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# Nasal Reflexes: Implications for Exercise, Breathing, and Sex

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## Abstract

Nasal patency, with both congestion and decongestion, is affected in a wide variety of reflexes. Stimuli that lead to nasal reflexes include exercise, alterations of body position, pressure, and temperature, neurological syndromes, and dentists. As anticipated, the vagal and trigeminal systems are closely integrated through nasobronchial and bronchonasal reflexes. However, perhaps of greater pathophysiological importance are the naso-hypopharyngea-laryngeal reflexes that become aggravated during sinusitis. None other than Sigmund Freud saw deeply beyond the facial adornment and recognized the deeper sexual tensions that can regulate nasal functions and psychoanalytical status. Wine, women and song are linked with airflow through the nose, the nose, that by any other name would still smell as sweetly.

## Introduction

The brainstem, autonomic, and systemic reflexes that regulate nasal airway patency are potent, and play second-by-second roles in regulating our breathing and all of the sensations associated with movement of air through mucosal passages of the bronchial offshoot of the foregut and more rostral structures. These are deep seated reflexes with a distant footing in the ontology of the first organisms to walk from the sea onto land. Despite their primacy, these reflexes are such a critical part of life that we generally forget to reflect on their presence, let alone their importance. Many of the subtleties and nuances of life that mingle sensory, autonomic, and supratentorial integration depend on these reflexes that climax with nasal patency.

### Peripheral Stimuli Leading to Nasal Reflexes Exercise

Sympathetic reflexes are active in the nasal mucosa. Exercise promotes a drop in total nasal airway resistance within 30 sec that is maximal at 5 min, and may persist for up to 30 min after completing the aerobic performance [1,2]. Nasal airway resistance drops in proportion to exertion, with a 39% reduction at a workload of 75 watts and 49% after 100 watts. Sympathetic vasoconstriction of nasal vessels is part of a general sympathetic effect to maintain the flow of oxygenated blood to the muscles [3]. Isocapneic hyperventilation does not alter nasal airflow, indicating that the workload, and not nasal or oral airflow, is the trigger for the nasal and systemic vasoconstrictor response. Body position also does not affect the nasal changes of exercise.

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Exercise [4], and α-adrenergic agonists [5,6] decrease the thickness of the mucosa and increase nasal and sinus ostial patency. Sympathetic nerves innervate arterial and venous vessels including arteriovenous anastomoses, with only occassional nerves found around glands. Sympathetic nerves contain either norepinephrine, or norepinephrine plus neuropeptide Y (NPY) [7]. Norepinephrine and NPY are both vasoconstrictors, but NPY is slower in onset, and very long in duration [8]. The presence of both NPY-containing nerves and NPY binding sites on arteriovenous anastomoses suggests that NPY acts as a vasoconstrictor at this key location in vivo. NPY nasal provocation leads to decreased nasal airflow resistance and reduced plasma exudation [9]. NPY agonists may be excellent long-acting vasoconstrictors that may augment or replace α-adrenergic agonists.

## Positional Nasal Obstruction and Patency

Positional regulation of nasal airflow has been demonstrated by having subjects lay in the right and left lateral decubitus positions to maximize nasal patency in the superior nostril and decrease patency in the inferior nostril [10]. Nasal peak flow rates were measured after 30 min. Position had no effect on peak flow in the superior nostrils, or if nostrils were 100% obstructed (zero flow in some rhinitis subjects). However, the inferior, reflexly obstructed nostrils had a significant reduction in mean peak flow of −12.8 L/min (SD = 4.1 L/min). This obstruction may have clinical implications. Fluid dynamics demonstrate that the physical force (frictional stress) exerted on the walls of a tube increase as tube diameter is decreased (increased airflow resistance). Reduced tube diameter may be equated with the reduction in cross – sectional area for airflow through the nostrils during rhinitis. If so, breathing through obstructed nostrils could generate mechanical forces that activate mechanosensitive neurons and the sensation of nasal obstruction, or even promote epithelial cell damage and apoptosis which may worsen nasal inflammation. This full hypothesis remains to be tested.

## Peripheral Cutaneous Temperature Exposures

Cold water immersion of one upper limb leads to unilateral nasal obstruction in normal nonrhinitic subjects. Both the afferent and efferent arms of the reflex were limited to the chilled side [11]. Chilling one foot in water also increases nasal airflow resistance [12].

Immersion of both feet in warm water (42°C) increased the temperature of the nasal mucosa from ~30°C towards core body temperature [13]. Lidocaine prevented this nasal mucosal temperature rise. This implicated a neural mechanism. Topical mucosal application of phenoxybenzamine, an α-adrenergic receptor antagonist also increase the mucosal temperature. These data suggested that foot warming led to a decrease in systemic sympathetic activity that resulted in decreased norepinephrine release, default vasodilation, and so an increase in arterial blood flow through the superficial vascular plexus. Foot warming may have induced a transient, organ – specific parasympathetic vasodilator effect. Acetylcholine was not involved, although it is conceivable that small diameter VIP/NO sphenopalatine vasodilator neurons were activated.

## Crutch Reflex

Axillary pressure leads to unilateral and systemic changes in sympathetic reflexes (crutch reflex). Five minutes of unilateral axillary pressure decreased the ipsilateral minimum nasal cross sectional area (median change = 0.09 $cm^2$, $P < 0.01$) [14]. This demonstrated that axillary pressure caused either a loss of sympathetic vasoconstriction in the anterior nasal valve, or increased parasympathetic tone. In either event, ipsilateral nasal obstruction ("congestion"?) was induced. The contralateral nasal minimum cross-sectional area was significantly increased (median change = 0.35 $cm^2$, $P = 0.01$) (median change = 0.35 $cm^2$, $P = 0.01$) suggesting a contralateral increase in sympathetic vasoconstriction. Systemic sympathetic effects were suggested by increases in heart rate and diastolic blood pressure, but systolic blood pressure was unaltered. The lost of parasympathetic cholinergic inhibition of the sinoatrial node may also have contributed to the increased heart rate.

## Neurological Syndromes

Trigeminal autonomic cephalgias are a headache class that includes cluster headache, paroxysmal hemicrania, short lasting neuralgiform pain with conjunctival injection and tearing (SUNCT), and a subset of migraine headache patients who develop unilateral cranial autonomic symptoms such as nasal congestion, rhinorrhea, conjunctival vasodilation and injection, lacrimation, and eyelid edema [15]. One open label study suggested that that this subset may have had better pain relief with sumitriptan than migraineurs without autonomic symptoms [16]. However, this serotonin 5-HT1B/1D receptor antagonist did not alter the migraine – associated autonomic responses. The absence of double blinding, randomization, placebo control, and study in migraineurs without unilateral cranial autonomic symptoms severely limits the value of this conclusion.

Patients with neurological degenerative diseases develop multiple system atrophy (MSA) with autonomic dysfunction and disabling orthostatic hypotension [17]. The absence of normal autonomic reflexes has uncovered a series of previously unknown reflexes. Meals induce profound hypotension. Conversely, commonly used nasal decongestants have substantial pressor effects, and ingestion of 500 mL of water can increase blood pressure by a previously unrecognized sympathetic reflex. Residual sympathetic tone can induce sustained supine hypertension that resolves after ganglionic blockade. These phenomena were not previously recognized because of the buffering capacity of the baroreflex, but were unmasked in these autonomic failure patients. Although unstudied, they may have nasal congestion as occurs in Horner's syndrome, and alterations of other nasal reflexes.

## Nonallergic Rhinitis

Non-eosinophilic non-allergic rhinitis (NENAR) may be a disease of autonomic imbalance. The roles of systemic stimuli on nasal patency were assessed [18]. The nasal response to axillary pressure is much reduced in NENAR patients compared with normal controls, and the normal decrease in nasal resistance in response to standing is abrogated. Isometric exercise has little effect in normal subjects, but those with NENAR demonstrate an increase in nasal resistance. A similar effect is seen in response to the cold pressor test. Treatment with topical fluticasone propionate normalized the damaged nasal reflexes seen in NENAR,

while placebo had no effect. However, the systemic, non-nasal autonomic reflexes imbalances were not affected by nasal treatment.

### Dentistry

Blood oxygen saturation decreases during dental procedures. The use of external nasal dilator strips decreased patient discomfort, but this was not correlated with changes in oxygen saturation [19]. This suggests that the sensation of nasal patency may be separated from fear, pain and hypoventilatory effects. Tooth stimulation activates sympathetic reflexes with elevation in heart rate and blood pressure and nasal mucosal vasoconstriction [20]. More intense and prolonged tooth stimulation induced a second vasodilator reflex limited to the lips.

### Photosensitivity

Infrared light emitted from a dark source and applied to the face or trunk induces the sensation of nasal congestion [21]. Entering a brightly lit area from a dark area stimulates sneezing in some subjects [22]. Mechanisms of these reflexes are unknown.

### Alcoholic Beverages

Alcohol induces nasal congestion, the sensation of laryngeal airway closure, and occasionally bronchoconstriction. Red wine followed by white wine are the most common causes [23]. Women are affected twice as often as men. Some men report profound nasal obstruction with malt – laden beers. The agents that trigger these responses are not identified, but may include tannins from grape skins, sulfite preservative, and volatile products of fermentation.

## Nasobronchial Reflexes

The classic nasobronchial reflex is a component of the diving reflex. Immersion of the head into cold water leads to immediate suppression of respiration (apnea), laryngospasm, and bronchoconstriction. The nasocardiac component of the diving reflex includes bradycardia, decreased cardiac output, vasoconstriction in the skin, muscles, gastrointestinal and renal circulation systems [12,24,25]. The reflex keeps water out of the lungs, decreases oxygen consumption while maintaining cerebral perfusion. In aquatic mammals, this reflex permits prolonged underwater diving [26]. Nasal inhalation of dust, smoke, ammonia, phenylethylacetate (perfume), sulfur dioxide, and other water soluble chemicals can induce immediate bronchoconstriction with cessation of respiration in the expiratory phase due to relaxation of inspiratory muscles.

The afferent pathway was established by studying these reflexes in tic douloureux subjects who had undergone unilateral transection of the 2$^{nd}$ branch of the trigeminal nerve for symptomatic pain relief [27]. Intranasal crystalline silica dust to the innervated nostril produced nasal mucosal burning, nasolacrimal reflexes, and significantly increased pulmonary airways resistance. Provocation of the nostril on the surgically transected side failed to produce either local nasonasal or nasobronchial responses. Further study localized

the afferent pathway to the maxillary nerve (V2) since neither the ethmoid nor olfactory nerve could induce these effects [28].

Interactions between the nose and lung, including neurogenic and nasobronchial reflexes and neural plasticity have been investigated in allergic and nonallergic rhinitis and asthma [29,30]. Activation of nasal afferent receptors can lead to significant bronchial obstruction [31] and cardiodepressor reflexes. Mechanosensitive nasal receptors can stimulate nasobronchial reflexes. Rubbing the middle meatus or inferior turbinate caused significant decreases in FEV1 in healthy nonsmoking subjects [32]. Nasal histamine provocation induced induced bronchoconstriction in 8/12 allergic rhinitis and asthma subjects in an early study [33].

Nasal inhalation of particulate material such as crystalline silica particles [34] or granulated charcoal [35] leads to bronchoconstriction that can be prevented by cooling the vagal nerve or inhaled atropine. This implicates the Xth nerve in the efferent limb of the reflex.

Chronic unilateral nasal obstruction in rabbits leads to ipsilateral hypoinflation and thoracic deformities [36]. This suggests that the bronchial obstruction does not attenuate over time. It is not known if prolonged unilateral nasal obstruction during the pediatric growth periods can lead to similar chest wall abnormalities or scoliosis.

Nasal stimulation with cold dry air significantly decreased proximal tracheal mucosal blood flow (Qaw) in nine healthy humans [37]. Topical nasal local anesthetic treatment mucosa prevented this reduction suggesting that a nasobronchial vasoconstrictor reflex was induced by nasal cold dry air. In contrast, airflow was not affected. Nasal cold dry air, nasal lidocaine application, and inhalation of an anticholinergic bronchodilator had no effects on either tracheobronchial specific airways conductance (SGaw) or nasal airways resistance. Nasal provocation with warm air may reverse bronchoconstriction in asthmatic, but not normal, subjects [38]. Nasal cold dry air can stimulate bronchoconstriction in asthmatics but not normal subjects [39].

## Work of Breathing and Nasal Reflexes

Afferent nasal, tracheobronchial and inspiratory muscle mechanoreceptors participate in the coordination of inspiratory efforts [40]. Dynamic inspiratory load, a measure of the changing muscular effort during inhalation, is active in awake subjects, and is modified by changing from a seated to supine posture, mouth to nose breathing, and rest to mild exercise. Deep nasal breathing can induce bronchodilation in asthma attacks [41] Sniff and gasp – like maneuveurs may reverse central apnea. These stimuli may activate adrenergic sympathetic reflexes.

Patients who have had laryngectomies do not use their nose for inhalation, exhalation, or environmental sensing. However, the nasal mucosa remains reactive for both the sensory afferent and efferent limbs of nasal bronchial and other reflexes [42]. Air blown into one nostril of patients with laryngectomies produced ipsilateral hyperinflation [12,36]. Pretreatment of the nose with local anesthetic prevented the hyperinflation, demonstrating

the neural afferent origin. The hyperinflation was prevented by atropine, implicating cholinergic bronchial constriction followed by air trapping.

Nasal intermittent positive-pressure ventilation (nIPPV) has been used for the treatment of respiratory failure in patients with neuromuscular disease. Interruption of the positive nasal air pressure increased nasal airflow resistance [43]. Nasal anaesthesia or inhalation of a cholinergic antagonist blocked these effects, suggesting the presence of nasonasal and nasobronchoconstrictor reflexes. These reflex effects were suppressed by adding CO2 to the inspired gas. This suggested that CO2 activated chemosensitive nasal reflexes could override the obstructive reflexes.

## Bronchonasal Reflexes

Inhalation of ultrasonically nebulized distilled water increased nasal airway resistance in 19/23 allergic rhinitis and 2/12 nonrhinitic subjects [44]. There was no sneezing or rhinorrhea, the latter suggesting that parasympathetic efferent reflexes were not recruited. The vagal afferent innervation from the lung falls into 3 categories: C-fibres, rapidly adapting stretch receptors (RARs), and slowly adapting stretch receptors (SARs) [45]. A noted above, the plasticity of nociceptive receptors, ion channels, and neurotrasmitters that can be induced by neutrophins released during different types of inflammation may lead to severe perturbations of these nerves and generate neurons with novel afferent sensitivities and efferent axon response and central effects.

## Extrathoracic and Intrathoracic Obstruction

Sinusitis and posterior nasal and adenoid inflammation also stimulate airflow obstruction. Nasal provocations in relatively mild disease leads to glottic reflexes and extrathoracic obstruction [46]. Variable extrathoracic obstruction can be identified by the flattening of the inspiratory loop during a spirometric maneuver. This can be distinguished from laryngeal pathology with fixed airflow obstruction that shows flattening of both the inspiratory and expiratory loops. More severe sinusitis with nasopharngeal epithelial sloughing and eosinophilia is associated intra – and extra – thoracic obstruction with bronchial hyperresponsiveness [47]. These changes can not be appreciated using spirometers that fail to measure inspiratory flows and volumes.

The extrathoracic reflexes are of great clinical importance. Many subjects who are given diagnoses such as multiple chemical sensitivity, *globus hystericus*, and malingering develop glottic or supraglottic muscular contractions following exposures to “harmless” citrus, cleaning agents, glutaraldehyde, and other small, water soluble chemical agents. The fermentation products of fungi may also precipitate this syndrome in the absence of atopy and positive allergen skin tests or provocations to the fungal proteins. These observations generate the hypothesis that these chemicals activate neural ion channels and other receptors leading to local pharyngeal – laryngeal reflexes with hoarseness, a sensation of throat tightness, cough, and extrathoracic obstruction. Treatment of these subjects with abrupt dismissal from the clinic heightens their sense of paranoia and fears that the problem is all in their heads. These subjects respond to an understanding approach, related inspiratory – expiratory flow volume loops during exposures that demonstrate the dysfunctional reflex,

attempts to reduce pharyngeal afferent activation with honey, menthol lozenge, hot tea and other stimuli that can modify transient receptor potential (TRP) ion channel sensitivity, and avoidance of the offending agents. A search for underlying acid reflux and dysfunction of the upper or lower esophageal sphincters is often beneficial. Erythema and mild edema may be seen in on rhinolaryngoscopy, especially if there is severe cough, hoarse, reflux, inflammatory post-nasal drip, asthma or chronic eosinophilic rhinosinusitis.

## The Sexy Nose

The intertwining of sexual arousal, genitalia, and the nose has been long been intimately linked [48]. Foreplay and coitus lead to increased sympathetic reflexes with nasal constriction. This may last for some time before the normal nasal cycle or bilateral nasal congestion occur.

Sexual intercourse is a poorly recognized and underappreciated trigger factor for attacks of asthma and/or rhinitis and the morbidity caused to the ego and self-image of these patients. Some subjects can develop an overactive cholinergic reflex with nasal discharge that responds to anticholinergic drugs. Acute severe asthma may require emergency department visits [49]. These events can strain a relationship and lead to high anxiety. Late asthmatic responses have been reported, suggesting that the asthmatics may have been undertreated. None of the patients developed wheezing, dyspnea, a fall in peak expiratory flow rates, or rhinitis after climbing two flights of stairs, an exercise considered equivalent to energy expended during sexual intercourse. Thus, sexual excitement rather than exercise appeared to be the cause of postcoital asthma and rhinitis. Adequate pharmacotherapy along with counseling of the patients and their spouses restored normal sexual function and control of asthma and rhinitis. Postcoital asthma and rhinitis can easily be overlooked due to patient embarrassment and lack of physician awareness.

Sex and nonallergic rhinitis played an influential role in Sigmund Freud’s development of concepts of neurosis and psychoanalysis. Freud’s closest friend and confidant was an eccentric Berlin otolaryngologist, Dr. Wilhelm Fliess [50]. Fliess postulated that “reflex nasal neurosis” was based on an important physiological connection between the nose and the genitals, and described specific genital spots located on the nasal inferior turbinate [51]. The syndrome remains familiar today with headaches, vertigo, widely distributed neuralgia, and vague, functional disturbances of the circulatory, respiratory, digestive and genitourinary tracts including sexual dysfunction. Fleiss’s tools were his clinical observations that he reduced to descriptive classifications. These he used to support his theories of innate bisexuality. In contrast, Freud, the academic, analyzed these clinical observations of psychological phenomena through the prism of his theory of sexuality that ran in parallel to Fleiss’s innate bisexuality.

This unlikely pair developed a joint research project in 1893 to study the clinical problem of “neurasthenia” [52]. This study became more of a dialogue and was never carried out. One outcome was the psychological component of Freud’s psychoanalytic theory. It would be of interest to speculate on the influence of the recumbent couch that may have elicited position

- dependent nasal reflexes, or its heavily carpeted upholstery with its dominions of dust mites that may have aroused nasal responses in his delicate clientele.

Fleiss also played a clinical role in Freud's personal neurasthenia. He performed one of his favorite operations, cauterization of the turbinate bones, at least twice to help relieve the chronic, bilateral maxillary sinusitis that plagued Freud. Freud's personal prescription for treatment of neurasthenia at the time was cocaine. This drug played a major role in Freud's own erotic and neurotic thoughts, and nasal mucosal erosions.

Another outcome of this relationship was Fleiss's theory of vital periodicities. He believed that the symptoms of his reflex nasal neurosis followed regular 28-day cycles like female menstruation, and proposed a 23-day male menstrual cycle that he centered specifically on the erectile nasal turbinate. Freud kept a diary of his own cycles to provide data for Fleiss. This theory eventually evolved into the concept of biorhythms.

Although these theories have been largely discredited, we remain with the issue of "neurasthenia" in its various guises, and psychosomatic syndromes. The latter include sudden anosmia [53], recalcitrant nose picking [54], intractable psychogenic sneezing [55–57], and the neurocognitive need to explain nasal symptoms in the context of affective or psychological dysfunction [58].

Why should rhinitis have had such strong influences on Freud and Fleiss? Cases of coital reflex nasal obstruction, the anxiety they produced, and nasal symptoms that changed throughout the menstrual period and in pregnancy probably played important roles. The anxiety and frustration of allergic rhinitis, and presumably nonallergic rhinitis, decrease quality of life and promote sexual dysfunction [59]. The significance of a protuberant midline structure with paired erectile tissue and their nasogenital reflexes would have been most intriguing to Freud [60]. Male and female menstrual cycles played strong roles in this pair's thinking. Nasal alterations during the female menstrual cycle have been evaluated using peak inspiratory nasal flow, acoustic rhinometry, anterior rhinomanometry, mucociliary clearance time and a rhinitis questionnaire [61]. Anterior rhinomanometry and mucociliary time were significant reduced at the time of ovulation compared to the onset of menstruation ($p < 0.05$). These obstructive changes coincided with the high serum estrogen levels found at ovulation. Changes in mucosal hyperresponsiveness have also been examined [62]. The nasal mucosa became hyperreactive to histamine at the time of ovulation. Hyperresponsiveness was not different from the menstrual level during the luteal phase. Relationships such as these have not been identified in earlier studies [63,64], perhaps because of limitations in assay techniques. However, receptor binding studies did not identify nasal mucosal receptors for estradiol or progesterone. Instead, potential pheromones such as extracellular human major histocompatability antigen proteins, volatile hexanoic acid, and acidic analogs may offer subtle, but tantalizing odiferous cues for fecund nubile fertile women seeking to breed with vigorous, outbred men who have the least similarity to their own paternal MHC alleles [65]. Had he been aware, Freund would likely have poked his nose into these sublime passions of sexual attraction, coital and nasal arousal.

The relationship between Freud and Fleiss eventually festered. First was the fiasco of Dora Case. Dora Case was the pseudonym for Emma Eckstein (1865–1924), a Viennese feminist. Freud evaluated her stomach complaints and suspected a diagnosis of Fleiss's "nasal reflex neurosis." Freud referred her to Fliess for inferior turbinate cautery. However, Ms. Eckstein's surgical wound would not heal. After weeks of hemorrhagic discharge, "the brave Frau Doctor" Rosanes probed the nostril and withdrew "at least half a meter of gauze" that was followed by such profuse hemorrhage that Freud interpreted it as nasal menstruation (http://library.med.cornell.edu/Library/HTML/sigmund_freud/essays_op.html#pho). After a second surgical inspection and turbinectomy, the wound healed promptly. Ms. Eckstein was left with a permanent nasal deformity. Freud blamed himself rather than Fleiss, and often dreamed of the nightmarish experience. Eventually, he dissected the dream as *"Irma's Injection",* which became the centerpiece of his book The Interpretation of Dreams and so a major event in the history of psychoanalysis.

The ultimate end of their relationship was Fleiss's use biorhythms to predict Freud's death at the age of 56. His credibility was crushed, as Freud lived on to the age of 83.

Unfortunately, sometimes a cigar was just a cancer stick. Freud developed cancer of the hard palate. This had a deep psychological meaning to him, since his speaking self (as developer of "speaking therapy") became linked via the erosion of his palate to reveal his nasal labia majorum and minorum in the form of his twinned inferior and middle turbinates. Where once he could speak, he now experienced frequent "menstrual" hemorrhages from his ulcerating tumor. Ultimately, at Freud's request, his friend and physician Max Schur administered three doses of morphine over many hours prompting Freud's death on September 23, 1939.

## Conclusion

This strange nasal theme that threaded through Freud's life evokes the curiosity and complexity of our meshwork of nasal reflexes. The nose is a central player as both afferent initiator and efferent responder to stimuli affecting many parts of the body. The subtle innuendo of these competing stimuli balances our noses on the cusp between congestion and clarity. The nose yet has many secrets to reveal about the neurological and erotic lives of men and women. These may be revealed through Type C and Aδ nerve fibres, transient receptor potential ion channels, G protein – coupled excitatory and inhibitory autoreceptors, and neurotransmitters, but with the hope that future modulation of these molecular mechanisms may enhance the patency of our noses and the pleasures of our lives.

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