

ORIGINAL ARTICLE

## Nasal tactile sensitivity in allergic rhinitis

FRANCESCO ANTONIO SALZANO<sup>2</sup>, RENZO MORA<sup>1</sup>, SARA PENCO<sup>1</sup>,  
DANIELA TRAVERSO<sup>1</sup>, GIOVANNA GAGGERO<sup>1</sup>, GIOVANNI SALZANO<sup>3</sup> &  
LUCA GUASTINI<sup>1</sup>

<sup>1</sup>ENT Department, University of Genoa, <sup>2</sup>ENT Department, University of Palermo and <sup>3</sup>University of Naples, Federico II, Naples, Italy

### Abstract

**Conclusion:** These preliminary data show a decrease in nasal tactile sensitivity and point out interesting aspects of the nasal chronic inflammatory condition in allergic rhinitis. **Objectives:** The aim of this study was to evaluate the effects of allergic rhinitis on nasal tactile sensitivity during the intercritical period. **Methods:** A total of 70 patients aged between 18 and 67 years (average 42 years), with a positive history of allergy caused by seasonal outdoor allergens, were included (group A). Patient outcome was assessed by the nasal monofilament test: a set of 20 Semmes-Weinstein monofilaments was used to detect nasal sensitivity for both nasal cavities. The sensitivity threshold was recorded as the minimum monofilament size with which patients could detect at least two of three stimuli. **Results:** When compared to the control group (group B), subjects in group A required a significantly ( $p < 0.05$ ) higher stimulus to trigger a touch response in the monofilament test, for both the inferior ( $195.1 \pm 0.39$  mg vs  $67.7 \pm 0.19$  mg) and middle turbinate ( $108.7 \pm 0.23$  mg vs  $67.7 \pm 0.19$  mg).

**Keywords:** Monofilament test, inferior turbinate, middle turbinate

### Introduction

The symptoms of nasal allergy are caused partly by the direct effect of chemical mediators released from mast cells and basophilic cells as a result of an antigen–antibody reaction on nasal glands and vessels and partly by reflexive excitation of the efferent nervous pathway resulting from stimulation of sensory nerve endings by chemical mediators [1].

The collection of fibers beneath the nasal epithelium is composed of mainly sensory fibers but also some autonomic fibers. Most of the fibers in the region of glands and blood vessels are secretomotor fibers, but sensory fibers are known to also innervate these structures. Sensory fibers may contribute to a hyperresponsive or hyporesponsive state, and secretomotor fibers contribute to congestion and rhinorrhea [2].

Although interest in measuring tactile sensitivity using objective methods is growing, at the moment

no specific study has been done to test the tactile sensitivity in the noses of allergic patients. In the literature, there are some reports on the allergic process of the nose, but most of them are about nasal epithelial change, olfaction or taste: no data are present on change of nasal tactile sensitivity with allergy.

Because previous studies have used semiquantitative forms of analysis (visual analogic scale, immunomarkers, etc.) to look nasal tactile sensitivity in the nose, we chose to use the monofilament test [3]. In the nose, it has been used as a useful diagnostic tool to establish regions of sensitivity, investigate hyposensitivity after rhinoplasty, determine efficacy of local anesthesia, and evaluate nasal sensitivity in the elderly [3–6].

The aim of this study has been to evaluate the effects of allergic rhinitis on nasal tactile sensitivity during the intercritical period through the use of the monofilament test.

## Material and methods

### Study population

The regional ethics committee approved the study protocol. A total of 70 patients aged between 18 and 67 years (average 42 years) were included. Objective evaluation of the intranasal findings was performed by anterior rhinoscopy and nasal endoscopy (rigid and flexible). Turbinate edema, nasal secretions, and crusts were graded using a five-point scale (0, absent; 1, mild; 2, moderate; 3, severe; and 4, very severe). Patients were included if they were: more than 18 years old; without turbinate edema, nasal secretions, and crusts; with a positive history of allergy to seasonal outdoor allergens (tree, grass, and ragweed pollens); the allergen was confirmed by skin testing performed by the prick method, before inclusion. All the patients in the study group presented an allergy to a single seasonal allergen: 22 patients had an allergy to *Betula* allergen, 19 to *Olea europaea* allergen, 15 to *Platanus* allergen, and 14 had graminaceous pollinosis. As a control group, 70 healthy, nonallergic patients were included.

Exclusion criteria were: genetic and congenital conditions (cystic fibrosis, primary ciliary dyskinesia); nasal polyps; anatomic abnormalities (severe septal deviation among others); acquired mucociliary dysfunction; neoplasms; nasal radiotherapy; acute contemporary bacterial, viral, and/or allergic rhinosinusitis; acute allergic crisis; middle ear and upper respiratory tract infections; bronchopulmonary disease; nasal trauma; smoker; previous nasal and sinus surgery. Additional exclusion criteria included contemporary and/or recent (previous 3 months) use of oral and nasal steroid and antihistaminics, local or systemic nasal desensitization, coagulation disorders, uncontrolled hypertension, diabetes, and anosmia.

### Study design

The patients with a proven seasonal allergy formed group A, while group B was formed by the healthy subjects (controls). After signing an informed consent, all subjects underwent medical history and ENT examination by an ENT specialist with nasal endoscopy and monofilament test.

### Monofilament test

A set of 20 Semmes-Weinstein monofilaments (Sammons Preston, ABOcare srl, Grugliasco, Turin, Italy) was used to detect nasal sensitivity for both nasal cavities.

The instrument originally described by von Frey has undergone several changes in becoming the instrument available today: the horse hairs he used were designed to measure only light thresholds of touch recognition. Later, Semmes and Weinstein needed a broader range of forces for their studies than those that were available with horse hairs. They designed and developed nylon monofilaments of increasing diameters set at right angles in acrylic resin rods. They did not intend to provide specific measurable thresholds of force or stress but a relative range of progressive pressures. They described a relationship, as did von Frey, in which the ordinal rank of the filaments arranged according to their diameters resulted in progressive increases in pressure. To deal with the data statistically, they expressed the values as  $\log(10 \times \text{force in mg})$  and indexed the filaments by numbers derived from this log scale [7] (Table I). The instrument consists of 20 nylon monofilaments, each precisely calibrated and of equal length (Figures 1 and 2).

During the test, nostrils were held open, the vibrissae were held back with a nasal speculum, and

Table I. Monofilament size: Von Frey (VFN) number and the amount of force exerted by the monofilament.

Fiber label	Monofilament sizes	
	VFN	Force (mg)
A	1.65	4.47
B	2.36	22.9
C	2.44	27.5
D	2.83	67.6
E	3.22	166.0
F	3.61	407.4
G	3.84	691.8
H	4.08	1202.3
I	4.17	1479.1
J	4.31	2052.0
K	4.56	3632
L	4.74	5500
M	4.93	8650
N	5.07	11 700
O	5.18	15 000
P	5.46	29 000
Q	5.88	75 000
R	6.10	127 000
S	6.45	281 500
T	6.65	447 000



Figure 1. Monofilament assessment. Monofilaments used in this study.

patients were asked to close their eyes [3,5,6]. The anterior aspect of both the inferior and middle turbinates (right and left side) were then probed with a series of 38 mm long monofilaments of increasing

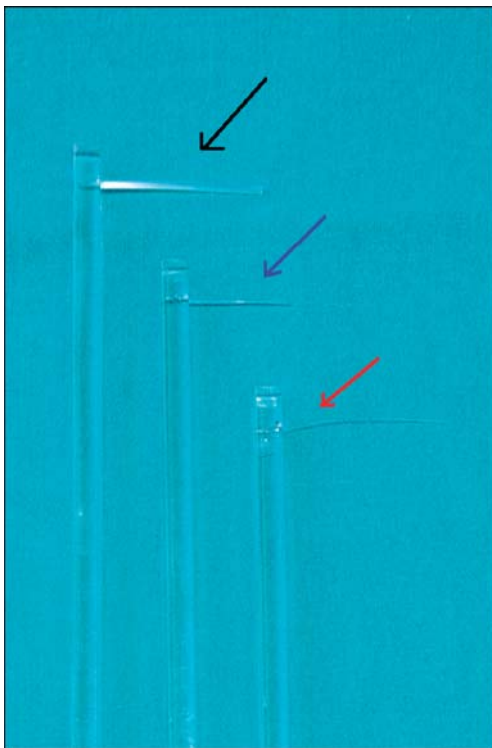


Figure 2. Particulars of the diameter of the filaments: arrows show the filaments able to trigger a touch response in the normal subject (red), at the level of the middle turbinates (blue) and inferior turbinates (black).

diameters, ranging from 1.65 mm (A) to 6.65 mm (T), and sized and numbered according to increasing force.

The microfilaments were labeled with logarithmic values ( $10 \times$  force in milligrams): the lowest force exerted by the series of microfilaments was 4.47 mg, and the highest was 447 g. Since the instrument markings were logarithmic values, they were first converted to force values for statistical testing [3,5,6] (Table I; Figure 1).

The examiner kept the filament perpendicular to the test site. The filament was bowed within about 1.5 s; the bow was maintained for approximately 1.5 s; and the filament was removed after an additional 1.5 s. The sensitivity threshold was recorded as the minimum monofilament size that patients could detect at least two of three stimuli from. The minimum filament size at which discomfort was caused was also noted. Discomfort was defined as discomfort, sneezing, eye tearing, or pain. For each stimulus, the amount of force in milligrams exerted by the monofilament, as determined by its size, was calculated. The 2.83 filament (67.6 mg) is considered to represent normal sensitivity in most areas of the body and was therefore presented first [3,5,6] (Table I; Figure 1)

#### Statistical analysis

All the data were evaluated by the paired or unpaired *t* test, and  $\chi^2$  analysis where appropriate; *p* values of  $< 0.05$  were regarded as significant. The results were reviewed and approved by the Institutional Review Board of the University of Genoa, Italy. Results for each group are expressed as means  $\pm$  standard deviation (SD).

#### Results

In the two groups, the nasal endoscopy revealed the absence of turbinate edema, nasal secretions, and crusts: the five-point scale showed a value of 0.

Considering the mean value of the two sides (right and left inferior and middle turbinates), when compared to the control group (group B), group A required a significantly ( $p < 0.05$ ) higher stimulus to trigger a touch response in the monofilament test, for both the inferior ( $195.1 \pm 0.39$  mg vs  $67.7 \pm 0.19$  mg) and middle ( $108.7 \pm 0.23$  mg vs  $67.7 \pm 0.19$  mg) turbinates (Table II; Figure 2).

#### Discussion

Different fiber types are involved in trigeminally mediated sensations. C fibers mediate dull and

Table II. Monofilament testing mean values ( $\pm$  SD) for both nasal cavities in each group.

Group	Parameter	Monofilament testing (mg)	
		Inferior turbinate	Middle turbinate
A	F	195.1 $\pm$ 0.39	108.7 $\pm$ 0.23
B	F	67.7 $\pm$ 0.19	67.7 $\pm$ 0.19
	<i>p</i> value*	< 0.05	< 0.05

F, minimum amount of force required to cause irritation.

\**p* value between the two groups.

burning painful sensations, while sharp and stinging sensations are known to appear in relation to excitation of A- $\delta$  fibers. These sensations follow different time courses and may have a different impact on olfactory sensations [8]. It has been shown that the responsiveness of A- $\delta$  fibers decreases with age while C-fiber function seems to be largely unaffected [9].

Among other nasal problems, allergic subjects are reported to have an abnormality of nasal secretion. Accordingly, it is unclear whether these different conditions could lead to altered perception of trigeminal stimulants simply because of differences in access of the stimulant to the trigeminal nerve endings [9].

Because allergic rhinitis has been shown to be associated with frequent respiratory tract infections, there is evidence from biopsy specimens of human nasal mucosa that damage, and perhaps irreversible damage, can occur as a result of these infections and that the degree of damage is correlated with the degree of nasal dysfunction [10]. Distortions in nasal tactile sensitivity function, observed in the study group (group A), could be a consequence of epithelial damage.

This suggests that the link between allergic rhinitis and nasal tactile sensitivity function may be caused in part by the pathophysiologic characteristics of allergic rhinitis, and not only by inflammatory diseases, such as nasal polyposis. This may also explain why, for a sizable number of patients in our earlier study, topical nasal steroid treatment for allergic rhinitis associated with nasal-sinus disease failed [11].

In allergic rhinitis there is an influx of inflammatory cells into the mucosa layer. These cells produce various cytokines, such as tumor necrosis factor (TNF)- $\alpha$ , interleukin (IL)-1 $\beta$ , and interferon (IFN)- $\gamma$  [12–14]. It has been reported that TNF- $\alpha$  induces expression of adhesion molecules such as intercellular cell adhesion molecule 1 (ICAM-1), vascular cell adhesion molecule 1 (VCAM-1), and endothelial-leukocyte adhesion molecule 1 (ELAM-1) on vascular endothelial cells, which may result in an inflammatory vascular lesion [14].

It can further be expected that ongoing inflammatory processes will increase a general occurrence of cell apoptosis in the affected airway tissue. TNF- $\alpha$  can induce the expression of inducible nitric oxide synthase (iNOS), which results in the generation of apoptosis in cultured human nasal microvascular endothelial cells [15].

Although the literature reports opposite evidence, different studies highlight that apoptosis is implemented by intracellular activity of a family of cysteine proteases called caspases. Activation of cascade caspases results in the dramatic morphological changes of the epithelium typical of apoptosis [16].

These morphological changes of the nasal epithelium may contribute to the decline in cutaneous tactile sensitivity. Our data show a decrease of tactile sensitivity in allergic patients, during the nonacute phase, this decrease in nasal tactile sensitivity may highlight a chronic nasal inflammatory condition, related to a chronic apoptotic process.

Past studies showed that the thickness of the nasal basement membrane zone was statistically significantly greater in allergic subjects than in nonallergic ones and highlighted that the activation of a collagen-producing system was involved in the tissue remodeling [17]. In particular, the thickened basement membrane zone of the nasal mucosa of the inferior turbinate was shown by different investigations [17,18]. These investigations explained that the collagen deposition on the basement membrane zone and allergic inflammation may determine a process of fibrosis.

Compared with the inferior turbinates, the reduced higher stimulus to trigger a touch response in the monofilament test on the middle turbinates may be related to their anatomic disposition and vascularization: the surface of the inferior turbinates is larger and more vascularized than that of the middle turbinates, thus the consequences of an inflammation process caused by allergens are greater. For this reason an examination of the nasal tactile sensitivity function can be useful.

The design of the filaments of constant length but increasing diameters to bend when a specific value is reached provides unique control. This design helps to control the variables that occur with any hand-held instrument. Any hand-held instrument, used as a stimulus, carries with it the vibration of the examiner's hand and the variable application amplitude of the examiner [7]. These variables, independent of the stimulus, exceed the normal touch recognition resolution of the cutaneous end organs and bombard them with stimuli at multiple frequencies. The bend of the filaments provides some control of the application amplitude and vibration. Even

though the diameters must change to produce heavier forces, the filaments provide a relatively more controlled testing stimulus than other hand-held instruments, which do not attempt to control these variables [7]. The constant length, related to each diameter, allows the filaments to produce application forces that are repeatable within a predictable range. For these reasons, among the objective tests, monofilament testing has become the standard means for repeatable testing and measurement of the threshold of mucosal sensory perception [5,6].

Although further studies are necessary, these preliminary data show that a decrease of nasal tactile sensitivity points out interesting aspects of the nasal chronic inflammatory condition in allergic rhinitis.

**Declaration of interest:** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

## References

- [1] Seiberling KA, Conley DB. Aging and olfactory and taste function. *Otolaryngol Clin N Am* 2004;37:1209–28.
- [2] McKeegan DE, Demmers TG, Wathes CM, Jones RB, Gentle MJ. Response characteristics of nasal trigeminal nociceptors in *Gallus domesticus*. *Neuroreport* 2002;13:1033–5.
- [3] O'Hanlon S, Facer P, Simpson KD, Sandhu G, Saleh HA, Anand P. Neuronal markers in allergic rhinitis: expression and correlation with sensory testing. *Laryngoscope* 2007;117:1519–27.
- [4] Bafaqeeh SA, al-Qattan MM. Alterations in nasal sensibility following open rhinoplasty. *Br J Plast Surg* 1998;51:508–10.
- [5] Salzano FA, Mora R, Dellepiane M, Zannis I, Salzano G, Moran E, et al. Radiofrequency, high frequency and electrocautery versus partial inferior turbinotomy: micro and macroscopic effects on nasal mucosa. *Arch Otolaryngol Head Neck Surg* 2009;135:752–8.
- [6] Salzano FA, Guastini L, Mora R, Dellepiane M, Salzano G, Santomauro V, et al. Nasal tactile sensitivity in elderly. *Acta Otolaryngol* 2010;130:1389–93.
- [7] Bell-Krotoski J, Tomancik E. The repeatability of testing with Semmes-Weinstein monofilaments. *J Hand Surg Am* 1987;12:155–61.
- [8] Frasnelli J, Hummel T. Age-related decline of intranasal trigeminal sensitivity: is it a peripheral event? *Brain Res* 2003;987:201–6.
- [9] Hummel T, Livermore A. Intranasal chemosensory function of the trigeminal nerve and aspects of its relation to olfaction. *Int Arch Occup Environ Health* 2002;75:305–13.
- [10] Apter AJ, Gent JF, Frank ME. Fluctuating olfactory sensitivity and distorted odor perception in allergic rhinitis. *Arch Otolaryngol Head Neck Surg* 1999;125:1005–10.
- [11] Klemens C, Rasp G, Jund F, Hilgert E, Devens C, Pfrogner E, et al. Mediators and cytokines in allergic and viral-triggered rhinitis. *Allergy Asthma Proc* 2007;28:434–41.
- [12] Salzano FA, d'Angelo L, Motta S, del Prete A, Gentile M, Motta G Jr. Allergic rhinoconjunctivitis: diagnostic and clinical assessment. *Rhinology* 1992;30:265–75.
- [13] Salzano FA. Specific nasal provocation test with powder allergen. *Allergy* 1997;52:32–5.
- [14] Nonoyama T, Harada T, Shinogi J, Yoshimura E, Sakakura Y. Immunohistochemical localization of cytokines and cell adhesion molecules in maxillary sinus mucosa in chronic sinusitis. *Auris Nasus Larynx* 2000;27:51–8.
- [15] Arai S, Harada N, Kubo N, Shen J, Nakamura A, Ikeda H, et al. Induction of inducible nitric oxide synthase and apoptosis by LPS and TNF-alpha in nasal microvascular endothelial cells. *Acta Otolaryngol* 2008;128:78–85.
- [16] Grzegorzczak J, Kowalski ML, Pilat A, Iwaszkiewicz J. Increased apoptosis of peripheral blood mononuclear cells in patients with perennial allergic asthma/rhinitis: relation to serum markers of apoptosis. *Mediators Inflamm* 2002;11:225–33.
- [17] Sanai A, Nagata H, Konno A. Extensive interstitial collagen deposition on the basement membrane zone in allergic nasal mucosa. *Acta Otolaryngol* 1999;119:473–8.
- [18] Agha-Mir-Salim P, Rauhut O, Merker HJ. Electron and fluorescence microscopic investigations on composition and structure of the epithelial basement membrane of the human inferior nasal concha. *Eur Arch Otorhinolaryngol* 1993;250:401–7.