Olfactory stimulation may modulate the sensation of nasal patency*

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Abstract

Background: The sensation of nasal patency can be induced by inhaling menthol, which predominantly produces trigeminal stimulation. It remains unclear whether olfactory stimulation can also induce or modulate the sensation of nasal patency.

Methodology: A total of 118 participants (normosmia: n=67, olfactory dysfunction: n=51) were exposed to four odors in a randomized order: 1) phenylethanol (PEA), 2) menthol, 3) a mixture of PEA and menthol, 4) nearly odorless propylene glycol. The odors were presented by nasal clips. After the nasal clip had been removed, the participants rated relative nasal patency (RNP) from - 50 to +50, and their peak nasal inspiratory flow (PNIF) was measured. Repeated measures analysis of variance was used to examine the difference of RNP and PNIF among the four conditions and the influence of olfactory function.

Results: The RNPs, other than PNIFs, differed between the four conditions. Menthol induced the highest RNP, followed by the mixed solution, PEA and the odorless condition. Normosmic participants, but not those with olfactory dysfunction, responded to PEA significantly higher than odorless condition with regard to RNP. The correlation analysis showed that the better the subjective or measured olfactory performance, the greater the PEA-induced sensation of nasal patency.

Conclusions: A specific olfactory stimulant that selectively induces olfactory perception can also evoke and modulate the sensation of nasal patency. Hence, patients might benefit from exposing themselves to odors in order to relieve the annoying nasal obstruction.

Key words: nasal patency, olfactory stimulation, trigeminal stimulation

Introduction

Nasal obstruction or nasal blockage is one of the most common presenting symptoms in otolaryngology practice and profoundly influences quality of life and general health [1, 2]. Great efforts are used to manage this complaint through medical or surgical treatment, which aims to physiologically improve mucosal swelling and hypersecretion, anatomically reduce the volume of nasal turbinates, correct the deviated nasal septum, and/or nasal valve collapse [3]. In some circumstances, patients still complain of a blocked nose despite a properly patent nasal cavity, even after surgery. Objective measurement, such as endoscopic examination, rhinomanometry (measures intranasal airflow and resistance), or acoustic rhinometry (measures intranasal cross-sectional areas) often demonstrates an adequately wide intranasal space and sufficient airflow, which is inconsistent with subjective experience and feedback [4-6]. This discordance suggests the important role of other factors that contribute to the perception of nasal patency, the receptive structures that mediate the sensation of intranasal airflow [7].

The intranasal trigeminal system can detect mechanical, chemical and thermal stimuli, and primarily conveys the sensation of burning, stinging and cold. Transient receptor potential melastatin subfamily member 8 (TRPM-8) is considered a thermoreceptor that conveys a cooling sensation during breathing, which, in turn, contributes to the perception of nasal patency [8, 9]. Some

substances (e.g. menthol or eucalyptol) can activate the TRPM-8 receptor, sensitize trigeminal nerve endings, and cause cooling and the sensation of nasal widening [10, 11]. Inhaling menthol can lead to an illusion of a decongested nasal airway and an 'open' nose without a change in anatomical structure, resistance to airflow or mucosal temperature [10, 12].

Almost all odorous substances stimulate both the trigeminal and olfactory systems [13], which interact closely in central [14] and peripheral [15] neural processing. Menthol predominantly produces a trigeminal stimulation, but still the olfactory component gives rise to its minty scent. The 'open' nose effect of menthol has always been attributed to trigeminal activation; however, the influence of olfactory stimuli on subjective perception of nasal patency has not been investigated yet. It is conceivable that an improvement in the sensation of intranasal airflow when inhaling menthol is due not only to the activation of the trigeminal, but also to the activation of the olfactory system.

This study aimed to clarify the role of olfactory stimuli in the perception of nasal patency. We regarded 2-phenylethanol (PEA) as a specific olfactory stimulus with negligible trigeminal component because it is one of the few exceptions for the dual-modality characteristic of all odorants [13]. Individuals with various degrees of olfactory function were involved to examine the effect of olfactory stimuli. We hypothesized that people with normal smell function can still improve their perception of nasal patency when exposed with selective olfactory stimuli.

Methods

Subjects

Healthy volunteers and patients with olfactory impairment were recruited. They were over 18 years of age and were non-smokers. All participants received detailed otorhinolaryngological examinations, including medical history, nasal endoscopy, peak nasal inspiratory flow (PNIF) measurements, and complete psychophysical evaluation related to olfaction. Subjective olfactory function and sense of airflow permeability in nasal breathing were also rated on a visual analogue scale (VAS 0 ~ 100, where 0 represents an inability to perceive odor or airflow at all, and 100 represents maximum sensitivity to odor or airflow) before the experiment. Since cognitive function and emotional states can affect olfactory function, participants also completed the Montreal Cognitive Assessment (MoCA) [16] to evaluate cognitive performance and the 'Allgemeine Depressions-Skala' (ADS_L) for the assessment of depressive symptoms [17]. Exclusion criteria were active rhinologic diseases (e.g., allergic rhinitis or rhinosinusitis), significant health impairments that can be accompanied by olfactory dysfunction (e.g., severe type II diabetes mellitus, Parkinson's disease, renal insufficiency), or pregnancy. Participants provided their written informed consent. All procedures were carried out in accordance with the Declaration of Helsinki and were approved by the local ethics committee of the Technical University of Dresden (application number EK557122019).

Experiment design and odor presentation

A total of four odors were presented to participants in randomized order and a blinded manner. The four conditions were: 1) phenylethanol (PEA, order #77861; all odorants came from Sigma-Aldrich, Steinheim, Germany) 20%, diluted with propylene glycol (PG, order #W294004), 2) menthol (order #2416) 50%, dissolved in PG, 3) a 1:1 mixture of (1) and (2), and 4) nearly odorless PG. These odors were presented by a nose clip (Aspuraclip, Berlin, Germany) filled with 0.3 ml of each solution (Figure 1). The nose clips were made of an elastic silicone tube in a horseshoe-like shape (limbs: 18 mm in length; tube: 3 mm in diameter). During the experiment, participants wore each nose clip for 2 minutes, when the clip limbs were inserted into the right and left nostrils and fixed on the nasal columella. Participants were instructed to breathe smoothly through the nose with their mouths closed. Immediately after each clip was removed, participants were asked to rate relative nasal patency (RNP) on a VAS from -50 to +50, where 0 represents unchanged, -50 represents maximum worsening, and +50 represents a maximum improvement in nasal breathing. We also measured PNIF after each trial of odor presentation. The participants took a 10-minute break between each trial. They did not feel any discomfort during the procedures.

Psychophysical evaluation of olfactory function

The olfactory function was examined using Sniffin' Sticks (Burghart Messtechnik GmbH, Holm, Germany), a set of felt-tip pens packed with scents. The examination comprised three subtests, i.e., odor detection threshold (T), odor discrimination (D), and odor identification (I) [18, 19]. The olfactory threshold for phenylethanol was assessed using an adaptive staircase procedure and a three-alternative forced-choice technique. The odor discrimination task employed 16 triplets of pens, two of which contained the same odor with the third containing a different one. The pens were randomly presented to the participants, who were asked to identify the different ones. Odor identification involved 16 common odors, which should be identified from a list of descriptors (four for each odor). The scores of each subtest were summed up to a composite TDI score, which reflected the general olfactory function of the participants. Although the participants were recruited from two distinct sources (patients from clinic and volunteers from outside), they were grouped according to the measured olfactory function no matter which source they came from. Based on previously normalized data, participants were grouped into a normosmia group (TDI > 30.5) and an olfactory dysfunction group (hyposmia/anosmia, TDI ≤

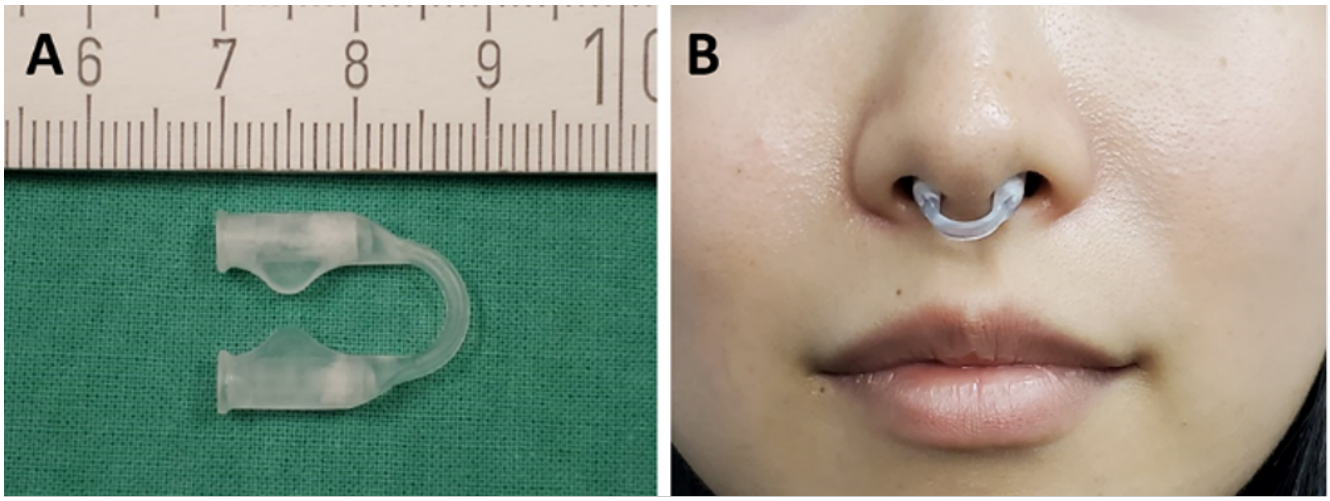

Figure 1. Photograph of the nose clip that contained the odor. The figure shows (A) the size of the clip, and (B) how the clip fixed on the columella of the nose.

30.5) [2].

Peak nasal inspiratory flow measurements

PNIF was measured using an In-Check portable nasal inspiratory flow meter (Clement Clarke International, Harlow, Essex, UK). Participants were in an upright position during the procedure. At the end of full expiration, the participants attached an anesthesia mask to their faces while making deep inspiration with the mouth closed. They were encouraged to inhale as hard and rapid as they could for three times. The measurement with the highest value was recorded [20, 21].

Statistical analysis

Statistical analysis was performed with IBM SPSS Statistics, version 28 (IBM Corp., Armonk, NY, USA). We used independent two-sample t (for continuous variables) and chi-squared (for categorical variables) tests to compare demographic and behavioral data between groups. Repeated measures analysis of variance (rm-ANOVA) was then used to check the effect of the odor-presenting conditions and olfactory function groups ('condition' as a within-subject variable; 'group' as a factor between subjects, and 'age' and 'gender' as covariates). Post hoc pairwise analysis was conducted using the Bonferroni method. Finally, we asked whether the olfaction-induced sensation of nasal patency is related to olfactory performance. Analysis was carried out to examine the correlation between the difference in RNP after exposure to PEA and PG and the rated or measured olfactory function in all subjects. In addition, the correlation of rated and measured nasal patency as well as olfactory function at the baseline were also analyzed. The correlation coefficient was estimated using Pearson's r. The level of significance was set at $p < 0.05$.

Results

Demographic data and baseline measurements

A total of 118 participants (81 women and 37 men, age range: 18-81 years) were recruited in our study. The results of demographic data and baseline measurements are shown in Table 1. Based on their TDI scores, participants were grouped into normosmic participants (n = 67) and participants with olfactory dysfunction (n = 51). Normosmics were significantly younger, had better MoCA scores, a less depressive state reflected by ADS_L, and a tendency for higher self-rated intranasal airflow ($t = 1.9$, $p = 0.07$). The sense of intranasal airflow was positively correlated with rated ($r = 0.34$, $p < 0.001$) and measured (TDI, $r = 0.20$, $p = 0.03$) olfactory function, but not the measured nasal patency (PNIF, $r = 0.13$, $p = 0.23$) (Table 2).

Difference in nasal patency in response to various stimuli

When using rm-ANOVA for the analysis of rated RNP and measured PNIF in response to the different stimuli under the four conditions, the results indicated a significant main effect of the condition on RNP ($F [3, 342] = 5.4$, $p = 0.001$). This showed a higher rating of RNP in response to menthol ($M = 13.6 \pm 1.7$, $p < 0.001$) and mixed solution ($M = 9.4 \pm 1.4$, $p < 0.001$) compared to PG, and menthol compared to mixed solution ($M = 4.2 \pm 1.5$, $p = 0.04$) and PEA ($M = 9.9 \pm 1.6$, $p < 0.001$). However, the pairwise comparison in PEA and PG only showed a trend of difference ($M = 3.6 \pm 1.4$, $p = 0.06$) (Figure 2A). For the objective measurement of nasal patency the ΔPNIF was calculated, which indicated the PNIF result in each condition minus the baseline PNIF value. Note that only 88 participants (40 normal smellers, 48 poor smellers) had received the PNIF examination throughout the study. The main effect of the condition on ΔPNIF was not significant ($F [3, 252] = 0.2$, $p = 0.88$) (Figure 2B). In summary, trigeminal stimuli (menthol) could induce a greater improvement in

Table 1. Demographic data and test results.

Mean ± SD	Total (n=118)	Normosmia (n=67)	Olfactory dysfunction (n=51)	t	χ^2	p
Gender, n					0.6	0.43
women	81	48	33			
men	37	19	18			
Age (years)	40.5 ± 16.6	34.9 ± 14.3	47.9 ± 16.7	-4.5		< 0.001
Rated olfactory function	64.1 ± 31.6	81.9 ±16.0	40.8 ± 31.9	8.4		< 0.001
Rated intranasal airflow permeability	80.0 ± 15.9	81.9 ± 14.5	76.5 ± 17.3	1.9		0.07
Threshold	13.5 ± 5.8	7.6 ± 2.2	3.4 ± 2.0	10.7		< 0.001
Discrimination	11.9 ± 3.0	13.6 ±1.4	9.6 ±2.9	9.1		< 0.001
Identification	12.0 ± 3.2	14.0 ± 1.2	9.4 ± 3.2	9.8		< 0.001
Composite TDI	30.0 ± 7.9	35.3 ±2.5	22.3 ± 6.5	13.4		< 0.001
PNIF*	78.0 ± 37.9	83.4 ± 37.8	73.5 ± 37.9	1.2		0.23
MOCA	28.1 ± 2.2	28.7 ± 1.8	27.2 ± 2.3	4		< 0.001
ADS_L†	12.6 ± 8.5	10.8 ± 7.8	14.8 ± 8.9	-2.5		0.01

* 88 subjects (40: normosmia, 48: olfactory dysfunction) had received the PNIF examination. † 113 subjects (62: normosmia, 51: olfactory dysfunction) had completed the ADS_L questionnaire. SD= standard deviation; TDI= composite threshold + discrimination + identification scores; PNIF= peak nasal inspiratory flow; MOCA= Montreal Cognitive Assessment; ADS_L= Allgemeine Depressionsskala (depression scale).

Table 2. Correlation between baseline nasal patency and olfactory function.

	Nasal patency				Olfactory function			
	rated [a]		measured [b]		rated		measured [c]	
	r	p	r	p	r	p	r	p
Rated nasal patency	1	-	0.13	0.23	0.34	<0.001*	0.2	0.03*
Rated olfaction	0.34	<0.001*	0.13	0.23	1	-	0.82	<0.001*

[a] Rated intranasal airflow permeability at baseline; [b] PNIF of 88 subjects; [c] composite TDI scores. *A p-value < 0.05 indicates significance.

subjective nasal patency, which was not observed in objective measurement by PNIF.

Group differences in nasal patency in response to varies stimuli

To clarify the effect of olfactory stimuli on the sensation of nasal patency, participants were grouped according to their measured olfactory function and the analysis was repeated. The ANOVA results showed that although there was no significant main effect of the group on RNP ($F [1,114] = 0.6$, $p = 0.5$), the interaction of the condition x group was significant ($F [3, 342] = 6.0$, $p < 0.001$). The post hoc test showed that the RNP in response to menthol compared to PEA and PG was significant in both normosmia (to PEA: $M = 12.2 \pm 2.2$, $p < 0.001$; to PG: $M = 19.7 \pm 2.3$, $p < 0.001$) and olfactory dysfunction groups (to PEA: $M = 7.7 \pm 2.6$, $p = 0.02$; to PG: $M = 7.4 \pm 2.6$, $p = 0.03$). Interestingly, when comparing the PEA and PG conditions, the normosmia group rated nasal patency higher in the PEA condition ($M = 7.5 \pm 1.9$, $p < 0.001$), while the olfactory dysfunction group did not rate them differently ($M = 0.2 \pm 2.2$, $p = 1.00$). Similarly, the response to mixed solution compared to PEA or PG was significant in normosmia (to PEA: $M = 8.0 \pm 2.2$, $p = 0.002$; to PG: $M = 15.5 \pm 1.9$, $p < 0.001$) but not in olfactory dysfunction groups (to PEA: $M = 3.4 \pm 2.6$, $p = 1.00$; to PG: $M = 3.2 \pm 2.3$, $p = 0.97$). Lastly, the response to the mixed solution compared to that to the menthol was not different in both the normosmia group ($M = 4.2 \pm 2.1$, $p = 0.28$) and the olfactory dysfunction group ($M = 4.3 \pm 2.4$, $p = 0.48$) (Figure 3A). Still, the main effect of the group ($F [1, 84] = 0.8$, $p = 0.36$) and the interaction of the condition x group ($F [3, 252] = 1.2$, $p = 0.32$) on ΔPNIF were not significant (Figure 3B). In this section, we discovered that normosmic participants, other than participants with olfactory dysfunction, respond to olfactory stimuli (PEA) in terms of subjective nasal patency.

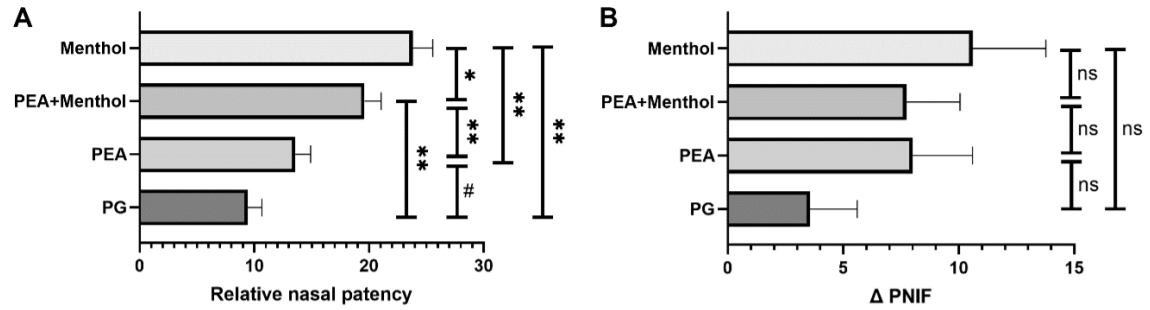

Figure 2. Differences in rated (left) and measured (right) nasal patency for all participants in four experimental conditions. Means and standard errors of means (error bars) of (A) rated relative nasal patency and (B) change of peak nasal inspiratory flow (PNIF). ** $p < 0.005$; * $p < 0.05$; # $p = 0.06$; ns: not significant. PEA = phenylethanol, PG = propylene glycol (odorless).

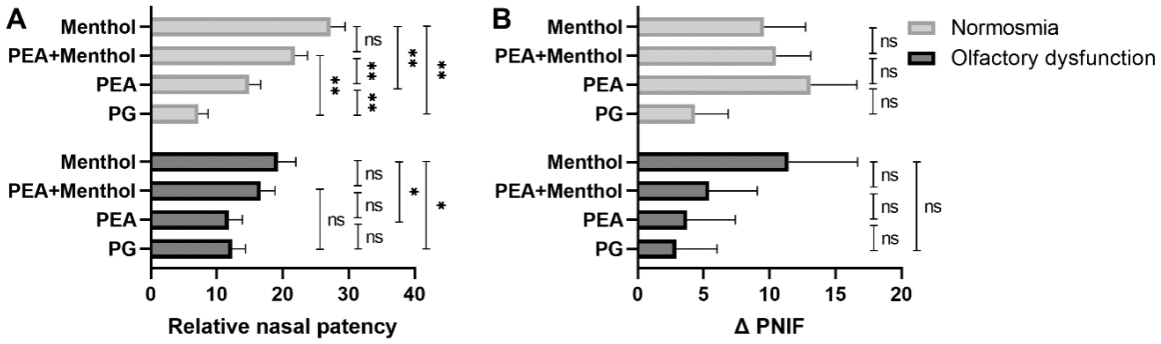

Figure 3. Different responses to PEA and menthol between normosmia and olfactory dysfunction groups. (A) Participants with olfactory dysfunction rated relative nasal patency at the same level between PEA and PG. (B) There was no significant difference in changes in PNIF in both groups. ** $p < 0.005$; * $p < 0.05$; ns: not significant.

The relationship between sensation of nasal patency and olfactory performance

In the last analysis, we found that even in the trial without odor (PG condition), participants still responded positively in terms of subjective nasal patency. To control this placebo effect and investigate the influence contributed by selective olfactory stimulation, we treated the difference in RNP between PEA and PG (RNP_{PEA-PG}) as an independent variable and examined its correlation with other variables related to olfactory function. We found that RNP_{PEA-PG} was positively correlated with self-rated ($r = 0.27$, $p < 0.01$) and measured olfactory function (TDI, $r = 0.24$, $p < 0.01$, and for subtests, refer to Figure 4). In contrast, the baseline rating for the sense of airflow permeability in nasal breathing was not correlated with RNP_{PEA-PG} ($r = 0.01$, $p = 0.91$). This finding corroborated the idea that the better the olfactory function, the greater the odor-induced sensation of nasal patency. However, these significant correlations were not observed in either group separately (supplementary Table S1).

Discussion

There is evidence showing that menthol can trigger the thermoreceptor in trigeminal endings that are also activated by cold stimuli [22, 23]. This TRPM-8 thermoreceptor is expressed in up to 60% of the trigeminal afferents distributed in the nasal mucosa [9], and regulates vascular tone by vasodilatation in response to a decrease in mucosal temperature [24, 25]. When inspired air flows largely or rapidly through the nasal cavity, fluid may vaporize and the temperature of the mucosa lining decreases, leading to TRPM-8 neuronal depolarization and subsequent signaling to the respiratory center in brainstem, i.e., the first relay in the trigeminal nuclei [15]. The sensory information is then transmitted to the primary and secondary somatosensory cortex to produce a cooling sensation, which is interpreted as a more open or patent intranasal space [26].

Besides trigeminal stimuli, our current study demonstrated that specific olfactory stimuli with low trigeminal potency (i.e., PEA) could also induce the sensation of nasal patency in normosmic subjects, but to a lesser extent. It is not clear where and how exactly the olfactory information induces the activation of trigeminal system. Although the olfactory and trigeminal systems differ in their respective neural transmission architecture, they share some common structures at both the peripheral and central levels where olfactory signals may interact with trigeminal system. The olfactory neuroepithelium and the olfactory bulb are two possible peripheral sites, as collaterals of trigeminal in-

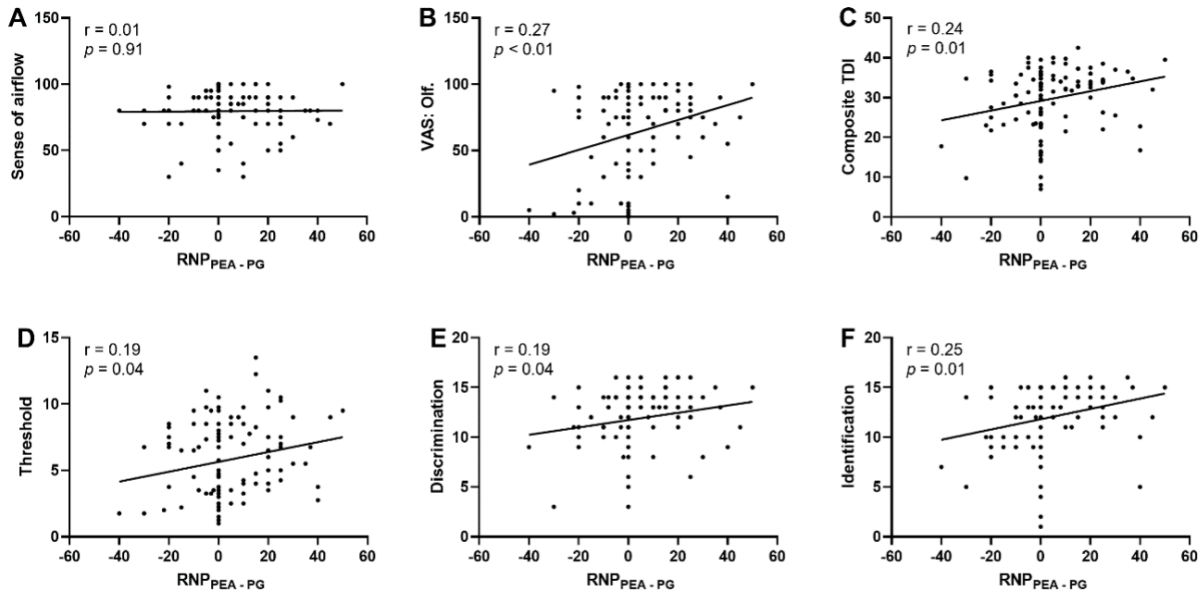

Figure 4. Correlations between the difference in relative nasal patency (RNP_{PEA-PG}) after exposure to PEA (odorous) and PG (odorless) and rated or measured olfactory function: (A) the rated sensation of airflow permeability in nasal breathing (VAS 0 to 100), (B) self-rated olfactory function (VAS 0 to 100), (C) composite TDI scores, (D) threshold, (E) discrimination, and (F) identification.

nervation were found to reach both the epithelium and bulb [27]. Substance P, calcitonin gene-related peptide (CGRP), and other peptides in these two structures can serve as neurotransmitters to facilitate cross-talk between the two systems, transferring olfactory information to the trigeminal pathway [28]. In addition, some of the central areas responsible for olfactory signal processing, such as the pyriform cortex, orbitofrontal cortex and insula, overlap with areas that process trigeminal information [14, 29]. These brains areas may serve as potential central hubs for producing trigeminal perception in response to an olfactory stimulation [30].

The improvement in open-nose sensation was not associated with an anatomically 'open' nasal cavity, as the PNIF measurement throughout our study kept statistically unchanged. This finding was in line with the previous study that the effect of menthol was based on trigeminal-mediated cooling sensation without an alteration of intranasal structures detected by objective assessment [10, 11]. Therefore, the nasal patency induced by specific olfactory stimuli also resulted from neurobiological perception, but not from actual structural patency.

Some studies showed that olfactory stimuli (specifically vanillin) can enhance the intensity of CO_2 trigeminal stimuli [31], and ipsilateral co-stimulation of trigeminal and olfactory triggers can increase the trigeminal lateralization test score [15]. On the contrary, we did not find an additive effect. The sensation of nasal patency evoked by the mixed solution was weaker compared to menthol alone. Similarly, in some circumstances for example, trigeminal irritation by CO_2 was suppressed by odorants such as amyl butyrate [32], carvone or H_2S [33]. The quality of the stimuli determined whether this suppressive effect was centrally or peripherally mediated [34]. After all, the interaction between olfactory and trigeminal system is difficult to predict. Whether a given olfactory component mediates additive or suppressive effect on trigeminal chemosensitivity is dependent on stimulus quality, stimulus intensity and the relative intensity of olfactory and trigeminal components [35]. It should also be noted that the measurement of the current study was the sensation of nasal patency, which was different from previous studies that focused on the intensity of trigeminal perception. To sum up, although PEA itself can induce the open-nose sensation, it may suppress menthol to modulate the sensation of nasal patency.

It has been known that olfactory deficits can lead to a decrease in trigeminal chemosensitivity [36, 37], a poorer temporal resolution of trigeminal lateralization [38], and smaller response amplitudes of trigeminal event-related potentials [39]. In our study, no between-group difference was observed in RNPs in response to the menthol ($M = 5.9 \pm 3.7$, $p = 0.11$), and only a trend of greater response to the mixed solution favoring normosmia group ($M = 6.0 \pm 3.1$, $p = 0.05$) was noted. Despite these, subjects in the olfactory dysfunction group did not rate higher RNP in the PEA exposure condition than in the PG condition, plus the positive correlations of the RNP_{PEA-PG} with olfactory measures, suggesting the important role of olfactory receptivity in contributing to the sensation of nasal patency.

Our findings implicated that patients complaining about nasal

congestion without olfactory dysfunction could benefit from nasal clip-based odor presentation in terms of gaining a sensation of nasal patency. Although the olfactory component contributes to a lesser extent compared to the trigeminal one, it may potentially be more pleasant and therefore increase patient compliance [40]. The nasal clip device that provided continuous release of odorants was also easy to wear without causing discomfort. Future applications should be directed toward customizing the presenting odors to maximize the effect of open-nose sensation.

One other finding worth noting was that participants with olfactory dysfunction had a trend of rating their intranasal airflow permeability at baseline lower than normosmics ($p = 0.07$, Table 1), while no significant structural difference revealed by PNIF was observed ($p = 0.23$). Again, the sense of airflow or nasal patency reflected the sense of trigeminal stimulation; therefore, patients with olfactory loss rate the intensity of proprionic acid [41], menthol gum [42] and ammonia [43] lower than healthy subjects as well. The analysis of correlations among the subjective and objective baseline measurements (Table 2) also supports the fact that rated nasal patency was associated with rated olfactory function, but not with measured nasal patency [44]. These findings add evidence to the literature that trigeminal and olfactory sensations interact closely enough to confuse ratings of functions.

The current study still had some limitations that need to be taken into account. First, the two groups were not perfectly matched since all subjects were randomly recruited. It was intuitive that subjects grouped into olfactory dysfunction tended to have more advanced age and therefore poorer scores in MoCA and ADS_L. We had considered 'age' as covariates in the analysis; however, it should be kept in mind that older people might have difficulties judging nasal patency. Second, the lasting duration of the nasal patency sensation was not measured. Given that continuous olfactory/trigeminal stimuli are subject to adaptation, the open-nose sensation may be a transient effect. Further work should focus on investigating the time of action and optimizing the frequency of nasal clip replacement. Lastly, objective trigeminal measurement was not included in the current study. A lateralization test is to examine the ability to localize a trigeminal cooling agent (i.e., eucalyptus), which may irritate and fatigue the trigeminal nerve and habituate the sensation that the nerve gives rise to [45]. If the test is implemented just before the experiment, it may profoundly influence the ratings of nasal patency. Although it would have been possible to include a test of trigeminal function at the end of the experimental session, it was decided against that extension of the study protocol in order not to overburden the participants but rather leave that for a separate future experiment.

Conclusions

A specific olfactory stimulant that selectively induces olfactory perception can also evoke and modulate the sensation of nasal patency, which was previously attributed to a trigeminal cooling effect. It is believed that patients could benefit from exposing themselves to odors in order to relieve the annoying nasal obstruction.

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Authorship contribution

Study idea and design: YC, TH, AN, AH, SP; data collection: AN, SP, TH; data analysis: YC, TH; manuscript writing: YC, TH; final approval: all authors.

Conflicts of interest

The authors claim that there is no conflict of interest.

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This manuscript contains online supplementary material

SUPPLEMENTARY MATERIAL

Table S1. Correlations between RNP_{PEA-PG} and various olfactory scores in different groups.

	Sense of airflow*		Rated olfaction		T		D		I		TDI	
	r	p	r	p	r	p	r	p	r	p	r	p
Normosmia	-0.08	0.50	0.01	0.93	0.03	0.81	0.02	0.90	-0.01	0.94	0.03	0.82
Olf. Dysfunction	0.02	0.90	0.23	0.10	-0.04	0.81	0.02	0.91	0.14	0.31	0.05	0.75

*The rated sensation of airflow permeability (VAS 0 to 100) at a baseline measurement. T, threshold; D, discrimination; I, identification; TDI, composite threshold + discrimination + identification score.