة المكونة من مرضى تم تشخيصهم سابقًا بألم العصب الخامس مجهول السبب ومجموعة ضابطة تتكون من مرضى يعانون من صداع التوتر. تم إعادة تقييم التصوير بالرنين المغناطيسي للقحف لمرضى العصب الخامس من قبل أخصائي الأشعة العصبية الغير معرفين. بمجرد التأكد من عدم وجود علامات على ضغط الأوعية الدموية أو أي أسباب ثانوية ، تم إجراء التصوير بالرنين المغناطيسي للغضروف العنقي لتقييم أمراض عنق الرحم. تم تقييم التصوير بالرنين المغناطيسي للقحف و الغضروف العنقي من قبل نفس أخصائي الأشعة العصبية.

النتائج: تم فحص عشرين مريضا لديهم تشخيصات مسبقة لألم العصب الخامس مجهول السبب و20 مجموعة تحكم. كان متوسط عمر مرضى العصب الخامس 64.9 ± 12.6، وكان متوسط عمر المجموعة الضابطة 61.3 ± 9.1 (ع = 0.305). كانت نسبة الذكور / الإناث في مرضى العصب الخامس 2.3 و 1.8 في المجموعة الضابطة (ع = 0.736). بينما لوحظ أن الضعط من خارج النخاع على المسار الشوكي للعصب الخامس الناجم عن اعتلال القرص العنقي العلوي أعلى من المستوى الفقري الرابع في 12 من 20 مريضًا ، لم يكن لأي من الضوابط أي مشاركة في نفس المنطقة (p <0.001).

الخلاصة: نتائج هذه الدراسة تشير إلى أن الضعط من خارج النخاع على المسار الشوكي للعصب الخامس الناجم عن اعتلال القرص العنقي العلوي قد يكون أحد العوامل المسببة المحتملة في ألم العصب الخامس.