Medical Hypotheses 100 (2017) 15–18

Contents lists available at ScienceDirect

Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy

Primary trigeminal neuralgia and the role of pars oralis of the spinal trigeminal nucleus

Selcuk Peker [a,*], Alperen Sirin [b]

[a] Koc University Hospital, Istanbul, Turkey
[b] Acibadem University School of Medicine, Istanbul, Turkey

ARTICLE INFO

Article history:
Received 1 August 2016
Accepted 12 January 2017

ABSTRACT

Trigeminal neuralgia is a painful condition that causes great discomfort. Although this disease has been known for more than 1000 years, there is still no consensus on its underlying mechanism or treatment. Many hypotheses have been reported to explain the cause and nature of trigeminal neuralgia. These include theories about peripheral mechanisms and central mechanisms. We put forward a new hypothesis that trigeminal neuralgia is associated with the pars oralis of the spinal trigeminal nucleus (POSTN). The main basis for this is the close similarity between trigger point distribution and the area of influence of the POSTN. We also highlight that the areas of influence for the trigeminal nerve divisions do not match the trigger point distribution; therefore, peripheral theories should be further investigated.

Trigeminal neuralgia is a condition that maps to the distribution area of one or multiple branches of the trigeminal nerve. This disease is typically unilateral and characterized by stabbing and paroxysmal pain [1]. The annual incidence of trigeminal neuralgia is 4–5 per 100,000 [2]. There are two etiological categories of this condition: primary (or idiopathic) and secondary (or symptomatic) [3]. While the primary form has no clear cause, the secondary form has multiple known causes, including tumor, multiple sclerosis, cysts, and others [3]. Trigeminal neuralgia due to neurovascular compression is considered to be primary [3]. The etiopathology of trigeminal neuralgia is not fully understood, but it is known that different mechanisms contribute to the establishment and persistence of this form of pain [4].

Current theories on etiology

Peripheral mechanisms

Peripheral theories suggest that trigeminal neuralgia is related to anatomical and physiological defects along the course of the nerve before enters the brainstem [1]. The most widely supported of these theories is vascular compression. This proposes that neuralgia occurs due to compression of the central-peripheral myelin transitional zone, the region where central myelin meets peripheral myelin [5]. However, it has been suggested that the root entry zone and transitional zone are distinct sites and that these terms should never be used interchangeably [5]. Dandy was the first researcher in modern medicine to point to vascular compression as the cause of trigeminal neuralgia [6]. Dandy observed that 66 of 215 patients with trigeminal neuralgia had vascular compression of the sensory root of the trigeminal nerve [6]. Gardner and Janetta concluded that compression of the central-peripheral myelin transitional zone (Obersteiner-Redlich line) causes ephatic transmission and subsequently trigeminal neuralgia [7]. McLaughlin et al. later postulated that the central myelin of the sensory root of the trigeminal nerve could extend along the entire cisternal segment of this branch [8]. They also stated that whereas vascular decompression of the root entry zone could relieve the pain of patients with trigeminal neuralgia, decompression performed anywhere along the entire length of the nerve (from the pons to the entry into Meckel's cave) could also be effective [8]. Further, another important study evaluated 3-Tesla magnetic resonance imaging of 200 trigeminal nerves in 100 asymptomatic patients using three-dimensional CISS sequences [9]. The authors detected neurovascular decompression in 92 of the 100 patients, with 83 cases bilateral and nine unilateral. In total, 175 of the 200 nerves examined showed vascular compression. The researchers concluded that vascular compression of the trigeminal nerve is not necessarily pathological [9].

Neto et al. have hypothesized that trigeminal neuralgia can be caused by maxillary and/or mandibular nerve entrapment [10]. Trigeminal neuralgia most commonly occurs on the patient's right side. The main basis for the theory proposed by Neto et al. is that, although vascular compression of the dorsal root the trigeminal

* Corresponding author at: Koc University Hospital, Department of Neurosurgery, Davutpasa Cad No 4, 34010, Topkapi, Istanbul, Turkey.
E-mail address: peker@selcukpeker.com (S. Peker).

http://dx.doi.org/10.1016/j.mehy.2017.01.008
0306-9877/

nerve by an aberrant loop of blood vessels is currently accepted to be the most common cause of trigeminal neuralgia, there is no anatomical reason for the loop to be more frequent on the right side of the cranial fossa [10]. They also note that anatomical and radiological studies have shown that the rotundum and ovale foramina of the human cranium are significantly narrower on the right side than on the left, and that the maxillary and mandibular nerves, respectively, pass through these foramina [10]. These are the two nerves most commonly affected in trigeminal neuralgia.

It is also thought that trigeminal neuralgia can be caused by demyelination. Some investigations of surgical biopsies from affected patients have revealed significant demyelination of trigeminal sensory fibers [11]. One study indicated that ectopic impulses can be caused by demyelination [12]. It has been suggested that demyelination can cause ectopic impulse generation and pain sensation, and can reduce the central pain-gating mechanism, thus leading to trigeminal neuralgia [13,14]. However, this does not align with the rapid electrophysiologic recovery and pain relief that usually occurs after a patient with trigeminal neuralgia undergoes microvascular decompression surgery [15]. A study that pursued this revealed that both demyelination and neurovascular decompression are needed to cause abnormal muscle response, whereas neither alone is sufficient to cause this [16].

Other peripheral causes of trigeminal neuralgia have also been identified. Several studies have demonstrated changes in anisotropy or diffusivity of the trigeminal nerve and grey matter in affected patients, and this suggests that microstructure abnormalities and demyelination without axonal injury are important pathogenetic factors [17–19]. Knight theorized that past herpes simplex virus infections cause chronic damage to nerve ganglia, which leads to development of trigeminal neuralgia [20]. Another study indicated that arachnoid thickening or granulomatous adhesion between the root and surrounding structures might lead to this condition [21].

It has also been speculated that an abnormality of the trigger zone could cause trigeminal neuralgia [22]. Specifically, it has been suggested that this type of abnormality could alter the function of calcium and sodium channels, thus affecting nerve transmission. In accord with this, authors have also suggested several related treatments for trigeminal neuralgia: local injection of carbamazepine into the trigger zone, or destruction of trigger zone via laser damage or freezing.

A bioresonance hypothesis has also been presented [23]. This states that when the vibration frequency of a structure near the trigeminal nerve approaches its natural frequency (e.g., reflecting blood pressure, heart rate, intracranial pressure, or pulsing of tortuous vessels near the nerve), the trigeminal nerve resonates with that frequency. Such resonance of the trigeminal nerve can damage nerve fibers, which leads to abnormal transmission and resulting facial pain.

Central mechanisms

Central mechanism theories for trigeminal neuralgia are based on the concept that this disease is characterized by focal epileptic and neuronal hyperactivity features [1]. Lewy and Grant reported that 50% of trigeminal neuralgia patients have cardiomegaly, angina pectoris, and advanced arteriosclerotic vascular disease [24]. They suggested that trigeminal neuralgia is caused by minor ischemic foci in the thalamus and resultant thalamocortical radiations. Black demonstrated that injecting epileptogenic agents into the trigeminal nucleus of cats and monkeys led to neuronal hyperactivity and pain syndrome [25]. Further, King observed that irritation of the descending tract of the trigeminal nerve and of the trigeminal nucleus increases electrical stimulation response in the peripheral portion of the nerve [26]. Considering this, King concluded that trigeminal neuralgia is caused by irritation of the trigeminal nucleus in the brainstem [26]. In other work, it has been observed that when the amplitude and frequency of a skin stimulus changes, there is a refractory phase prior to the next paroxysm [27]. It has been observed that a rapid fall in excitability following the cessation of the stimulus is followed by a refractory period of up to two to three minutes, depending upon the duration and intensity of the pain following the attack [27]. It has been also observed that anti-epileptic drugs, such as lidocaine and hydantoin, raise the attack threshold and shorten the duration of the attack by diminishing its tendency to self-maintenance [27]. The study has been concluded that there are several reasons that suggest the paroxysmal pain is situated centrally, probably in the brain-stem in structures related to the spinal V nucleus [27]. These reasons are: long summation times, the tendency of the attack to be self-maintained, the effect of antiepileptic drugs as well as the long-lasting refractory period [27].

List and Williams reported that the pain in trigeminal neuralgia is caused by a pathological multineuronal reflex that occurs in the trigeminal system within the brainstem [28]. A separate study revealed that grey matter volume is decreased in the thalamus, primary and secondary somatosensory cortex, and other central nervous system structures of trigeminal neuralgia patients, and that greater reductions were associated with longer disease duration [29]. The authors suggested that patients exhibit a neuroplastic adaptation phenomenon in response to chronic trigeminal neuralgia [29].

Research has also shown that injection of certain substances into the trigeminal nucleus caudalis causes hypersensitivity that resembles trigeminal neuralgia [30]. As well, Hu et al. hypothesized that atypical trigeminal neuralgia can be a consequence of central sensitization [31].

Several case reports have described different central causes of trigeminal neuralgia. One report notes two patients who developed this condition due to vascular malformations of the brainstem [32]. In both cases, it was thought that the neuralgia was caused by damage to the intra-axial trigeminal nerve pathways [32]. A second case study described a patient afflicted with trigeminal neuralgia due to pontine infarction [33]. The patient had a trigger point on the left upper lip. Imaging demonstrated a pontine infarct suspected to be caused by an arterial embolism. The condition was treated with carpamazepine.

Another report noted a patient with trigeminal neuralgia who had mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) [34]. The latter condition is an autosomal-recessive disease associated with multiple deletions of mitochondrial DNA in skeletal muscle [35]. It is a multisystem syndrome that affects muscle, the peripheral and central nervous systems, and the gastrointestinal tract [36]. The patient was a 25-year-old male who presented with a 3-year history of right-sided trigeminal neuralgia. In this case, a parallel was suggested between multiple sclerosis and MNGIE as a cause for trigeminal neuralgia [34].

Anatomy

Anatomy of the sensory portion of the trigeminal nerve

The pseudounipolar perikarya of the sensory portions of the trigeminal nerve are in the semilunar or gasserian ganglion, which is situated near the apex of the petrous bone in the middle cranial fossa. From this ganglion, the fibers of the sensory root (portio major) enter the substance of the pons, course dorsomedially, and terminate in three major nuclear complexes within the brainstem: the nucleus of the spinal tract of the trigeminal nerve, the