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Review Article

What is Sluder's neuralgia?

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Abstract

In 1908 Sluder described a symptom complex consisting of neuralgic, motor, sensory and gustatory manifestations that he attributed to the sphenopalatine ganglion. He stated that treatment directed at the ganglion successfully alleviated these symptoms. Over the last 90 years several reports have described patients as having sphenopalatine neuralgia and have directed treatment at the ganglion. The symptoms described and the criteria for patient selection in these studies has often been varied and deviated from Sluder's description. In reports claiming cures with treatment directed at the ganglion the duration of post-treatment follow-up has been short. This article discusses Sluder's description and attempts to analyse its features in the light of current understanding of the different mechanisms and categories of facial pain. It is proposed that the condition described by Sluder is a neurovascular headache that most closely resembles cluster headache in its aetiology and clinical manifestations. We propose that the term Sluder's neuralgia should be discarded as there are serious flaws in its original description and many authors have misused the term leading to persistent confusion about it.

Key words: Facial Pain Syndromes; Ganglia, Autonomic; Cluster Headache; Disease Management

Introduction

In 1908 Sluder observed that occasionally patients who recovered from a high-grade inflammatory reaction in the posterior ethmoid and sphenoid sinuses were left with a characteristic neuralgic picture.[1] He described the syndrome as a sphenopalatine ganglion neuralgia[2,3] which included a symptom-complex of neuralgic, motor, sensory and gustatory manifestations that he attributed to the extension of inflammation or the transmission of toxins into the sphenopalatine ganglion. He described an all encompassing entity, but never recorded a case presenting with a combination of all the signs and symptoms he described.[2,3] Sluder lacked the benefit of both nasal endoscopy, current imaging techniques and the range of drugs available today.

Neurological features

Sluder described an ipsilateral pain that could be constant with exacerbations, cyclical or episodic. The pain was classically described as beginning at the root of the nose, spreading ipsilaterally in and around the eye, involving the upper jaw and teeth and sometimes the lower jaw and teeth. It occasionally extended beneath the zygoma to the ear and sometimes it affected the mastoid, but was nearly always most severe at a point about 5 cm posterior to the mastoid. Sluder called this group of symptoms 'lower half headache'. The pain could extend to the occiput, neck, shoulder blade, shoulder and breast. In severe attacks it spread to the axilla, arm, forearm, hand or fingers. It could also produce a sore throat on the affected side.

Sensory signs

Many patients experienced slight anaesthesia of the soft palate, oropharynx, tonsils and the anterior lower part of the nose on the affected side while some patients experienced hyperaesthesia in the distribution of the trigeminal nerve. Before, or during, an attack of a migraine-like episode, some patients had an aura of a distorted sense of taste described as 'metallic' or like a 'peculiar acid'.

Motor signs

The palatine arch was often, but not always, higher on the affected side when compared with the normal side. A dimple formed in the raphe just above the uvula in the act of gagging and the uvula was inclined obliquely to the normal side.

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Parasympathetic (vasomotor and secretory) signs

Patients complained of ipsilateral swelling of the nasal membrane, a serous nasal discharge, nasal obstruction, lacrimation and conjunctival injections. Some patients experienced salivation on the affected side.

Role of the sphenopalatine ganglion in Sluder's neuralgia

Sluder described the sphenopalatine ganglion as a small triangular body placed deep within the sphenomaxillary fossa, behind the posterior tip of the middle turbinate, 1–9 mm from the lateral nasal wall and separated from the nasal cavity by mucous membrane and fatty tissue.[2] He believed that irritation of the ganglion resulted from the extension of inflammation from the sphenoid and the posterior ethmoid sinuses.[3]

Sluder attempted to treat the syndrome by destruction of the sphenopalatine ganglion intranasally via the sphenopalatine foramen. He reported that patients who had refused surgery for ethmosphenoid inflammation that had been active for two years, later developed sphenopalatine neuralgia. In these patients the pain was controlled by the local application of cocaine or cured by injection of phenol into the ganglion, in spite of the persistence of any nasal inflammation. In patients with pain attributed to 'systemic toxicity' in the absence of nasal inflammation, cocaine applied to the sphenopalatine foramen was always effective in stopping the pain. He concluded that pain of 'systemic' origin was more susceptible to treatment than pain following local inflammation.[3]

Sluder recommended that pain should initially be treated with cocaine, followed by an application of formaldehyde or silver, failing which he advised an injection of phenol. He treated pain of moderate intensity with one to three applications of a drop of 20–67 per cent cocaine. In moderate to severe pain of longer duration he used one to three injections of alcohol into the ganglion. In the most severe chronic cases, treatment produced temporary relief with a return of symptoms at a diminished intensity. He found there was a variable response to treatment. It was proposed that the variability of pain relief from chemoneurolytic agents depended upon the depth of the sphenopalatine ganglion (1–9 mm) from the lateral nasal wall, the size of the sphenopalatine ganglion (2–6 mm $\times$ 1–3 mm) and the degree of nerve arborization.[2]

Sluder was confident that there was a direct association between the sphenopalatine ganglion and the manifestations he described. No pain relief was obtained when cocaine was applied to other areas in the nose. He also said that while treatment to the sphenopalatine ganglion could temporarily relieve these symptoms, the pain could recur following a recurrence of inflammation or 'toxic conditions'.[3]

A review of the treatment strategies advocated for the symptom-complex fitting Sluder's description

A study of Puig *et al.*[4] advocated the use of intranasal cauterization of mucosa over the area of the sphenopalatine ganglion with 88 per cent phenol. Eight patients were diagnosed with 'Sluder's neuralgia'. The nature of their pain and its similarity with that of Sluder's description were not mentioned in this study and the patients were selected on the basis that local anaesthesia of the sphenopalatine ganglion with xylocaine relieved their symptoms of their head and face pain (but this was not also done using a placebo such as saline which the senior author has sometimes found to work). The patients were treated with phenol-soaked cotton carriers applied to the region of the sphenopalatine ganglion for 15–30 seconds on an average of 13 occasions and this resulted in 90 per cent experiencing a decrease in pain for an average of 9.5 months.

Various surgical techniques have been attempted for treating patients with a symptom complex similar to that described by Sluder. A 70-year-old woman with neurogenic and autonomic features similar to that described by Sluder and consistent pain relief for several hours with a series of three lidocaine blocks of the sphenopalatine ganglion was diagnosed as having sphenopalatine neuralgia.[5] Computerized tomography (CT) scans of the patient's sinuses revealed no bone or soft tissue abnormalities and no evidence of acute or chronic sinusitis. Stereotactic radiosurgical treatment on this patient caused total symptomatic relief by eight months. However, the pain then recurred and she required repeat radiosurgery and the patient was followed-up for a further seven months with no recurrence of pain.[5]

Sphenopalatine ganglion neuronectomy in 12 patients with hemifacial pain associated with ipsilateral autonomic discharge showed a high incidence of recurrent pain on follow-up, although their pain was less severe.[6]

A patient with bilateral pain in the jaw, teeth, and eyes that radiated to the arms with associated rhinorrhoea, nasal obstruction and no radiological evidence of sinusitis was treated by bilateral ganglionectomy performed four years apart. The patient was followed up for a further year and had intermittent episodes of pain and altered sensation in the cheek and hard palate.[7]

It has been suggested that a contact point on the middle nasal turbinate can cause the neurogenic features described by Sluder, although Sluder did not describe the presence of such a point. In 1934 McAuliffe *et al.*[8] stimulated the lower, middle and upper turbinates mechanically with a probe or by a faradic current and reported that this process produced referred pain with a specific distribution depending on the area stimulated.[8] However, these findings were not found in a recent study which compared the application of pressure, adrenaline, substance P and a placebo topically to mucosa of the nasal floor, septum, lateral nasal wall and inferior and middle turbinates. The study suggested that the presence of a nasal mucosal contact point and facial

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pain was a coincidence and not causal.[9] The prevalence of contact points has also been found to be the same in an asymptomatic control population as in a symptomatic population.[10]

Anatomy and physiology of the sphenopalatine ganglion

The sphenopalatine ganglion is a parasympathetic ganglion that lies just below the maxillary nerve near the sphenopalatine foramen. It receives fibres from the maxillary nerve, greater petrosal nerve and deep petrosal nerve.

The branches of the maxillary nerve that pass through the sphenopalatine ganglion supply sensation to the nose, palate, tonsils and gingivae. The greater petrosal nerve, a branch of the facial nerve carries taste and parasympathetic fibres. Taste fibres pass through the sphenopalatine ganglion to the palate. The parasympathetic fibres synapse in the ganglion and postsynaptic fibres supply the lacrimal gland and mucosa of the palate, nasopharynx and nasal cavity. The deep petrosal nerve is a branch of the internal carotid plexus and carries postganglionic fibres from nerve cell bodies in the superior cervical sympathetic ganglion. The sympathetic nerve fibres pass through the sphenopalatine ganglion without synapsing and join branches of the maxillary nerve where they are distributed to the nasal cavity, palate and superior part of the pharynx. The greater petrosal nerve and deep petrosal nerve join at the foramen lacerum to form the vidian nerve, which travels through the pterygoid canal to the sphenopalatine ganglion.

Possible mechanisms for the clinical manifestations described by Sluder

Hypothetical neurological mechanisms

A possible origin for the symptom-complex described by Sluder is the trigeminal nerve. Irritation of the pterygopalatine nerves could cause a 'lower half headache' along the distribution of the maxillary nerve. There is an overlap between cervical and trigeminal root afferents in the most caudal part of the spinal nucleus of the trigeminal nerve. Hence there is a potential for stimulation of the trigeminal nerve to cause pain in dermatomes supplied by cervical nerves C2–4 in the neck, shoulder and mastoid process regions, so that theoretically, disorders of the nose and sinuses could elicit pain almost anywhere in the head and neck region.

Stimulation of the medial pterygoid nerve, a branch of the mandibular nerve that supplies the tensor veli palatini could cause tension of the soft palate and explain the higher palatine arch on the affected side. The lacrimal nucleus, a parasympathetic nucleus of the facial nerve is situated in the lower part of the pons. It receives afferent fibres from sensory nuclei of the trigeminal nerve for reflex lacrimation secondary to irritation of the cornea or conjunctiva. However, the parasympathetic fibres that end in the submandibular gland originate in the superior salivary nucleus and are separate from the sphenopalatine ganglion and trigeminal nerve although it accompanies the lingual nerve for part of its course. Therefore, in theory, the trigeminal nerve could potentially initiate the parasympathetic manifestations of lacrimination, hypersecretion and congestion of the nasal mucous membrane but not gustation. A pathological mechanism for initiating pain has been proposed in a recent study on small diameter nociceptive trigeminal afferent fibres that project to the trigeminal nucleus where they excite further nociceptive neurones.[11] The nociceptive neurones can be modified by peripheral tissue trauma and inflammatory conditions resulting in neuroplastic changes (an alteration at the neural junctions or the formation of new connections) in trigeminal neurones in the brainstem.[11,12] Neuroplastic changes may underly the development and maintenance of chronic pain as well as influence the acute pain associated with injury and inflammation. It has been proposed that the neuroplastic changes that occur may be involved in the spread and referral of pain and may also contribute to the tenderness and hyperalgesia of superficial tissues.[11,12]

Proposed vascular mechanisms

The majority of sphenopalatine ganglion neurones possess vasoactive intestinal polypeptide (VIP), nicotinamide-adenine dinucleotide phosphate (NADP) diaphorase and nitric oxide (NO) synthase.[13–16] VIP in cerebral arteries acts as a vasodilator and enhances cerebral blood flow. NADP-diaphorase-positive and NO-containing nerves are known to induce non-adrenergic, non-cholinergic vasodilation in cerebral arteries. Relatively abundant NADP-diaphorase positive fibres were found in the zygomatic nerve, a branch of the maxillary nerve, that conveys sensory fibres as well as postganglionic parasympathetic fibres from the sphenopalatine ganglion via the zygomaticotemporal nerve to the lacrimal gland. The origin of NADPH-diaphorase-positive fibres in the zygomatic nerve appeared to be from the sphenopalatine ganglion.[13]

In the cat, VIP-positive fibres in the nose were shown to arise from parasympathetic nerves originating from the sphenopalatine ganglion.[17,18] This was supported by the finding that stimulation of the sphenopalatine ganglion detected by laser Doppler flowmetry produced vasodilatation and increased bloodflow to the cat nasal mucosa.[19] A study attempting to identify the origin and distribution of NADP-diaphorase-positive fibres in rat nasal mucosa, revealed that the fibres originating from the sphenopalatine ganglion were distributed around blood vessels, submucosal glands and the subepithelial layer of rat nasal mucosa. It has also been suggested that nitric oxide may be co-localized to the cholinergic innervation and be involved in vasomotor and secretory control of nasal mucosa.[20] In chronic paroxysmal hemicrania and cluster headache levels of calcitonin gene-related peptide and vasoactive intestinal polypeptide have been found to be raised in the cranial circulation during attacks.[21]

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Therefore the presence of vasodilator positive fibres in parasympathetic nerves originating from the sphenopalatine ganglion, may be responsible for the secretory and vasolidatory changes in the nasal cavity and the migraine-like vascular pain of Sluder's description.

Interestingly, a study identified that branches of the external carotid artery receive innervation from parasympathetic, sympathetic and C fibres containing substance P. Encephalins, known antagonists of substance P, were also identified in the arterial branches. It has been hypothesized that a desequilibrium between sympathetic and parasympathetic firing from the sphenopalatine ganglion may result in the release of substance P or cause a blockade of local encephalins, resulting in vasodilatation of the external carotid and its branches producing pain in the distribution of the sphenopalatine ganglion.[22]

Neurovascular headaches

Assimilating the above theories one can reason that the symptom complex described by Sluder has a neurovascular basis. In keeping with Sluder's theory it is possible that the sphenopalatine ganglion is involved as part of the symptom-complex. Furthermore neuroimaging of primary headache syndromes such as cluster headache and migraine have shown that they have a neurovascular basis rather than being primarily vascular.[23–25] Experimental and clinical data in cluster headache suggests involvement of pain afferents of the ophthalmic nerve and involvement of vasoactive neuropeptides such as calcitonin gene-related peptides produced by the parasympathetic fibres of the facial nerve.[23,24]

Furthermore functional imaging with positron emission tomography (PET) has documented specific activation of the hypothalamus in cluster headache, with activation of the midbrain and pons in migraine.[24,25]

Classification of the condition described by Sluder

The International Headache Society (IHS)[26] described Sluder's neuralgia as a previously used term for cluster headache. It divided cluster headache into the following subgroups: cluster headache periodicity undetermined, episodic cluster headache and chronic cluster headache unremitting from onset or evolved from episodic. Many authors have suggested that Sluder's neuralgia is categorized as cluster headache[27] because of the similarities between the two conditions, particularly in those where the midface and jaw are involved.[28,29] A minority dispute an association between the two conditions.[30]

The classification of chronic pain by the International Association for the Study of Pain (IASP)[31] did not recognise Sluder's syndrome. It described classic migraine (V-1), cluster headache (V-6) and clustertic syndrome (V-9) of which the main features have been presented in Table I. These categories of facial pain appear to have several characteristics in common with the symptom-complex described by Sluder.

Sluder's description and classic migraine

Sluder described patients with migraine-like pain as a characteristic of his syndrome and identified a few patients who complained of an aura preceding the development of a headache as seen in classic migraine. Intranasal lidocaine treatment used during the aura in one patient suffering from migraine prevented the development of a headache in 73 out of 75 episodes over an 18-month period.[32] Whilst there are some similarities between the two conditions, there are also many significant differences, as shown in Table I.

Sluder's description and cluster headache

Table I shows several similarities in the distribution of pain, the autonomic manifestations, precipitating factors and the age of onset in Sluder's description and cluster headache. However, the characteristic features of cluster headache which are its periodicity, groups of attacks when the patient is in an active bout that distinguishes the 'on' period from the 'off' period are lacking in Sluder's description. While cluster headache appears to be mediated by the ophthalmic division of the trigeminal nerve[23,24] Sluder described pain that extended outside this distribution. A study on 66 patients who suffered from cluster headache that did not respond to pharmacological management, showed a significant therapeutic effect following radiofrequency treatment of the sphenopalatine ganglion via an infrazygomatic approach. Sixty per cent of the patients with episodic cluster headache and 30 per cent of patients with chronic cluster headache experienced complete pain relief over a 12–70 month period.[33] It has been recommended that radiofrequency treatment to the sphenopalatine ganglion is an effective treatment option for cluster headache resistant to pharmacological treatment.

A double-blind placebo study on 15 patients suffering from cluster headache offered further support to the therapeutic effects of treatment to the sphenopalatine ganglion. An attack of pain was induced using a standard nitroglycerine test and when patients experienced a pain intensity measuring 5 on the visual analogue scale after five to 10 minutes, either a 10 per cent solution of cocaine hydrochloride, a 10 per cent lidocaine solution or saline was applied using a cotton swab in the area corresponding to the sphenopalatine fossa, under anterior rhinoscopy. All patients had complete cessation of induced pain after approximately 30 minutes. In cases where saline was used pain severity increased.[34] These studies support the hypothesis that the sphenopalatine ganglion is involved in cluster headache as it has many similarities to Sluder's description.

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TABLE I

COMPARISON OF SLUDER'S SYNDROME, CLASSIC MIGRAINE, CLUSTER HEADACHE AND CLUSTER-TIC SYNDROME

Characteristics	Sluder's syndrome[3]	Cluster headache [IASP (V-6)][26]	Classic migraine [IASP (V-1)][26]	Cluster-tic syndrome [IASP (V-9)]26
Pain quality and intensity	Burning or aching pain which was either a constant pain with exacerbations or a pain that stopped and reappeared cyclically or stopped and reappeared with stabbing sharpness.	Excruciating severe attacks of constant stabbing, burning or even throbbing pain.	Throbbing, pulsating pain, mild to severe in intensity.	Cluster headache: Agonizingly severe, long-lasting, burning or throbbing pain. Tic Douloureux: Sharp, agonizing, electric-shock-like stabs of pain felt superficially in the skin or buccal mucosa, triggered by a light tactile stimuli from a restriction trigger point. Both elements of the combined syndrome are among the most severe pains.
Site	Typically unilateral pain starting at the root of nose, involving the cheek, eye, teeth, frontotemporal region, mastoid region. Maximum pain intensity was experienced 5 cm posterior to the mastoid. Occasionally bilateral pain.	Unilateral pain, no alternation in side characteristic. Pain in ocular, frontal, temporal areas; less frequently involving infraorbital, upper teeth, back of head, entire hemicranium, neck and shoulder. Maximum pain in ocular, retro-ocular or peri-ocular areas.	Typically unilateral pain beginning most commonly in fronto-temporal area, may involve whole hemicranium, alternating sides between or during an attack.	Pain limited to head and face, with both parts of the syndrome appearing on the same side. Cluster headache element was located in the ocular area while the tic pain was most commonly along the distribution of the 2nd and 3rd division of the trigeminal nerve.
Frequency	Attacks could last hours to several days. Attacks could occur daily.	Attacks occur during cluster periods of 4–12 weeks. Attacks last 30 minutes to 2 hours and occur 1–3 times a day. Nocturnal attacks were typical. No attacks occur during the remission period, which last 6–18 months.	Attacks last 4–72 hours if unmodified by drugs. Attacks most commonly occur 1–4 times a month.	The cluster episode comprises severe episodes of steady pain lasting 10–120 minutes, frequently occurring at night, in cluster periods lasting 4–8 weeks. Remission periods may last 6–12 months. At times it may enter a chronic phase when attacks may occur daily for months. The 2 components of the syndrome may occur concurrently with or temporarily separated from each other.
Associated symptoms and signs	Sensory signs: Anaesthesia of soft palate, pharynx, tonsils, nose. Hyperesthesia along distribution of trigeminal nerve. Motor signs: Palatine arch higher on affected side, the deviation of uvula to normal side. Parasympathetic signs: Ipsilateral lacrimation, conjunctival injections, nasal obstruction, rhinorrhoea, serous nasal discharge, inflamed mucosa. Gustatory signs: Delayed or diminished perception of taste.	Sensory signs: Dysaesthesia on touching scalp hairs in ophthalmic division of trigeminal nerve, Photophobia. Motor signs: Ipsilateral miosis or ptosis. Parasympathetic signs: Ipsilateral lacrimation, conjunctival injection, nasal obstruction, rhinorrhoea. Reduced heart rate, irregular in severe attacks. Nausea and vomiting may occur.	Anorexia, nausea, vomiting, photophobia and phonophobia. Redness and swelling of the mucous membrane of the nose and conjunctival injection may also occur with migraine.	Prominent autonomic features with the cluster type pain, similar to cluster headaches.
Aura	Distorted sense of taste described as 'metallic' or 'peculiar acid' before or during an attack.		Visual disturbances; unilateral paresthesia of hand and mouth or mild paresis; dysarthria and aphasic disturbance occurred before or during an attack.	

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Treatment	Pain relieved by anaesthetization of SPG, ganglionectomy, clonazepam	Pain improved with triptans, pizotifen, ergot preparations, oxygen, $5HT_1$ agonists, steroids, verapamil, lithium methysergide.	Pain relieved by triptans, pizotifen, ergotamines, beta-blocking agents, calcium channel blocking agents, NSAIDs, $5HT_1$ agonists.	Carbamazepine and/or baclofen, rather than the conventional drugs used for cluster headache.
Precipitating factors	Alcohol, tobacco, changes in climate or exposure to drafts	Alcohol or smoking. Long lasting stress may predispose to bouts.	Numerous, including changes in stress, mood changes, relaxation, dietary factors.	Alcohol can stimulate the cluster component, while a trigger phenomenon exists for the tic component. Speaking, swallowing, washing the face or shaving can precipitate an attack.
Prevalence	Rare	7 per 10 000 population	High	Rare
Sex ratio	Female : Male 2:1	Male : Female 4:1	Female > Male	Male : Female 1:1
Age of onset	30–50 years	18–40 years	Childhood to 35 years	Middle age, rarely in the elderly.

Sluder's description and cluster-tic syndrome

In an attempt to combine the cluster headache manifestations and the trigeminal component of Sluder's description, one might imply that Sluder's description is a variant of the cluster-tic syndrome. However, the clinical manifestations, triggering factors and periodicity of the tic-douloureux component showed striking differences to Sluder's description (see Table I).

- **Sluder's neuralgia was originally described as being due to irritation of the sphenopalatine ganglion in the sphenoid and posterior ethmoid sinuses that was treated with local anaesthetic applied to, or destruction of, the ganglion**
- **Later descriptions argued in favour of a contact point on the middle turbinate as the origin of this pain, these have now been discredited**
- **This article describes the anatomy and physiology of the sphenopalatine ganglion and advances hypothetical mechanisms for the origin of pain in patients with Sluder's neuralgia**
- **While patients also have some features that are migraine like, the authors suggest that patients with Sluder's neuralgia have features that are consistent with a variant of cluster headache**

Conclusion

Over 90 years ago Sluder described a 'sphenopalatine ganglion neuralgia' that encompassed an array of symptoms and signs that he treated by local anaesthesia of the sphenopalatine ganglion. His definition did not describe a single entity but a diverse symptom-complex and he never reported a case presenting with a combination of all its features. Recent studies have attempted to reproduce his findings. However, there is no diagnostic test to identify patients with Sluder's description and the criteria for diagnosing patients in the reported studies often differ from that used by Sluder.

Current classification categorizes Sluder's description as a cluster headache[28] as it has many of the features that he described. Several studies have shown that the sphenopalatine ganglion is involved in a cluster headache.

The classification of facial pain is evolving, as there is no 'test' by which a condition can be diagnosed. At present the 'best fit' for patients with the symptoms that Sluder described is cluster headache. Whilst cluster headache and Sluder's description can be placed together by their trigeminovascular pathogenesis, one fundamental question is the nature of the pathology initiating these conditions. There are some similarities with migraine, including its response to treatment, but we have more to learn. The term Sluder's syndrome is used loosely and it should be discarded as his description differs from most clinical entities.

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