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NEUROMODULATION (M GOFELD, SECTION EDITOR)

Neurostimulation at Pterygopalatine Fossa for Cluster Headaches and Cerebrovascular Disorders

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Abstract There are numerous neural structures (parasympathetic, sympathetic, and trigeminal sensory) that are compacted in a small well defined area of the pterygopalatine fossa (PPF). These targets can be readily accessed via minimally invasive neuromodulation techniques making the methods more desirable than neurosurgical deep brain or hypothalamic intervention. Recent research has shed light over the important role of the sphenopalatine ganglion (SPG), which is located within the PPF, in cerebrovascular autonomic physiology as well as in the pathophysiology of different headache disorders (cluster headache, migraine, and trigeminal autonomic cephalalgias). Accordingly, neuromodulation of the autonomic fibers (parasympathetic and sympathetic) may play a key role in the management of headaches, stroke, or cerebral vasospasm. Another important structure within the PPF is the maxillary nerve (V2), which passes through the roof of the fossa. Here the trigeminal system is accessible for a reliable neuromodulation by targeting its second branch -the maxillary nerve- and this could be utilized in various painful conditions of the head and face.

Keywords Pterygopalatine fossa neuromodulation · Sphenopalatine ganglion · Trigeminal nerve neurostimulation · Cluster headache

Introduction

Over the past decade, there was a renewed interest in the application of radiofrequency modulation to the neural structures within the pterygopalatine fossa (PPF), mainly the sphenopalatine ganglion (SPG) and the maxillary nerve. More recently, electrical stimulation has emerged as a reversible and adjustable method for modulating the activity of these autonomic fibers within the SPG as well as the trigeminal sensory fibers thought the maxillary nerve (Fig. 1).

SPG is an autonomic ganglion located within the pterygopalatine fossa. It is mainly a parasympathetic ganglion; however, it conveys both sensory and sympathetic fibers as well. The parasympathetic fibers are the only fibers that synapse in the ganglion, while the sensory and sympathetic fibers only pass through the ganglion without synapsing.

SPG mediates cluster headache symptoms through its connections to the trigemino-vascular system and as well as its parasympathetic outflows, which results in the associated autonomic features [1, 2]. Recently, it was shown that experimental activation of the SPG in humans provokes cluster-like attacks [3]. It also influences cerebral blood flow because of its parasympathetic cerebrovascular innervations, and SPG stimulation has been shown to reverse cerebral vasospasm and induce partial reperfusion of ischemic lesions in animal models [4–6].

Pterygopalatine Fossa (PPF) Anatomy

The pterygopalatine fossa is a small, upside-down pyramidal space 2 cm high and 1 cm wide on average. It is located behind the posterior wall of the maxillary sinus.

Pterygopalatine Fossa (PPF) Contents

(1) Maxillary artery and its branches
(2) Maxillary nerve (V2)
(3) SPG and its afferent and efferent branches.

This article is part of the Topical Collection on *Neuromodulation*

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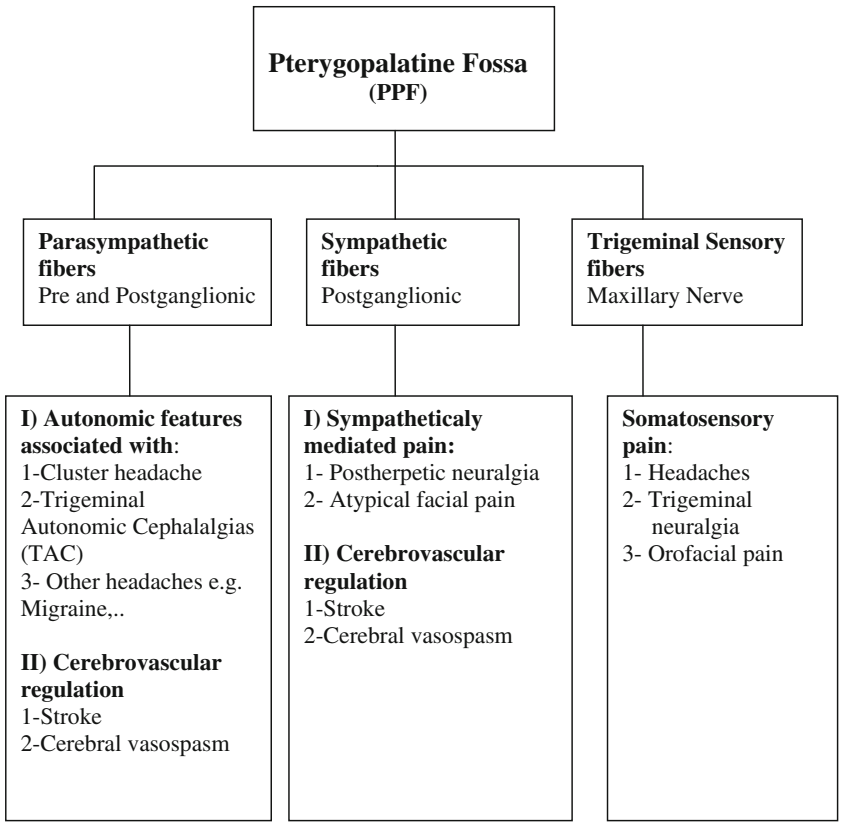

Fig. 1 Potential applications for neuromodulation at the pterygopalatine fossa (PPF).

Pterygopalatine Fossa (PPF) Openings

- Foramen rotundum (posterior wall, roof)
- Pterygoid canal (posterior wall , medial)
- Palatovaginal canal (posterior wall)
- Palatine canal (inferior)
- Sphenopalatine foramen (medial wall)
- Inferior orbital fissure (anterior wall, roof)
- Pterygomaxillary fissure (lateral)

Approaches to the Pterygopalatine Fossa (PPF)

Traditionally the PPF has been accessed by nasal applications of topical local anesthetics or injections through the greater palatine foramen [7, 8]. However, neuromodulation is clinically feasible through either the percutaneous infrazygomatic approach or the transoral approach.

Percutaneous Infrazygomatic Approach

The SPG is located within the pterygopalatine fossa and it is best approached using infrazygomatic approaches. The infrazygomatic approach could be either anterior to the mandible or through the coronoid notch of the mandible. The technique is described in details by Narouze et al [9, 10••].

Minimally Invasive Trans-Oral Approach

This new approach utilizes a small inductive coupled SPG stimulator implant that is activated by an external energy delivery control device [11]. The implant is placed by a minimally invasive trans-oral approach with an incision in the gingival mucosa above the maxillary molars. The stimulator implant is surgically placed below the cheek-bone with the electrode tip close to the sphenopalatine ganglion.

Neuromodulation at the Pterygopalatine Fossa (PPF)

Augmentation of Cerebral Blood Flow in the Treatment of Acute Ischemic Events

SPG stimulation has been shown to increase regional cerebral blood flow, induce partial reperfusion of ischemic lesions and reverse cerebral vasospasm in animal models [4–6].

The animal studies were encouraging and now there are human trials evaluating the safety and effectiveness of

SPG stimulation in the treatment of acute ischemic stroke [12].

Treatment of Cluster Headache

Original SPG stimulation technique employed transient neurostimulation with a temporary electrode using the standard lateral infrazygomatic approach [9].

Tepper et al performed electrical stimulation of the SPG for the acute treatment of intractable migraine. In 10 migraine headache trials, acute SPG stimulation resulted in complete relief in 2, partial relief in 2, and no relief in 6 instances [13]. It was noted that patients with medication overuse headaches (MOH) were resistant to SPG stimulation. In general, SPG stimulation for migraine has achieved variable results.

On the other hand, SPG stimulation for cluster headache has been promising. Ansarina et al reported the effectiveness of SPG stimulation in the treatment of cluster headaches. In 18 distinct cluster headache attacks, acute SPG stimulation resulted in complete resolution of the headache in 11, partial resolution in 3, and no relief in 4 instances. Interestingly, SPG stimulation resulted in complete resolution of the associated autonomic features of cluster headaches such as nasal congestion and periorbital swelling in all cases presented with autonomic features [14].

Recently, Schoenen et al conducted a multicenter randomized, sham-controlled study evaluating SPG stimulation implants in chronic cluster headaches [15••]. They used an on-demand mini SPG neurostimulator that was implanted through a transoral approach into the PPF in 32 patients. Each cluster headache attack was randomly treated with full, sub-perception, or sham stimulation. Pain relief was achieved in 67.1 % of full stimulation-treated attacks compared with 7.4 % of sham-treated and 7.3 % of sub-perception treated attacks. The authors concluded that SPG stimulation was effective in both acute pain relief as well as attack prevention, and has an acceptable safety profile compared with similar surgical procedures.

Brainstorming and Challenges with PPF stimulation

- The key question to answer is; can we selectively stimulate the parasympathetic, sympathetic, or sensory trigeminal fibers within the PPF? Is there a specific set of stimulation parameters that can modulate one neural structure than the other?
- What are the parameters to augment vs blocking the signals in those different fibers? Since the only cell bodies located in the SPG are the postganglionic parasympathetic neurons, can we presume that we always stimulate the parasympathetic system *first* before recruiting other nerve fibers?

Answering these questions will allow modulating or shifting the balance between the sympathetic and parasympathetic innervations of the cerebral vasculature, to selectively stimulate difference components of SPG and trigeminal system, and to find specific targets to manage separate clinical syndromes.

More animal and human data is needed to address the above questions. It is critical to know how to consistently shift the balance between the sympathetic and parasympathetic drives. Animal models can help us understand how to selectively modulate the autonomic fibers (sympathetic or parasympathetic) vs the trigeminal sensory fibers within the PPF. This might open a new horizon for the application of neuromodulation in various cerebrovascular as well as headache and facial pain disorders.

Compliance with Ethics Guidelines

Conflict of Interest Samer Narouze declares that he has no potential conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:
•• Of major importance

1. Goadsby PJ. Pathophysiology of cluster headache: a trigeminal autonomic cephalgia. Lancet Neurol. 2002;1:251–7.
2. Bartsch T, Goadsby PJ. The trigeminocervical complex and migraine: current concepts and synthesis. Curr Pain Headache Rep. 2003;7:371–6.
3. Schytz HW, Barløse M, Guo S, Selb J, Caparso A, Jensen R, et al. Experimental activation of the sphenopalatine ganglion provokes cluster-like attacks in humans. Cephalalgia. 2013;33:831–41.
4. Goadsby PJ. Sphenopalatine ganglion stimulation increases regional cerebral blood flow independent of glucose utilization in the cat. Brain Res. 1990;506:145–8.
5. Yarnitsky D, Lorian A, Shalev A, Zhang ZD, Takahashi M, Agbaje-Williams M, et al. Reversal of cerebral vasospasm by sphenopalatine ganglion stimulation in a dog model of subarachnoid hemorrhage. Surg Neurol. 2005;64:5–11.
6. Hennerici MG, Kern R, Szabo K. Non-pharmacological strategies for the treatment of acute ischaemic stroke. Lancet Neurol. 2013;12:572–84.
7. Sluder G. The role of the sphenopalatine ganglion in nasal headache. N Y State J Med. 1908;27:8–13.
8. Ruskin SL. Techniques of sphenopalatine therapy. Eye Ear Nose Throat Mon. 1951;30:28–31.

9. Narouze S, Kapural L, Casanova J, Mekhail N. Sphenopalatine ganglion radiofrequency ablation for the management of chronic cluster headache. Headache. 2009;49:571–7.
10.•• Narouze SN. Role of sphenopalatine ganglion neuroablation in the management of cluster headache. Curr Pain Headache Rep. 2010;14:160–3. *This article describes in details the neuroanatomy of the SPG, the pathophysiology of cluster headache, and the techniques to access the PPF.*
11. Oluigbo CO, Makonnen G, Narouze S, Rezai AR. Sphenopalatine ganglion interventions: technical aspects and application. Prog Neurol Surg. 2011;24:171–9.
12. Khurana D, Kaul S, Bornstein NM. For the ImpACT-1 study group. Implant for augmentation of cerebral blood flow trial 1: a pilot study evaluating the safety and effectiveness of the Ischaemic Stroke System for treatment of acute ischaemic stroke. Int J. Stroke. 2009;4:480–5.
13. Ansarinia M, Rezai A, Tepper SJ, Steiner CP, Stump J, Stanton-Hicks M, et al. Electrical stimulation of sphenopalatine ganglion for acute treatment of cluster headaches. Headache. 2010;50:1164–74.
14. Tepper SJ, Rezai A, Narouze S, Steiner C, Mohajer P, Ansarinia M. Acute treatment of intractable migraine with sphenopalatine ganglion electrical stimulation. Headache. 2009;49:983–9.
15.•• Schoenen J, Jensen RH, Lantéri-Minet M, Láinez MJ, Gaul C, Goodman AM, et al. Stimulation of the sphenopalatine ganglion (SPG) for cluster headache treatment. Pathway CH-1: a randomized, sham-controlled study. Cephalalgia. 2013;33:816–30. *This is the first RCT evaluating the safety and efficacy of permanent SPG stimulation for cluster headaches.*