

The physiology and pathophysiology of the parasympathetic nervous system in nasal disease: An overview

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The nose functions as an organ of respiration, as the first line of host defense against inspired microorganisms, as the organ of olfaction, as the source of liquid to humidify and cleanse inspired air, and to provide resonance. The human nasal mucosa is lined by ciliated pseudostratified columnar epithelium and nonciliated goblet cells. Beneath the epithelium is a lamina propria rich in seromucous acinar glands, blood vessels, and nerves. Deeper in the tissue is an area of venous sinusoids. The nasal mucosa has a relatively limited set of responses to irritation, infections, and allergic reactions. The tissue may swell because of increased vascular permeability or sinusoidal engorgement; secrete mucous, serous, or goblet cell products; or become irritated with a reduced threshold to either swell or secrete. Stimulation of sensory nerves leads to itching and sneezing. These responses are orchestrated by sets of regulatory processes, which are now being defined.¹ What follows is a brief summary of the findings relevant to the response of the nose to parasympathetic stimulation.

The mucosa is richly innervated by parasympathetic, adrenergic, and sensory nerves. Parasympathetic discharge will release acetylcholine, vasoactive intestinal polypeptide, and the closely related peptide, peptide histidine methionine (the latter two neuropeptides are colocalized to cholinergic nerves) and will result in glandular discharge, vasodilation, and possibly sinusoidal engorgement.²

Secretions (a runny nose) come from three major sources—the seromucous glands, goblet cells, or as part of the process of vascular permeability. Nasal secretions consist of proteins, glycoproteins, lipids, cells resident in the mucosa and plasma, and electrolytes and water secreted from the epithelial lining

cells. These secretions kill or retard growth of bacteria, viruses, or fungi that are inspired and reach the mucous blanket; lubricate, humidify, waterproof, and insulate the mucous membrane; retard proteins, particulate matter, or microorganisms from accessing the mucosa; provide an extracellular surface for enzymes and IgA to interact with microorganisms; neutralize noxious fumes; provide an appropriate milieu for ciliary action; and provide a disposable fluid with which to clear trapped materials from the nose.³

By using quantitative analysis of the proteins found in secretions, it has become possible to determine what conditions will cause certain secretions. Stimulation of parasympathetic nerves results in glandular secretions rich in mucous glycoproteins, lactoferrin, lysozyme, secretory leukoprotease inhibitor, neutral endopeptidase, and secretory IgA.⁴ We surmise that the production of this type of fluid enriches secretions with antimicrobial factors that might be important in keeping the mucosa free of infection.³ Glandular secretions are increased after eating hot and spicy foods (gustatory rhinitis syndrome),⁵ late in the course of respiratory tract infections,⁶ as a part of the response to allergen challenge (as a reflex response to mediator release, including histamine),⁷ and after any mechanical irritation of the nasal mucosa.

Edema formation, vasodilation, and sinusoidal engorgement create nasal congestion. Edema occurs in response to injury, allergic reactions, or inflammation, and it causes thickening of the mucosa and turbinates. Edema is associated with the secretion of a plasma protein-rich fluid.⁴ Vasodilation also occurs with inflammation and the normal process known as the “nasal cycle,” or alternating unilateral increased nasal airway resistance. Sinusoidal engorgement is regulated by the cholinergic nervous system, perhaps through the release of the neuropeptide vasoactive intestinal polypeptide or the generation of nitric oxide, as well as acetylcholine stimulation of muscarinic M3 receptors.⁸ Vasoactive intestinal polypeptide, nitric oxide, and acetylcholine cause arteriolar dilation, which allows blood to flow into the sinusoids and causes engorgement. This is the mechanism responsible for tumescence of erectile tissues elsewhere in

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the body and likely is the mechanism for this form of nasal congestion.

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Sensory, parasympathetic, and sympathetic neural influences in the nasal mucosa

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Neural mechanisms contribute to many nasal symptoms and syndromes. Sensory nerve stimulation by irritants, mast cell products, and inflammatory mediators leads to sneezing and other systemic reflexes. Parasympathetic reflexes and sensory axon responses combine to increase nasal blood flow, fill venous sinusoids (which thickens the mucosa and reduces nasal patency), induce plasma extravasation, and stimulate glandular secretion of mucous and serous cell products. These putative roles for nerves and neuropeptides in pathologic events open new therapeutic avenues. Anticholinergic agents, peptide neurotransmitter agonists and antagonists, drugs to reduce or modulate sensory or parasympathetic nerve function, potent topically applied glucocorticosteroids, and agents to inactivate inflammatory, secretory, or vascular cells may be of use. Ablation of sensory nerves by topical application of the chili pepper neurotoxin capsaicin has been successful in reducing the symptoms of refractory vasomotor rhinitis. (J ALLERGY CLIN IMMUNOL 1992;90:1045-50.)

Key words: Vasoactive intestinal peptide, parasympathetic reflexes, rhinitis, neuropeptide

Sneezing, rhinorrhea, and cyclic changes in nasal patency and discharge rates are normal, healthy responses to the varied conditions of inhaled air and noxious stimuli. Nasal nerves play a central role in the regulation of nasal patency and secretion production.¹ Stimulation of sensory nerves leads to parasympathetic reflex-mediated glandular secretion, whereas sympathetic influences contract the mucosa.² Alter-

ations in the neural control of vascular and secretory processes may contribute to the symptoms of rhinitic syndromes.

Abbreviation used

VIP: Vasoactive intestinal peptide

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NOCICEPTIVE SENSORY NERVES

The discovery that many neurons use peptides as neurotransmitters has revolutionized our understanding of the nervous system in general and the innervation of human nasal mucosa in particular.³ Trigeminal sensory neurons contain calcitonin gene-related