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Correlation between olfactory function, trigeminal sensitivity, and nasal anatomy in healthy subjects

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Abstract

Purpose Few studies have investigated the correlation between chemosensory function (trigeminal and olfactory) and nasal volume in humans, even though nasal anatomy is crucial for the sense of smell. Aim of this study was to evaluate these correlations in normosmic subjects.

Methods Two hundred and fifty-six healthy volunteers (age range 19–69 years) participated. Olfactory function was investigated for (the rose-like) phenylethyl alcohol odor threshold and odor identification (OI) using the Sniffin' Sticks test, while nasal structure was evaluated by acoustic rhinometry (AR); trigeminal sensitivity was assessed in terms of detection "thresholds" for the odorless carbon dioxide (CO_2).

Results There were negative correlations between olfactory sensitivity at threshold level and minimum cross-sectional area (MCSA) in both nostrils. No significant correlations were found between OI and nasal anatomy. Similar to olfactory sensitivity, with regard to the trigeminal stimulus CO_2 for the right nostril subjects were the more sensitive the smaller the MCSA.

Conclusions The current results emphasize the significance of nasal anatomy for trigeminal/olfactory threshold perception. Interestingly, correlations were not found between suprathreshold odor identification and nasal anatomy. Other than odor identification, odor thresholds appear to depend on subtle differences in nasal anatomy.

Keywords Acoustic rhinometry · Chemosensory system · Nasal anatomy · Olfactory function · Sniffin' Sticks

Introduction

The nasal anatomy plays a crucial role for olfactory function, as shown in a number of studies that evaluated the correlations between nasal airflow and olfactory abilities [1–4]. Still, relatively few studies investigated the relationship between olfactory function and the nasal volume [e.g., 5, 6]. To our knowledge, only one study [7] examined the correlation between intranasal volume and olfactory function in normosmic subjects. In particular, Damm et al. [7] classified each nasal cavity in 11 segments according to previous studies [6, 8]. They found that only two of these segments, the upper meatus below the cribriform plate and an anterior segment comprising the nasal valve area, played an important role for the explanation of inter-individual differences in odor thresholds.

Some studies looked at the relationship between olfactory function and the trigeminal system [9–11]. However, only the study of Konstantinidis et al. [12] described the interaction between nasal anatomy and trigeminal sensitivity. They reported a positive correlation between the size of the nasal cavity and the trigeminal system.

There are no studies where the association between nasal anatomy and both trigeminal and olfactory sensitivity would have been investigated simultaneously in healthy subjects. To fill this gap the aim of this study was to evaluate these correlations in normosmic subjects.

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Materials and methods

Participants

Two hundred and fifty-six healthy participants were enrolled, with an age range from 19 to 69 years and a mean age of 29.3 years (SD 9); 112 were men (mean age 27 years; SD 0.6) and 144 women (mean age 31.1 years; SD 0.8). Participants were divided into two age groups: 19–30 years (A, $n = 184$), 31–69 (B, $n = 72$) years. Inclusion criteria were 18 years and older, overall good health, normal olfactory function, and the ability to comprehend and perform adequately the test procedure. The following exclusion criteria had been defined: major head trauma, dementia, psychiatric conditions interfering with study participation, chronic/acute rhinosinusitis, diabetes, stroke, any systemic disease associated with smell disorders like chronic renal failure or thyroid disorders, and impaired sense of smell.

Procedure

The following procedures were performed for all subjects in this chronological order: (1) collection of medical history; (2) self-assessment of olfactory function; (3) psychophysical evaluation of olfactory function for phenyl ethyl alcohol odor threshold, and odor identification; (4) acoustic rhinometry; and (5) evaluation of trigeminal function.

The self-assessment of olfactory function (smell ratings) was carried out using the following classification: better than normal, normal, less than normal and no function.

Participants were instructed not to eat anything and to drink only water 1 h prior to the experiment, and not to wear any scented products on the day of testing. All olfactory assessment was carried out in a well-ventilated room. The study was approved by the local Ethic Committee and it was performed according to the Declaration of Helsinki. Participants received an explanatory statement and gave their written informed consent prior to participation in the study.

Assessment of olfactory function

Olfactory function was evaluated using the "Sniffin' Sticks" test (Burghart, Wedel, Germany) [13–17]. Felt-tip pens filled with odors were used to deliver the olfactory stimuli. For odor presentation, the cap was removed by the experimenter for approximately 3 s and the pen's tip was placed approximately 2 cm in front of both nostrils [18]. Two different olfactory functions were assessed: first, odor threshold (OT) was determined for (the rose-like) phenyl ethyl alcohol (PEA) with 16 stepwise dilutions staring at a 4% solution (dilution ratio 1:2 in propylene glycol). The threshold was measured using the single-staircase technique based on a three-alternative forced-choice task (3AFC). The subjects score ranged from 1 to 16. Then, odor identification (OI) was assessed by presenting 16 common odors, each presented with four verbal descriptors in a multiple forced-choice format (three distractors and one target). The interval between odor presentations was 20–30 s. Trigeminal sensitivity was assessed in terms of quasi-detection thresholds for the odorless carbon dioxide (CO_2) [19]. The stimuli were presented to both nostrils using a custom-built computer-controlled stimulator. The CO_2-pulses had different durations, starting at a duration of 50 ms, with increments of 50 ms and a maximum of 2000 ms. Quasi-CO_2-thresholds were assessed using a single staircase. Participants pushed a button as soon as they perceived a slightly tingling stimulus. According to that response, stimulus duration was decreased or increased, until seven reversals of the staircase had been reached; the threshold was calculated as the average of the last four reversals of that staircase.

Anatomical measures using acoustic rhinometry

A computer-aided rhinometer (GM Instruments LTD, acoustic Rhinometer, Kilwinning, KA13, 6PU, UK) was used to assess the anterior portion of the nasal cavity. Acoustic rhinometry (AR) is considered a rapid, non-invasive and objective technique to evaluate the morphology of the anterior nasal cavity using the reflection of sound waves [20, 21]. The rhinometry tube, with a length of 24 cm, is placed against each nostril. The AR allows to obtain measurements of the anterior nasal cavity in rapid succession, separately for the left and right sides. Variations in the cross-sectional area (e.g., created by the lower turbinate) reflect the sound waves [22]. The measurements include the minimum cross-sectional area (cm^2) (MCSA) [21], and the volume (cm^3) calculated at a distance from 0 to 4.7 cm, separately for each nostril.

Statistical analysis

Normal distribution of the data was assessed using the Shapiro–Wilk test. All statistical analyses were performed using SPSS 23 software for Windows (IBM, Armonk, NY, USA). The data were not normally distributed. Statistical differences between women and men and among the two different age groups were performed using Mann–Whitney test. Non-parametric Spearman's rank correlation coefficients (ρ) were computed to evaluate the relations between olfactory function and nasal anatomy. Moreover, multivariate linear regression analyses were performed using OT, OI and CO_2 sensitivity as dependent variables, while independent variables were MCSA, volume in the right and left nostrils, age, and sex.

All data are presented as mean ± standard deviation (SD). A p value < 0.05 was considered to be statistically significant.

Results

The mean values ± SD for odor threshold (OT, in dilution steps), odor identification (OI, in correctly identified items), CO_2 sensitivity (in ms), and smell ratings (in rating units) were 8.6 ± 2.486, 14 ± 1.342, 786.9 ± 41.074, and 2 ± 0.875, respectively (Table 1a). Mean scores of OT and OI were relatively high, and all participants were classified as normosmic according to normative data [14, 17].

Table 1 Evaluations of chemosensory function (trigeminal and olfactory) and acoustic rhinometry for all participants

	Mean ± SD
(a) Chemosensory function	
OT (dilution steps)	8.6 ± 2.486
OI (number of correct items)	14 ± 1.342
CO_2 (ms)	786.9 ± 41.074
Smell rating (units)	2 ± 0.875
(b) Acoustic rhinometry	
MCSA R (cm^2)	1.23 ± 0.663
Volume R (cm^3)	7.02 ± 3.010
MCSA L (cm^2)	1.28 ± 0.837
Volume L (cm^3)	6.73 ± 2.623

AR acoustic rhinometry, *CO_2* carbon dioxide, *OI* odor identification (number of correct items), *OT* odor threshold, *R* right nostril, *L* left nostril, *MCSA* minimum cross-sectional area (cm^2), *SD* standard deviation

In the acoustic rhinometry (AR) evaluations, the average MCSAs were 1.23 ± 0.663 cm^2 and 1.28 ± 0.837 cm^2 in the right and left nostrils, respectively. The volumes were 7.02 ± 3.010 cm^3 and 6.73 ± 2.623 cm^3 in the right and left nostrils, respectively (Table 1b). No significant differences ($p > 0.05$) were observed for the MCSA and the volume between right and left nostrils. For OT, OI, CO_2 and smell rating no statistical differences were found in relation to sex and age (Table 2a). However, in the acoustic rhinometry evaluations women exhibited significantly larger MCSA in both nostrils ($p < 0.01$ and $p < 0.001$ in the right and left nostrils, respectively), while men had significantly larger nasal volume ($p < 0.05$ in both nostrils) (Table 2b). Between the two age groups no statistically significant differences were observed for acoustic rhinometry. As regards relationships between chemosensory function (trigeminal and olfactory) and nasal anatomy, low negative correlations were observed between OT and MCSA ($\rho = -0.23$, $p < 0.01$; $\rho = -0.20$, $p < 0.01$, for the right and left side, respectively; Fig. 1a, c). In contrast, positive correlations were present between OT and AR volume ($\rho = 0.23$, $p < 0.01$, $\rho = 0.22$, $p < 0.01$, in the right and left nostrils, respectively; Fig. 1b, d). No significant correlations were found between OI and nasal anatomy. For CO_2, the trigeminal stimulus, a positive correlation was detected only between CO_2 sensitivity measures and MCSA for the right nostril ($\rho = 0.20$, $p < 0.01$; Fig. 2), indicating that subjects were the more sensitive the smaller the MCSA.

Moreover, no correlations were observed between OT, OI, CO_2 sensitivity and smell ratings.

Multivariate linear regression analyses were performed to predict olfactory function and trigeminal sensitivity based on MCSA, volume in both nostrils, age and sex. A significant regression equation was established only for OT [$F_{(6,210)} = 4.217$, $p = 0.0001$, $R^2 = 0.108$], and CO_2

Table 2 Evaluations of chemosensory function (trigeminal and olfactory) and acoustic rhinometry in relation to age and sex

	A Group Mean ± SD	B Group	p	Women Mean ± SD	Men	p
(a) Chemosensory function						
OT (dilution steps)	8.8 ± 2.9	8.4 ± 2.6	$p > 0.05$	9.4 ± 2.5	9.1 ± 2.4	$p > 0.05$
OI (number of correct items)	13.8 ± 1.4	13.1 ± 1.2	$p > 0.05$	13.9 ± 1.3	13.7 ± 1.4	$p > 0.05$
CO_2 (ms)	760.5 ± 609.7	860.2 ± 643.2	$p > 0.05$	882.9 ± 666.8	686.5 ± 549.6	$p > 0.05$
Smell rating (units)	1.5 ± 0.9	1.6 ± 1	$p > 0.05$	1.5 ± 0.9	1.5 ± 0.9	$p > 0.05$
(b) Acoustic rhinometry						
MCSA R (cm^2)	1.2 ± 0.8	1.3 ± 0.6	$p > 0.05$	1.4 ± 0.7	1 ± 0.5	**$p < 0.01$**
Volume R (cm^3)	7.2 ± 3	6.7 ± 2.9	$p > 0.05$	6.4 ± 2.7	7.8 ± 3.1	**$p < 0.05$**
MCSA L (cm^2)	1.3 ± 0.9	1.4 ± 0.6	$p > 0.05$	1.5 ± 0.9	1 ± 0.5	**$p < 0.001$**
Volume L (cm^3)	6.8 ± 2.6	6.5 ± 2.7	$p > 0.05$	6.3 ± 2.7	7.2 ± 2.4	**$p < 0.05$**

Bold indicated statistical differences $p < 0.05$

A Group 19–30 years, *B Group* 31–69 years, *AR* acoustic rhinometry, *CO_2* carbon dioxide, *OI* odor identification, *OT* odor threshold, *R* right nostril, *L* left nostril, *MCSA* minimum cross-sectional area (cm^2), *SD* standard deviation

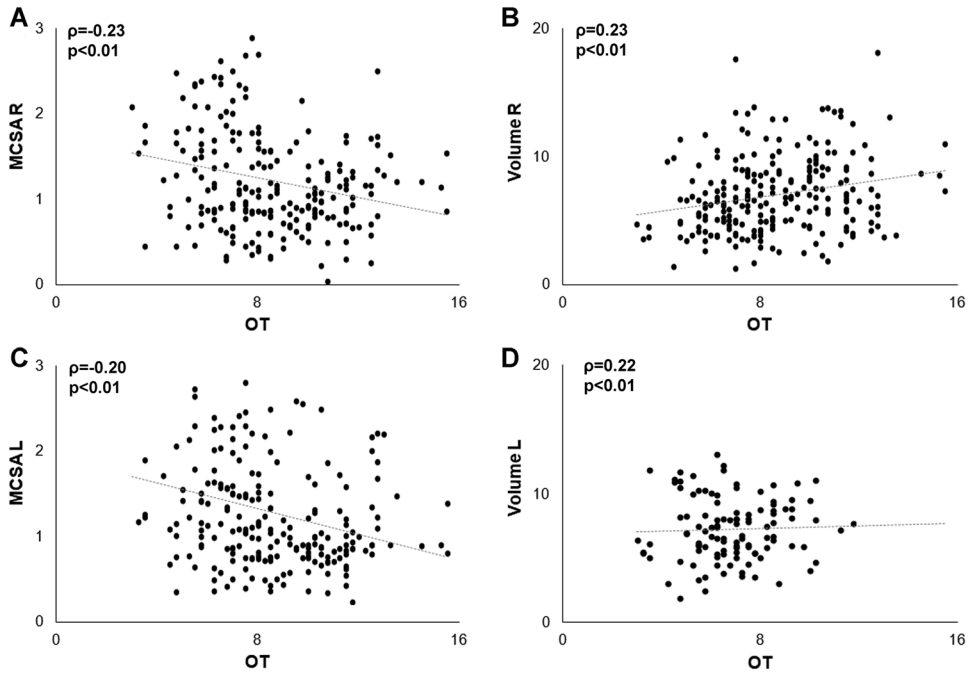

Fig. 1 Scatterplots of the relationship between odor threshold (OT) and nasal anatomy such as minimum cross-sectional area (cm^2) (MCSA) in the right nostril (**a**), in the left nostril (**c**), volume in the right nostril (**b**) and in the left nostril (**d**)

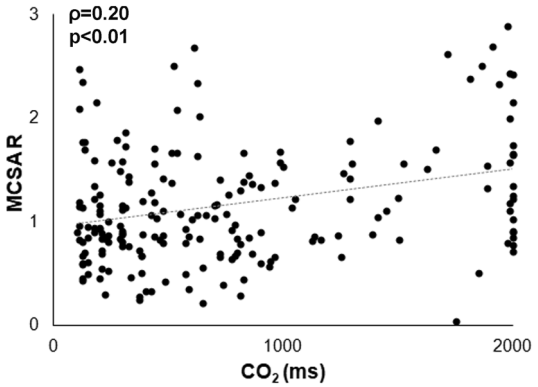

Fig. 2 Scatterplots of the relationship between CO_2 (ms) and minimum cross-sectional area (cm^2) (MCSA) in the right nostril

sensitivity [$F_{(6,191)} = 4.071$, $p = 0.001$, $R^2 = 0.113$], but not for OI [$F_{(6,210)} = 1.520$, $p = 0.173$, $R^2 = 0.042$] (Table 3). These results indicated that changes in volume and MCSA were significant predictors of OT and trigeminal sensitivity (CO_2), respectively.

Discussion

The current results indicate negative correlations between odor threshold and MCSA, while no correlations were observed between OI and MCSA. These results, in line with previous work [7], suggest that a decrease in MCSA is related to an increase in olfactory sensitivity. The current results are also supported by the MRI-based observations of

Table 3 Multiple linear regression analyses

Model	Unstandardized coefficients		Standardized coefficients		Significance
	B	Std error	Beta	*t*	
(a) Odor threshold (dependent variable)					
Volume R	0.153	0.071	0.175	2.167	**0.031**
MCSA R	−0.511	0.308	−0.132	−1.659	0.099
MCSA L	−0.295	0.230	−0.097	−1.281	0.202
Age	−0.021	0.020	−0.073	−1.066	0.288
Volume L	0.065	0.077	0.067	0.841	0.401
Sex	0.038	0.372	0.008	0.103	0.918
(b) Odor identification (dependent variable)					
MCSA L	−0.234	0.127	−0.145	−1.842	0.067
Volume R	−0.052	0.039	−0.111	−1.323	0.187
Sex	−0.172	0.206	−0.063	−0.835	0.405
Volume L	−0.018	0.043	−0.034	−0.411	0.682
MCSA R	0.082	0.171	0.040	0.484	0.629
Age	0.010	0.011	0.064	0.910	0.364
(c) CO_2 (dependent variable)					
MCSA R	191.673	78.420	0.199	2.444	**0.015**
Age	6.222	5.359	0.082	1.161	0.247
Volume L	−36.985	19.325	−0.156	−1.914	0.057
MCSA L	−3.745	57.350	−0.005	−0.065	0.948
Volume R	15.624	17.108	0.076	0.913	0.362
Sex	−118.297	92.438	−0.095	−1.280	0.202

CO_2 carbon dioxide, *R* right nostril, *L* left nostril, *MCSA* minimum cross-sectional area (cm^2), *Std* standard

Bold indicated statistical differences $p < 0.05$

Damm et al. [7] indicating a significant correlation between PEA odor threshold and the anatomy in the anterior portion of the nasal cavity, while no such correlations were found for suprathreshold odor identification. Moreover, multivariate linear regression analyses showed that a change in volume was associated only with OT, but not OI. Overall, these data suggested that odor thresholds are modified in relation to the morphology of the anterior portion of the nasal cavity, while this relation is less pronounced for odor identification.

It is interesting to note that the correlation between olfactory sensitivity and MCSA was negative, while it was positive between olfactory sensitivity and nasal volume. The negative correlation is best explained by the valve function of the MCSA. The laminar airflow outside of the nasal cavity becomes turbulent when entering the nasal cavity. This turbulence then guarantees that a small portion of the inhaled air reaches the olfactory cleft [23]. It appears that, within limits, this mechanism functions best in terms of olfactory sensitivity if the MCSA is small. In our results, there were no significant differences between the age groups for the MCSA and nasal volume. This is in contrast to previous studies which reported an increase of the MCSA and the nasal volume in relation to age [24, 25]. The current finding might be due to age range of the participants and the inclusion criteria which were different from previous work. Hence, part of this age-related change may also be explained by a change in nasal anatomy.

Moreover, specific conditions such as deviated septum or turbinate hypertrophy may induce an impairment in olfactory function [26–29].

Our data, according to previous work [5], suggested significant correlations between odor threshold and nasal anatomy, while no such correlations were observed between odor identification and volume. Moreover, multivariate linear regression analyses showed that a change in volume was associated only with OT, but not OI. A possible explanation for these results could be that odor threshold is more dependent on the nasal anatomy with the periphery of the olfactory system [29–32]. Minimal changes in airflow may change the number of molecules reaching the olfactory cleft—which is less than 10% of the overall nasal airflow [33]. As a consequence odor thresholds would be modified by changes in nasal anatomy. In contrast, odor identification, as a suprathreshold olfactory task, seems to be less dependent on such subtle anatomical changes.

Odor thresholds were positively correlated to intranasal volume which was expected considering previous work. This may be interpreted in the sense that larger volume may also be related to a larger surface with more receptive structures. Since interactions between nasal anatomy and airflow have been reported [33, 34], it may also be that the larger volume affects nasal airflow such that it results in a higher olfactory sensitivity.

The present results (obtained in healthy, normosmic volunteers) are in accordance with Leopold et al. [5] who suggested that changes in the volume of the nasal cavity near the middle turbinate were responsible for the alterations in olfactory function. Moreover, this data also supports Vainio-Mattila results [35], suggesting that a distortion in the nasal cavity could reduce olfactory ability by altering the airflow through the nose. Structural changes in the nasal cavity change the airflow so that it becomes turbulent [33]. As previously reported by Masing [36], a turbulent airflow increases the number of molecules that reach the olfactory epithelium. Furthermore, a turbulent airflow seems to enhance olfactory functions by removing smoke, dust, bacteria and viruses that are present in the inspired air [37].

Similar to the olfactory system, there was also a positive correlation between MCSA and trigeminal sensitivity for CO_2 in the right nostril. While, this compares very well to olfactory sensitivity, it is interesting to note that the correlation between anatomy and trigeminal sensitivity was only found for the right side, but not for the left side. Although, this side diversity may be related to subtle differences in hemispheric specialization for the processing of lateralized stimuli with a small advantage of the right hemisphere [38, 39], the results clearly suggest that the nasal anatomy also relates to trigeminal sensitivity, although the effects are small. In turn, surgical manipulations of the anterior portion of the nasal cavity may affect both olfactory and trigeminal sensitivity by modifying the intranasal airflow.

Conclusion

The results of this study highlight the significance of nasal anatomy for trigeminal and olfactory threshold perception. In particular, changes in volume and MCSA were predictors for odor threshold and trigeminal perception, respectively. Interestingly, using bivariate correlations and multiple linear regression analyses we did not find any significant correlation between suprathreshold odor identification and nasal anatomy. Further information is needed to instruct nasal surgery in terms of improvement of olfactory function.

Compliance with ethical standards

Conflict of interest Authors declare that they have no conflicts of interest.

Ethical approval This study was approved by the local Ethics Committee and was performed according to the Declaration of Helsinki.

Informed consent Participants were informed on aims and possible risks of the study, both orally and in writing, and gave their written informed consent to participate in the study.

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