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Mechanical Obstruction of the Olfactory Cleft Reveals Differences Between Orthonasal and Retronasal Olfactory Functions

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Abstract

Following up on recent observations in patients with nasal polyposis (NP), the present study aimed to investigate whether a mechanical obstruction of the anterior olfactory cleft (OC) would produce differential effects on orthonasal and retronasal olfactory functions. To this end, we studied 33 healthy subjects in a randomized trial. Sponges with high content of saline were either placed in the OC or on the respiratory epithelium, such that this was blinded to both subject and observer. The results indicated that orthonasal ($P = 0.04$) but not retronasal ($P = 0.15$) olfactory identification ability was lower when the OC was blocked. This confirms the idea that differences between orthonasal and retronasal olfactory functions, as observed in NP patients, are, at least to some degree, due to mechanical obstruction of the anterior portion of the OC. The present data also suggest that mechanical obstruction is a means to induce reversible hyposmia void of side effects which can be performed in a blinded fashion. This might become a valuable model of hyposmia for future investigations.

Key words: hyposmia model, interaction, olfaction, retronasal, Sniffin' Sticks, sponge

Introduction

The aim of the present investigation was to investigate a clinical observation in nasal polyposis (NP) patients (Landis *et al.*, 2003). We recently demonstrated that NP patients had better retronasal olfactory function compared to orthonasal olfaction. This difference appeared to be attributed to the growth pattern of the nasal polyps. In case the same obstruction pattern was induced in healthy subjects, it should result in the same pattern of discrepancies between orthonasal and retronasal olfactory functions as observed previously in NP patients.

To pursue this aim, we opted for the use of small sponges currently used in the control of nasal bleeding. Before placing them on the epithelium, the sponges are soaked in saline so that they have a very high water content and are very soft. As the clinical use of these sponges has been demonstrated to be safe, no side effects of the treatment were expected.

Materials and methods

Subjects

Participants were 33 healthy volunteers (14 female, 19 male; mean age: 33.2 ± 2.5 years), without any history or endoscopic signs of chronic rhinosinusitis and/or nasal polyps. All subjects underwent nasal endoscopy by an experienced otolaryngologist. None of the subjects received intranasal treatments; they did not take medication known to significantly influence olfactory function (Doty and Bromley, 2004). The study was approved by the Ethics Committee of the University of Dresden Medical School; all subjects gave written informed consent.

Design and material

The mechanical devices used were small (1 cm^3) hemostatic sponges (Gelita Tampon, Braun, Melsungen, Germany)

manufactured for control of nose bleeding. They are made out of deformable self-decomposable sponge-like material (odorless gelatine), which becomes very soft as soon as wetted (Figure 1). The gelatine sponges are not impreganted with any drug. During all experimental procedures, two sponges were put unilaterally either in the anterior olfactory cleft (OC) or in the respiratory epithelium (RE) below the insertion of the middle turbinate. The subjects were randomized and divided into two groups. Two pieces of the sponges were placed either in the OC (n = 20) or in the RE (n = 13) under endoscopic control (Figure 1a). The two sponges were placed directly adjacent to each other with little or no gap between them, and they were "stacked" horizontally (Figure 1b). The two groups did not differ in terms of age or gender distribution.

Olfactory thresholds were determined orthonasally only, and odor identification was obtained for both retronasal and orthonasal administration of odors. During orthonasal and retronasal testing, the untreated (no sponges) nostril was blocked with an adhesive tape, preventing nasal airflow at this side. Subjects participated in two sessions (mean session duration: 35 min) separated by at least 1 day (maximal interval 2 days), with sponges either in the OC or in the RE and without sponges, the sequence of which was randomized (sessions with and without sponge were randomly chosen) across subjects. Sponge placement was performed by an experienced otolaryngologist (O.P.), and the testing started approximately 15 min later; neither the subjects nor the investigator doing the olfactory testing knew about the placement of the sponges. Testing was performed in a well-ventilated, quiet room.

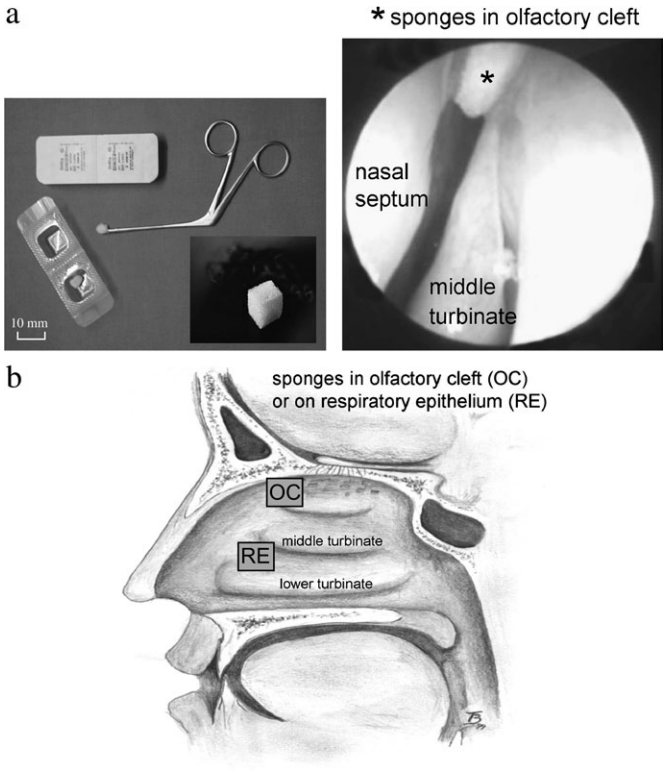

Figure 1 **(a)** Left: devices used to insert sponges in the OC; the insert photograph shows the cubical-shaped sponge with a length of 10 mm before they are wetted. Right: endoscopic view. **(b)** Schematic drawing of the lateral wall of the nasal cavity. Two sponges were either placed in the anterior OC or in the middle meatus, between lower and middle turbinate, on the RE.

Olfactory testing

Psychophysical testing of orthonasal olfactory function

All participants had orthonasal olfactory function tested by means of the "Sniffin' Sticks" (Burghart Instruments, Wedel, Germany), a validated odor identification test (Kobal *et al.*, 2000). The Sniffin' Sticks test is based on commercially available felt-tip pens. For odor presentation, the pen's cap was removed by the experimenter. The pen's tip was then placed approximately 2 cm in front of the nostril for approximately 2 s. Odor thresholds for phenyl ethyl alcohol (PEA) were assessed using a single-staircase, three-alternative forced-choice procedure. Sixteen dilutions were prepared in a geometric series starting from a 4% PEA solution (dilution ratio 1:2; diluent: propylene glycol). Three pens were presented in a randomized order, with two containing the solvent and the third containing the odorant at a certain dilution. The patient's task was to identify the odor-containing pen. Triplets were presented at intervals of 20 s. Reversal of the staircase was triggered when the odor was correctly identified in two successive trials. Threshold was defined as the mean of the last four out of seven staircase reversals. In addition, odor identification was tested for 16 common odors. Using a multiple forced-choice task, odors were identified from lists of four descriptors each. The subject's score ranged from 0 to 16. The coefficient of correlation for measures of test–retest reliability has been found at r = 0.94 for odor thresholds and at r = 0.76 for odor identification (Hummel and Mayer, 2003).

Psychophysical testing of retronasal olfactory function

For retronasal stimulation, a validated test was used (Heilmann *et al.*, 2002) which is based on grocery store condiments and food items available in powder form (e.g., spices or instant drinks). The 20 substances were applied using squeezable plastic vials with a 6-cm-long spout. While the powder was applied by the experimenter, subjects were free to sample as much stimulant as needed for identification. In a typical trial, through the wide-open mouth, the experimenter placed approximately 0.05 g on the middle of the tongue inside the oral cavity. Before the application of the stimulant, subjects rinsed their mouths with tap water. Each substance was identified by means of a closed set with four verbal items using a forced-choice procedure. Scores were obtained by adding the number of correct identifications of retronasal stimuli. The test–retest reliability of this test has been reported with r = 0.76 (Heilmann *et al.*, 2002).

Statistical analysis

Results were analyzed using SPSS 10.0 for Windows (SPSS Inc., Chicago, IL). To eliminate intraindividual differences in olfactory function, differences were calculated between results from measures with sponges inserted and those without sponges. Using these data, analyses of variance were exploited to investigate differences between OC and RE groups. The alpha level was set at 0.05.

Results

Introduction of the sponges was tolerated well by all subjects; no side effects were recorded. All subjects had threshold and orthonasal identification scores compatible with normosmia (Kobal *et al.*, 2000).

Comparing the changes induced by the sponges between groups, the decrease of odor thresholds was significantly more pronounced in the OC group compared to the RE group (F = 5.2; P = 0.03; Figure 2). Further, orthonasal (F = 4.5; P = 0.04; Figure 3), but not retronasal (F = 2.2; P = 0.15; Figure 4), olfactory identification ability was significantly lower when the sponges were in the OC compared to results with sponges in the RE.

Discussion

Results from the present study suggested that the previous findings in NP patients regarding differences in the orthonasal and retronasal olfactory functions are due to the mechanical obstruction of the anterior OC.

In a previous study (Landis *et al.*, 2003) based on a clinical observation, retronasal olfaction had been reported to be more resistant to NP growth than orthonasal olfactory function. The authors speculated that this might be related to the growth pattern of nasal polyps obstructing first the anterior access of odors to the OC sparing the retronasal access for odorant molecules during a long time of the course of NP disease (Landis *et al.*, 2003). Only when polyps reach a certain size, blocking the whole nasal cavity and rendering any nasal airflow (orthonasal and retronasal) impossible, is retronasal olfactory function also extinguished in these patients. The present findings seem to corroborate the hypothesis that

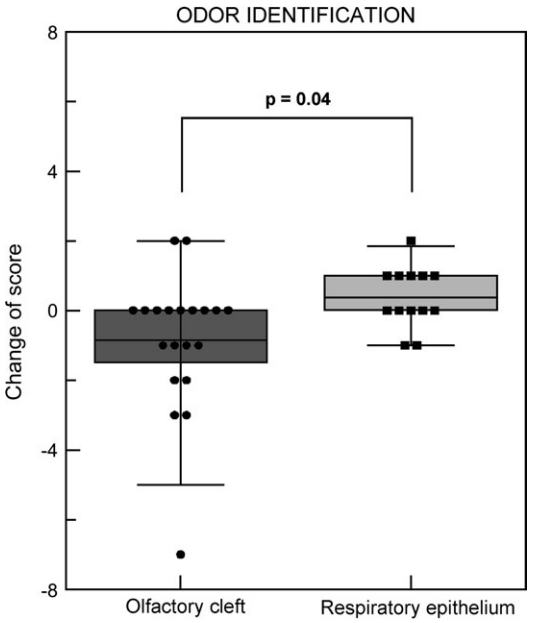

Figure 3 Changes in orthonasal olfactory identification units with and without sponges between the two treated groups.

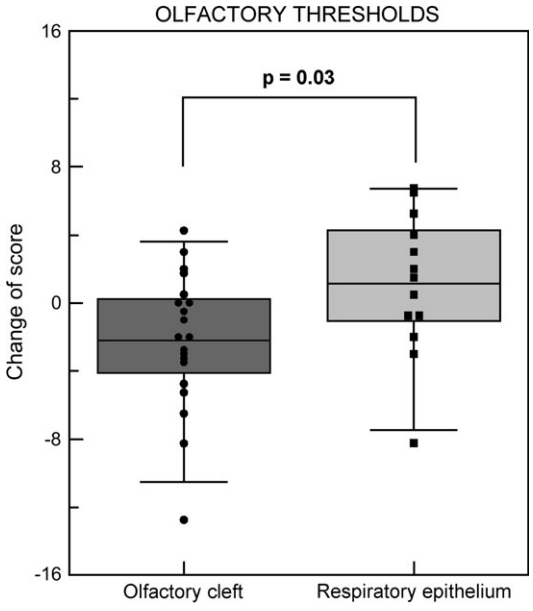

Figure 2 Changes in orthonasal olfactory threshold units with and without sponges between the two treated groups.

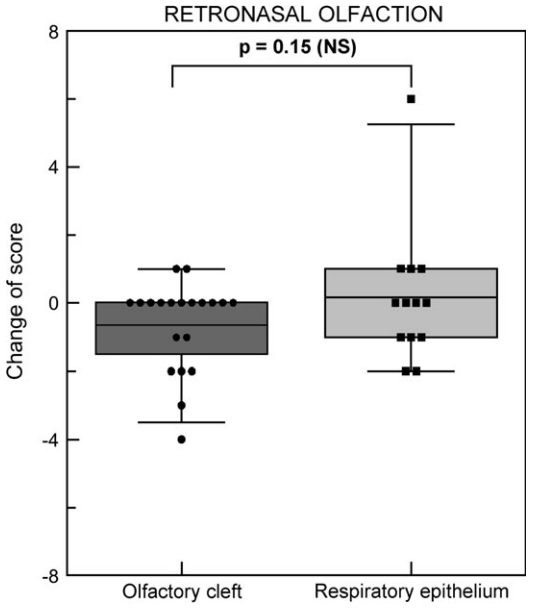

Figure 4 Changes in retronasal olfactory identification units with and without sponges between the two treated groups.

the observed difference between orthonasal and retronasal olfaction in NP patients is mainly based on the alteration of the anterior flow pattern, preventing odorants from entering the OC during sniffing. The reproduction of the same pattern of orthonasal versus retronasal olfaction in healthy subjects that has been observed in NP patients previously should theoretically be possible to simulate aspects of NP. Comparison of the results from the present paper and those of Landis *et al.* (2003) reveals that the absolute difference between orthonasal and retronasal olfactory functions is smaller in the present experimental study. The main reasons for this could be that the subjects in the present study were younger on average than the typical NP patients, rendering their olfactory function less vulnerable to mechanical obstruction. Further, NP is a mucosal inflammatory disease of the entire nasal mucosa. It is likely that the modification of olfactory function observed in the previous paper (Landis *et al.*, 2003) not only is due to the mechanical obstructive aspect of the polyps but also reflects inflammatory changes within the olfactory epithelium. Finally, the NP patients in the previous study (Landis *et al.*, 2003) had mainly stage II polyps, meaning that the extent of obstruction was bigger than the extent of obstruction achieved with the presently used hemostatic sponges. However, the present data might be an interesting model in a clinical setting. Further, this model which creates a difference between orthonasal and retronasal olfactions might be interesting for chemosensory studies or even food research. Orthonasal and retronasal olfactory information has been shown to be differently processed on a cerebral level (Small *et al.*, 2005). Recent studies even suggest that the structures responsible for orthonasal and retronasal olfaction are functionally, but maybe also structurally, different maybe even at the level of the olfactory epithelium, the olfactory bulb, and not only at the cerebral levels (Landis *et al.*, 2005). Thus, the proposed model could be used to induce differences between orthonasal and retronasal olfaction in order to investigate consecutive cerebral changes in information processing. It is also imaginable to test foods for their retronasal perception with little or no orthonasal interference.

The present data also provide preliminary evidence for the feasibility of models of mechanically induced olfactory loss. Since the present study was conducted to investigate effects of the blocking of the anterior OC, further elaboration of this model with either more sponges or differently placed sponges within the OC could be used to gauge the degree of inducible olfactory loss. For studies aimed at questions related to interactions between the chemical senses, this approach appears to be relatively attractive especially in light of the absence of side effects and the ease of administration of the sponges by trained experimenters. The interaction between the three chemical senses of olfaction, gustation, and the trigeminal system has been, and still is, of interest for the chemosensory research community (Krause, 1895; Cain and Murphy, 1980). It has been postulated that loss of one chemical sense alters the function of the remaining senses (Kobal and Hummel, 1988). However, most studies have been conducted on patients (Cain, 1974; Hummel *et al.*, 1996; Gudziol *et al.*, 2001), and there is a lack of a good hyposmia model in healthy subjects. Previous studies with local anesthetics achieved good results regarding the induced decrease of olfactory function (Welge-Lussen *et al.*, 2004). However, considerable side effects have been recorded such as headaches lasting up to several hours (Welge-Lussen *et al.*, 2004). The explanation of headaches induced by a local anesthetic (lidocaine), which is not known for this, probably relates to the site of administration. The OC has been considered a potential weak point within the brain barrier (Perl and Good, 1991), a fact that seems to be confirmed by some experiments on the so-called ''nose–brain barrier'' (Okuyama, 1997; Born *et al.*, 2002). This gives rise to the question to which extent substances applied to the olfactory epithelium might also penetrate into the olfactory bulb or even in the cerebrospinal fluid, thereby affecting olfactory and maybe cognitive functions. By improving the presently described model, it could become a valuable tool for chemosensory researchers interested in interactions between the three chemical senses. Considering the reversibility of the method, the investigated subjects could also participate in crossover trials.

Taken together, the present study confirms the idea that differences between orthonasal and retronasal olfactory functions, as observed in NP patients, are at least to some degree due to mechanical obstruction of the anterior portion of the OC. The presented model might also serve as a valuable tool in chemosensory research.

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