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Opinion

Insights on the terminology and on some pathophysiological aspects of cluster headache and related conditions

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Abstract

Introduction

Cluster headache and the more recently reported "related conditions", namely Chronic Paroxysmal Hemicrania, Short-lasting, unilateral, Neuralgiform Headache with Conjunctival Injection and Tearing (SUNCT) Syndrome and (possibly also) Hemicrania Continua, are one of the fascinating groups of conditions in Neurology whose cardinal features are the almost absolute unilaterality of pain, its excruciating severity, besides the prominent mainly facial autonomic disturbances and overall the intriguing biorhythmicity. Beyond any doubt, the progress of our knowledge about the mechanisms of these conditions has been considerable, but there is always room for reflection on where we are and where we can go.

Objective

The objectives of the present study are to analyze the metrics of publications on the pathophysiology of these conditions, to explore in detail how proper the term "Trigeminal Autonomic Cephalgia" is, and to comment on their numerous synonyms.

Comment

Much is needed to know the exact structures and circuitry involved in the pathophysiology of these conditions; accordingly, a non-compromising and just descriptive term might be useful. Along this line of reasoning and bearing in mind the cardinal points of such conditions, namely, pain in the trigeminal territory, prominent autonomic symptoms, prominent chronobiological features, and the excruciating character of the pain, a terminological possibility would be: Unilateral with Prominent Rhythmicity and Autonomic Symptoms Excrutiating Cephalgia (UPRASEC).

Keywords:
Trigeminal autonomic cephalgias
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Cluster headache (CH) and the more recently reported "related conditions", namely Chronic Paroxysmal Hemicrania, Short-lasting, unilateral, Neuralgiform Headache with Conjunctival Injection and Tearing (SUNCT) Syndrome and (possibly also) Hemicrania Continua are one of the fascinating group of conditions in Neurology whose cardinal features are the almost absolute unilaterality of pain, its excruciating severity, besides the prominent mainly facial autonomic disturbances and overall the intriguing biorhythmicity.

Beyond any doubt, the progress of our knowledge about the mechanisms of these conditions has been considerable, but there is always room for reflection on where we are and where we can go. The objectives of the present study are to analyze the metrics of publications on the pathophysiology of these conditions, to explore in detail how proper the term "Trigeminal Autonomic Cephalgia" is, and to comment on their numerous synonyms.

Number of publications on CH pathophysiology

From a longitudinal perspective, the Cluster Headache (CH) history had some "ages" over the last 90-100 years. From circa 1930 through the fifties, the Horton's age, when the underpinning was histamine. From 60's through the nineties, the Sjaastad's age may be decomposed into: (a) to debunk the role of histamine in CH; (b) the rise of CH to the category of a nosologic entity by its own; (c) later Sjaastad's group together with Nappi's Italian group in a reasonable amount of papers, shed some light on the role of hormones on CH and the meticulous objective measurements of CH accompanying autonomic symptoms and accordingly, aiming to find correlations with CH intimate mechanisms. From 1996 on, *grosso modo*, we enter Goadsby's age, with May's seminal crucial study on the hypothalamic involvement in CH[1] as well as a series of very elegant experiments, culminating with the postulation of the core role of the so-called trigeminal-autonomic reflex in CH pathophysiology.

From another perspective, the number of publications on CH pathophysiology (period 1966-2022) drew our attention and, accordingly, was studied. Aiming such a study, a search at the Pubmed site[2] from 1966 through 2022, January, was performed. Results are seen in Table 1 and Figure 1, where it becomes obvious the entry "Pathophysiology of cluster headache) (1,384 publications will be our focus).

Table 1. The number of publications with entries of cluster headache mechanisms from 1966 to 2022 (see text).

Entry	Link	Number of publications (respective years)
Cluster headache pathophysiology	https://pubmed.ncbi.nlm.nih.gov/?term=clusterheadache%20pathophysiology&timeline=expanded	2: 1991, 1996
Cluster headache mechanisms	https://pubmed.ncbi.nlm.nih.gov/?term=clusterheadache+mechanisms	2. 2001, 2008
Pathophysiology of cluster headache	https://pubmed.ncbi.nlm.nih.gov/?term=Pathophysiology%20of%20cluster%20headache&timeline=expanded	1384

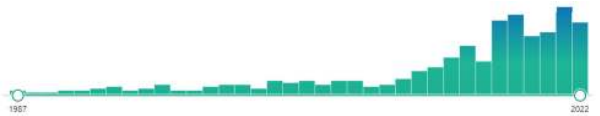

Figure 1. Distribution of the number of publications with the entry "Pathophysiology of migraine" from 1987 to 2022.

As far as the number of publications on CH, there seem to be three different periods with three other trends: a- 1966- 1990 from 1 article a year to 26 (a peak in 1988, 35 articles), an increase of 35 times in 24 years; from 1991 - 2005, from 29 to 51 an increase of 1.75 times in 14 years, from 2006 (47 in 2006 to 41 in 2021) onwards, the increase ratio was .87, lesser than one, pointing to a possible decrease in the number of publications. Therefore, the global trend was a crescent curve, but its convexity was upwards, indicating that the number of publications is decreasing in the long run. Such a decrease has already happened from 2019 on. The possible explanations for this finding are that we already know the main features of CH pathophysiology or, for some reason, as limitations in current scientific methods, restrictions of funding, or some other reasons the topic is not attracting investigators.

In such a scenario, the present study aims to foster discussion and enhance interest in some aspects of the pathophysiology of CH and its terminology.

On the terminolgy of cluster headache and related conditions

The issue terminology in "cluster headache" has been drawing the attention of headache specialists for decades. Sjaastad made an excellent review on this

Figure 3. Schematic drawing of the Trigeminal Autonomic Reflex (see text)

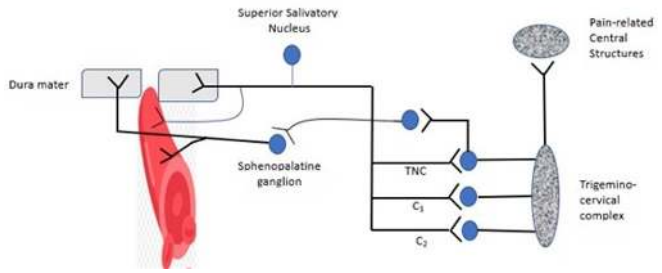

Figure 2. Schematic drawing of the Trigeminal Autonomic Reflex (see text)

topic.[3] As early as 1939, Horton et al. used the term "erythromelalgia" of the head[4], and in 1941, Horton coined the term "histaminic cephalgia".[5] The familiar term "cluster headache" was coined by Kunkle et al.[6] in 1952. Kunkle's "cluster headache" illustrated the typical trait of this condition, the accumulation of attacks within a limited time span. Ekbon[7] warned about the chronic form of CH; in his own words, "chronic migrainous neuralgia". In my opinion – not least from the linguistic aspect is to be preferred to the synonymous term chronic CH". In such a scenario, even as late as 1969, the Research Group of the World Federation of Neurology placed CH together with "facial migraine", "ophthalmoplegic migraine", and "hemiplegic migraine" under the heading: "Conditions which may fall within the category of migraine".

From 1988 onwards, in the first International Headache Classifications[8] CH appears as a condition on its own. Such terminology continued to evolve in the following IHS Classifications (Table 2).[9,10]

Table 2. The International Headache Classifications. The evolution of their item 3 terminology (Currently, Trigeminal autonomic cephalalgias)

Classification	Term	Definition
ICHD-1 (1988)	Cluster headache and chronic paroxysmal hemicrania	Cluster headache: Attacks of severe strictly unilateral pain orbitally, supraorbitally and or temporally, lasting 15-180 minutes and occurring from once every other day to 8 times a day.
ICHD-2 (2004)	Cluster headache and other trigeminal autonomic cephalalgias	The trigeminal autonomic cephalalgias share the clinical features of headache and prominent cranial parasympathetic autonomic features. Experimental and human functional imaging suggests that these syndromes activate a normal human trigeminal-parasympathetic reflex with clinical signs of cranial sympathetic dysfunction being secondary.
ICHD-3 (2018)	Trigeminal autonomic cefalalgias.	The TACs share the clinical features of unilateral headache and, usually, prominent cranial parasympathetic autonomic features, which are lateralized and ipsilateral to the headache. Experimental and human functional imaging suggests these syndromes activate a normal human trigeminal-parasympathetic reflex, with the clinical signs of cranial sympathetic dysfunction being secondary.

Following the timeline, it may be observed that the

terminological pendulum swung from a position close to vascular theory to the trigeminal-autonomic reflex. In this context is noteworthy to quote Goadsby[11] "Although both migraine and cluster headache are commonly called "vascular headaches", I suggest that they should be referred to generically as "neurovascular headaches", in which the vascular change that is seen in the cranial circulation is driven by the trigeminal-autonomic reflex (TAR) and thus is a marker of brain activation, not a driver of the syndrome.

The trigeminal autonomic reflex

The very concept of TAR seems to arise from headache researchers. Drummond obtained lacrimation and cutaneous vasodilation in the face following painful stimulation of the nasal ala and upper lip12, Goadsby and Duckworth[13] performed electrical activation of the trigeminal ganglion in cats, which led to a selective increase in regional blood flow in the frontal and parietal cortex; that was bilateral, even though, the unilateral intracranial section of the facial nerve blocked the response in the ipsilateral frontal and parietal cortex. Trigeminal fibers constitute the sole sensory (afferent) innervation of the cerebral vessels. It is noteworthy, nevertheless, that these fibers also have an efferent potential in pathophysiological settings.

Following a series of elegant experiments, Goadsby[11] conceived the trigeminal-autonomic reflex as follows: "Stimulation of the trigeminal ganglion in cats or monkeys leads to a decrease in carotid resistance, with increased flow and facial temperature, predominantly through a reflex mechanism. The afferent limb of this arc is the trigeminal nerve, and the efferent is the facial/greater superficial petrosal nerve (parasympathetic) dilator pathway. About 20% of the dilatation remains after the facial nerve section, and it is probably mediated by

antidromic activation of the trigeminal system directly. The portion running through the parasympathetic outflow traverses the sphenopalatine (pterygopalatine) and otic ganglia. The cells of origin for the cranial parasympathetic autonomic vasodilator pathway are in the superior salivatory nucleus in the pons, which can be activated with stimulation of a trigeminovascular nociceptive input, such as that from the superior sagittal sinus. This vasodilator reflex is a normal physiological reflex (Figure 2) that depicts the anatomy of trigeminal-autonomic cephalgias.

May et al.[1] also reported that in humans, an injection of capsaicin (painful stimuli) produces dilation of the internal carotid artery when administered into the skin innervated by the first (ophthalmic) division of the trigeminal nerve. However, when capsaicin is injected into the skin innervated by the third (mandibular) division or into the leg, there is no response in the ipsilateral carotid artery, despite the experience of pain.[14,15] Thus, the first (ophthalmic) division of trigeminal pain produces reflex activation of the cranial parasympathetic outflow.

According to Möller and May[16], the TAR is a physiological reflex with a protective function. Any irritation (trigeminal input) of the facial skin and specifically the eye, the upper lip, or the ala of the nose initiates parasympathetic output, such as lacrimation, miosis, an increase in facial blood flow in the respective area, as well as facial sweating. This mechanism protects especially the eye and the sensitive areas of the facial skin but is also involved in intracranial structures such as the meninges.

The term "Trigeminal Autonomic Cephalgias"

As early as 1997, it was suggested[17] that primary headache syndromes in which the TAR is prominently activated might be usefully classified together as trigeminal autonomic cephalgias (TACs).

Yet, according to Goadsby[11], TCAs pathophysiology may be seen as follows:

1. "Pain afferents from the trigeminovascular system traverse the ophthalmic division of the trigeminal nerve, taking signals from the cranial vessels and dura mater;
2. These synapses in the trigeminocervical complex, trigeminal nucleus caudalis (TNC), and dorsal horns of C1 and C2;
3. And then project to the thalamus and lead to activation in cortical areas, including the frontal cortex, insulae, and cingulate cortex, resulting in pain;
4. There is reflex activation of the parasympathetic outflow from the superior salivatory nucleus (SSN) via the facial (VIIth cranial) nerve;
5. Predominantly through the pterygopalatine (sphenopalatine) ganglion, which acts as a positive feedback system to dilate the vessels;
6. And irritate trigeminal endings further;
7. This autonomic activation leads to lacrimation, reddening of the eye, and nasal congestion; and a local third-order sympathetic nerve lesion due to carotid swelling results in a partial Horner's syndrome;
8. The key site in the CNS for triggering the pain and controlling the cycling aspects is in the posterior hypothalamic grey matter region (now known to be active on PET in patients.

Having in mind that the cardinal features of CH are (a) pain in the trigeminal territory, (b) the autonomic symptoms, (c) the chronobiological features, (d) the excruciating character of the pain, and that currently, since a unifying theory encompassing all such features are not available, but admitting the participation of the trigeminal vascular system for the former two features and hypothalamic grey activation for the remaining ones, the term TAC might be appealing.

In the same line of reasoning, Goadsby[18] would emphasize that the term would encompass the two major shared clinical features characteristic of this group: the trigeminal distribution of pain and ipsilateral cranial autonomic features. In this article, it is stated: (a) The term was coined to reflect a part of the pathophysiology of these conditions that is a common thread—that is, excessive cranial parasympathetic autonomic reflex activation to nociceptive input in the ophthalmic division of the trigeminal nerve; (b) The ipsilateral autonomic features (the underline is from us) seen clinically are consistent with cranial parasympathetic activation (lacrimation, rhinorrhoea, nasal congestion, and eyelid edema) and also "It is highly desirable that headache classification moves to a more biological and pathophysiological basis and the TACs are a step in that direction.

In this context, we feel that some comments may be useful. As early as 1986, in an Editorial on Cephalalgia, Sjaastad and Fredriksen[19] made crucial observations on the interrelationship of autonomic phenomena and pain in TCAs. Based on a sound body of studies concerning the measurement of autonomic symptoms in TAC patients, the authors stated, "It was clear that changes are almost invariably **bilateral**, provided the attacks are pronounced enough". This might be seen as a paradox: a unilateral

headache and **bilateral** autonomic phenomena.[7] For the authors, the players were: a "central generator ("origin"), the dysautonomic symptoms and pain. Figure 3 displays their possible interactions.

Figure 3. Possible interactions among "origin", dysautonomic symptoms and pain in CH attacks

A. Origin provokes pain and this provokes dysautonomic symptoms O → P → D
B. Origin provokes dysautonomic symptoms and this provokes pain O → D → A
C. Origen provokes both
   a. dysautonomic symptoms
   b. pain

The first possibility is the one that fits best with the concept of the core role of TAR in TACs.

Concerning such a possibility, we should go to Sjaastad et al.[20,21], who performed elegant experiments on chronic paroxysmal hemicrania (CPH) and the interrelationship between forehead sweating and pain. In one CPH patient, it was possible to precipitate attacks with flexion in the neck. A striking increase in sweating could start almost immediately on head flexion or after a few seconds. It was noteworthy that according to their own words, "During a real pain attack sweating usually started 15-30 seconds ahead of the pain", continuing, "Without sweat increase, there will be no ensuing pain." These findings were interpreted as follows: "Either the activation of the sweat production has to reach a certain level to give rise to pain, or the fact that the sweat activation has reached a certain level is only a sign that the local "irritation" has reached a level at which a *coactivation* of the pain may take place. In other words, it may still be that pain and autonomic phenomena are activated independently from a common source.

Moreover, it was demonstrated that both parenterally administered atropine and stellate ganglion blockade might abolish forehead sweating but not the surge of the pain. A dichotomy between pain and autonomic phenomena may, in other words, be obtained. Sweat production (or other autonomic phenomena, like tearing and nasal secretion) is not necessary for the generation of pain The authors concluded that possibility A is not correct. Furthermore, possibility B was highly unlikely that the autonomic phenomena generated the pain (possibility

B). "It seems most likely that pain and autonomic phenomena are activated in parallel during the attack. In other words, there may be a coactivation of two separate phenomena (possibility C). The interdependence of pain and autonomic phenomena is thus probably not causal." Such findings, therefore, clearly point against the hypothesis that autonomic dysfunction was secondary to pain; besides, it shows that autonomic symptoms are usually bilateral. So, neither does the hypothesis that autonomic signs are secondary to pain seem bearable, nor the statement that autonomic symptoms are ipsilateral to pain.

More recent papers on the topic deserve further comments as well.

Matharu and Goadsby[22] reported a case of a patient who had a complete surgical section of the left trigeminal sensory root, but the attacks continued to occur; this implies that even when one loop of the reflex is lacking, the attack may bring up. One study by Massoud Ashina's group[23] and another one from May's group[24] shed some light on the topic.

The Danish group study was based on the premise that sphenopalatine ganglion (SPG) stimulation with high-frequency stimulation might abort CH attacks. They hypothezed that low-frequency (LF) stimulation of the SPG would increase parasympathetic outflow, activate sensory afferents, and provoke a cluster-like attack. CH patients implanted with an SPG neurostimulator were to receive LF SPG stimulation, by this mean stimulating the efferent branch o TAR. As a matter of fact, it was found that "In the immediate phase (0–60 min), 80% of patients experienced cranial autonomic symptoms (CAS) after LF stimulation, even though, 45% of patients) reported CAS after sham (p=0.046) stimulation". No difference was found in the induction of cluster-like attacks between LF stimulation and sham stimulation (p=0.724). It was concluded that increased parasympathetic outflow (efferent branch) is insufficient to initiate CH attacks in patients.

In Möller et al. study[24] it was used kinetic oscillation stimulation (KOS) of the nasal mucosa, by this mean stimulating trigeminal afferents and, through TAR, provoking CAS. KOS was applied to 29 CH patients, including both episodic and chronic courses. KOS generated ipsilateral marked autonomic symptoms, including lacrimation significantly superior to rest. Nevertheless, it was not sufficient to induce CH attacks.

Goadsby in a Cephalagia's editorial[25] commented that Gou et al. and Möller et al.[24] papers were consistent with Matharu and Goadsby's[22] about the patient with a complete section of trigeminal nerve. It was concluded that "brain drives CH attacks", but did not comment that stimulation none branches of TAR were able to provoke full-blown CH attack; moreover, it was argued that such findings raise the question of the mode of action of SPG stimulation in CH, and support the notion that neurostimulation modulates the higher order processing centers of the brain.

As for the participation of TAR, the experiments of a complete section of trigeminal nerves, the studies by Mölller et al.[24] and by Gou et al. might indicate that TAR is neither necessary nor sufficient for the attack of CH and other TACs.

In short, it seems improbable that trigeminal pain through TAR in CH provokes autonomic symptoms. Even though it is well accepted that the *primum movens* in CH is the brain, researchers are so far arduously working to discover how central events turn into CH attacks; moreover, the involvement of TAR needs to be made more evident.

Let's make some comments on each word of TAC.

Trigeminal: The term presents flaws. First, it is very unspecific if we have in mind that the vast majority of headaches are "trigeminal"; besides, it has already been reported that TACs may occur in non-trigeminal territories.[26, 27]

Headache. Is CH a **headache** *sensu stricto*? It is noteworthy we could not find a definition of headache in IASP pain terms[28], IASP chapter concerning . Relatively Localized Syndromes Of The Head And Neck.[29] According to the site of the Cleveland Clinic[30], the main symptom of a headache is pain in the head or face. In a similar way, for Norman Harden for Scientific America[31], headache is pain in the head or face, and sometimes also includes pain in the upper neck.

On the other hand, in ICHD-3, officially called The International Classification of Headache Disorders, 3rd edition, even though there are not definitions for either headache or facial pain, it seems to be implicit that they are different terms. In three situations both terms appear together, **Head or facial pain** attributed to inflammation of the stylohyoid ligament, **Headache or facial pain** attributed to other disorder of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth or other facial or cervical structures and painful lesions of the cranial nerves and other **facial pain** and in one stance it appears only facial pain (painful lesions of cranial nerves and other facial pain. This may be interpreted that headache and facial pain are different symptoms, probably headache is pain

Table 3. Main Criteria for the terminology Cluster Headache

Term	Eponym	Phenomenology	Anatomic-physiopathological aspects
Naso-Ciliary neuralgia (Harris)	√		√
Sluder's neuralgia	√		√
Espheno-palatine neuralgia			√
Vidian neuralgia	√		√
Petrosal neuralgia (of Gardner)	√		√
Chronic Migrainous neuralgia (Ekbom)	√	√	√
Harris-Horton's disease	√		
Horton's headache	√	√	
Cluster headache (Kunkle)	√	√	
Histaminic Cephalalgia (Horton)	√	√	√
Erythro-melalgia of the head (Horton)	√	√	
Erythroprosopalgia of Bing	√	√	
Hemicrania angioparalytica (Eulenburg)	√	√	√
Hemicrania neuralgiform chronica		√	√

Table 4. Main Criteria for naming CH criteria for naming CH and related Conditions in IHS Classifications.

Term	Eponym	Phenomenology	Anatomic-physiopathological aspects
ICHD-1 Cluster headache and chronic paroxysmal hemicrania		√	
ICHD -2 Cluster headache and other trigeminal autonomic cephalalgias		√	√
ICHD-3 Trigeminal autonomic cepha-lalgias		√	√
Hemicrania Paroxística Crónica		√	
SUNCT		√	
UPRASEC		√	

felt above a straight line between the tragus and the outer canthus and facial pain, the ones felt beneath this line. Having in mind such distinction, Bahra et al.[32] report: "The site of pain was predominantly retro-orbital (92%) and temporal (70%). However, the pain was experienced over a wide area, including the forehead, jaw, cheek, upper and lower teeth, and, less commonly, the ear, nose, neck, shoulder, and other regions of the hemicranium. Thus, the pain predominantly was in areas under the distribution of the first division of the trigeminal nerve". Thus, CH and TACs in general are, as a matter of fact, "headache and facial pain". This means that TA cephalgia is a proper term; nevertheless, CH would better be cluster **cephalgia**. On **cranial autonomic symptoms**. Cranial autonomic symptoms are not a prerogative of CTS. It is not uncommon reports of cranial autonomic symptoms in migraine. Barbanti et al.[33] reported that up to 45.8% of migraine patients reported unilateral autonomic symptoms ocular symptoms alone or in combination with nasal symptoms) during their migraine attacks. Uluduz et al.[34], in 2,955 consecutive patients with definite migraine with and without aura, 89 display unilateral cranial autonomic symptoms. Togha et al.[35], in 493 migraineurs, 70% of subjects with chronic migraine and 56.2% of those with episodic migraine reported one or more cranial autonomic symptoms. Danno et al.[36] reported that 42.4% of patients with migraine had CAS. In short, CAS is far from being a prerogative of TACs.

On terminology

One question that deserves comments is the following: Trigeminal Autonomic Cephalgia, fancy term or constructive change to the IHS classification?[18] Despite the aforementioned comments, we believe it is not a fancy term and represents a constructive change to IHS Classification. But. Can we move further?

Along the timeline, the conditions we are dealing with have been classified sometimes as an eponym, sometimes according to its phenomenology or yet according to alleged anatomic-physiopathological aspects. Table 3 and Table 4 display, respectively, ancient terms and IHC Classifications terms. Nevertheless, two of the most important pillars in CH, namely, the chronobiological aspects and the excruciating pain have not been (with the exception of Kunkle's Cluster Headache) contemplated in the aforementioned terminology, not even in IHS Classifications.

Much is needed to know the exact structures and circuitry involved in the pathophysiology of these conditions; accordingly, a non-compromising and just descriptive term might be useful. Along this line of reasoning and bearing in mind the cardinal points of such conditions, namely, pain in the trigeminal territory, prominent autonomic symptoms, prominent chronobiological features and the excruciating character of the pain, a terminological possibility would be: Unilateral with Prominent Rhythmicity and Autonomic Symptoms Excrutiating Cephalgia (UPRASEC).

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References

1. May A, Bahra A, Büchel C, Frackowiak RSJ and Goadsby PJ. **Hypothalamic activation in cluster headache attacks**. *The Lancet* 1998; 352(9124): 275-278 Doi:10.1016/s0140-6736(98)02470-2
2. PubMed. **Migraine pathophysiology number of publications by year:** *PubMed*; 2023 [updated; cited 2023]. Available from: https://pubmed.ncbi.nlm.nih.gov/?term=migraine%20pathophysiologynumber%20of%20publications%20by%20year&show_snippets=off&timeline=expanded.
3. Sjaastad O. **Handbook of Clinical Neurology**. 48 ed. Elsevier Publishers B.V; 1986. 217 p.
4. Haane DYP, Dirkx THT and Koehler PJ.**The history of oxygen inhalation as a treatment for cluster headache.** *Cephalalgia* 2012; 32(12): 932-939 Doi:10.1177/0333102412452044
5. Horton BT. **Histaminic cephalgia**. *J Lancet* 1952; 72(2): 92-98
6. Kunkle EC, Pfeiffer JJB, Wilhoit WM and Hamrick LW. **Recurrent brief headache in cluster pattern**. *Trans Am Neurol Assoc* 1952; 56(77th Meeting): 240-243
7. Kunkle E. **Chronic Migrainous Neuralgia**. In:Rose. Handbook of Clinical Neurology. 4. 48 ed. 1986. p. 247.
8. **Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. Headache Classification Committee of the International Headache Society**. *Cephalalgia* 1988; 8 Suppl 7(1-96).
9. Olesen J. **Preface to the Second Edition**. *Cephalalgia* 2016; 24(1_suppl): 9-10 Doi:10.1111/j.1468-2982.2003.00824.x
10. **The International Classification of Headache Disorders, 3rd edition (beta version)**. *Cephalalgia* 2013; 33(9): 629-808 Doi:10.1177/0333102413485658
11. Goadsby PJ. **Pathophysiology of cluster headache: a trigeminal autonomic cephalgia**. *The Lancet Neurology* 2002; 1(4): 251-257 Doi:10.1016/s1474-4422(02)00104-7
12. Drummond PD. **Lacrimation and cutaneous vasodilatation in the face induced by painful stimulation of the nasal ala and upper lip**. *Journal of the Autonomic Nervous System* 1995; 51(2): 109-116 Doi:10.1016/0165-

1838(94)00121-y
13. Goadsby PJ and Duckworth JW. **Effect of stimulation of trigeminal ganglion on regional cerebral blood flow in cats**. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology* 1987; 253(2): R270-R274 Doi:10.1152/ajpregu.1987.253.2.R270
14. May A, Kaube H, Büchel C, Eichten C, Rijntjes M, Jüptner M, . . . Diener CH. **Experimental cranial pain elicited by capsaicin: a PET study**. *Pain* 1998; 74(1): 61-66 Doi:10.1016/s0304-3959(97)00144-9
15. May A, Büchel C, Turner R and Goadsby PJ. **Magnetic Resonance Angiography in Facial and other Pain: Neurovascular Mechanisms of Trigeminal Sensation**. *Journal of Cerebral Blood Flow & Metabolism* 2016; 21(10): 1171-1176 Doi:10.1097/00004647-200110000-00005
16. Möller M and May A. **The unique role of the trigeminal autonomic reflex and its modulation in primary headache disorders**. *Current Opinion in Neurology* 2019; 32(3): 438-442 Doi:10.1097/wco.0000000000000691
17. Goadsby P. **A review of paroxysmal hemicranias, SUNCT syndrome and other short- lasting headaches with autonomic feature, including new cases**. *Brain* 1997; 120(1): 193-209 Doi:10.1093/brain/120.1.193
18. Goadsby PJ. **Trigeminal autonomic cephalalgias: fancy term or constructive change to the IHS classification?** *Journal of Neurology, Neurosurgery & Psychiatry* 2005; 76(3): 301-305 Doi:10.1136/jnnp.2004.036012
19. Sjaastad O, Fredriksen T. **Cluster Headache Syndrome: Interrelationship of Autonomic Phenomena and Pain—an Editorial**. *Cephalalgia* 2016; 6(1): 3-5 Doi:10.1046/j.1468-2982.1986.0601003.x
20. Sjaastad O, Russell D and Saunte C. **Chronic Paroxysmal Hemicrania. VIII. The Sweating Pattern**. *Cephalalgia* 2016; 3(1): 45-52 Doi:10.1046/j.1468-2982.1983.0301045.x
21. Sjaastad O, Aasly J, Fredriksen T and Bakowska MMW. **Chronic Paroxysmal Hemicrania: X. On the Autonomic Involvement**. *Cephalalgia* 2016; 6(2): 113-124 Doi:10.1046/j.1468-2982.1986.0602113.x
22. Matharu MS and Goadsby PJ. **Persistence of attacks of cluster headache after trigeminal nerve root section**. *Brain* 2002; 125(5): 976-984 Doi:10.1093/brain/awf118
23. Guo S, Petersen AS, Schytz HW, Barløse M, Caparso A, Fahrenkrug J, . . . Ashina M. **Cranial parasympathetic activation induces autonomic symptoms but no cluster headache attacks**. *Cephalalgia* 2017; 38(8): 1418-1428 Doi:10.1177/0333102417738250
24. Möller M, Haji AA, Hoffmann J and May A. **Peripheral provocation of cranial autonomic symptoms is not sufficient to trigger cluster headache attacks**. *Cephalalgia* 2017; 38(8): 1498-1502 Doi:10.1177/0333102417738248
25. Goadsby PJ. **Cluster headache and the trigeminal-autonomic reflex: Driving or being driven?** *Cephalalgia* 2017; 38(8): 1415-1417 Doi:10.1177/0333102417738252
26. Sanin LC, Mathew NT and All S. **Extratrigeminal Cluster Headache**. *Headache: The Journal of Head and Face Pain* 1993;33(7):369-371 Doi:10.1111/j.1526-4610.1993.hed3307369.x
27. Rossi P, Di Lorenzo G, Faroni J and Sauli E. **Seasonal, extratrigeminal, episodic paroxysmal hemicrania successfully treated with single suboccipital steroid injections**. *European Journal of Neurology* 2005; 12(11): 903-906 Doi:10.1111/j.1468-1331.2005.01106.x
28. Goadsby PJ. **Cluster headache and the trigeminal-autonomic reflex: Driving or being driven?** *Cephalalgia* 2017; 38(8): 1415-1417 Doi:10.1177/0333102417738252
29. Sanin LC, Mathew NT and All S. **Extratrigeminal Cluster Headache**. *Headache: The Journal of Head and Face Pain* 1993;33(7):369-371 Doi:10.1111/j.1526-4610.1993.hed3307369.x
30. Rossi P, Di Lorenzo G, Faroni J and Sauli E. **Seasonal, extratrigeminal, episodic paroxysmal hemicrania successfully treated with single suboccipital steroid injections**. *European Journal of Neurology* 2005; 12(11): 903-906 Doi:10.1111/j.1468-1331.2005.01106.x
31. International Association for the Study of Pain, **IASP Terminology Background** Washington, D.C.: International Association for the Study of Pain; 1979 [update cited. 2. Available from: https://iaspfiles.s3.amazonaws.com/production/public/2021/Part_III-PainTerms.pdf.
32. Bahra A, May A and Goadsby PJ. **Cluster headache: A prospective clinical study with diagnostic implications**. *Neurology* 2002; 58(3): 354-361 Doi:10.1212/wnl.58.3.354
33. Barbanti P, Fabbrini G, Pesare M, Vanacore N and Cerbo R. **Unilateral Cranial Autonomic Symptoms in Migraine**. *Cephalalgia* 2016; 22(4): 256-259 Doi:10.1046/j.1468-2982.2002.00358.x
34. **Noro Psikiyatr Ars**. Turk Noropsikiyatri Derneği Nin Yayin Organidir; 1964. p.
35. Togha M, Jafari E, Moosavian A, Farbod A, Ariyanfar S and Farham F. **Cranial autonomic symptoms in episodic and chronic migraine: a cross sectional study in Iran**. *BMC Neurology* 2021; 21(1): Doi:10.1186/s12883-021-02513-0
36. Danno D, Wolf J, Ishizaki K, Kikui S, Yoshikawa H and Takeshima T. **Cranial Autonomic Symptoms of Migraine in Japan: Prospective Study of 373 Migraine Patients at a Tertiary Headache Center**. *Headache: The Journal of Head and Face Pain* 2020; 60(8): 1592-1600 Doi:10.1111/head.13888