ORIGINAL CONTRIBUTION

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Anatomy of the nasal cavity determines intranasal trigeminal sensitivity*

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SUMMARY

Background: *Aim of this study was to investigate whether intranasal anatomy plays a role in intranasal trigeminal sensitivity.*

Material and Methods: *A total of 65 healthy subjects (30 female, 35 male) participated in this study (age range 18-35 years). Nasal cavities were assessed using magnetic resonance imaging (MRI). The area of the nasal cavity was measured in 5 coronal sections distributed across the length of the nasal cavity. Trigeminal function was assessed by determining thresholds for CO_2, and responses to suprathreshold stimulation with CO_2 and menthol (intensity ratings; event-related potentials). In addition, rhino-manometric measures were obtained.*

Results: *A positive correlation was found between the size of the nasal cavity and trigeminal event-related potentials in response to suprathreshold CO_2 and menthol stimuli. By contrast, no such correlations were found between nasal cavity size and CO_2 thresholds. Results from rhino-manometry correlated only with the size of the nasal cavity in the nasal valve area.*

Conclusions: *These data suggest that, at least at a suprathreshold level, nasal anatomy plays a significant role in determining interindividual differences in the sensitivity to trigeminal stimuli.*

Key words: trigeminal, nasal anatomy, event-related potentials, smell, olfaction

INTRODUCTION

The nasal trigeminal nerve mediates sensations such as irritation, tickling, burning, warming, cooling, or stinging. In conjunction with respiratory reflexes, trigeminal activation serves to protect an organism from harmful stimuli [(1)]. In addition, trigeminal fibers mediate sensations of temperature and pressure, including the perception of nasal airflow during breathing [(2)].

There is evidence that functionally different areas can be distinguished within the nasal mucosa [(3,4)]. For example, it has been shown in humans that perception of chemosensory stimuli seems to be most accurate in the anterior portion of the nasal cavity [(3)].

Numerous factors influence trigeminal sensitivity. However, a possible relation between the size of the nasal cavity and trigeminal sensitivity has not been examined thus far. In the present study this was undertaken using MRI-based measurements of cross sectional areas of the nasal cavity and responses to the trigeminal stimuli, CO_2 and menthol, in human participants.

MATERIALS AND METHODS

Subjects

Sixty-five healthy volunteers participated in this study (30 women, 35 men; mean age 24.4 years, range 18 to 35 years). The study was performed according to the "Ethical Principles for Medical Research Involving Human Subjects" (World Medical Association, Helsinki). Informed written consent was obtained following oral and written explanation of benefits and potential risks of the study. The study had the approval of the Ethics Committee of the Medical School of the University of Dresden.

Medical history

A detailed medical history was taken from each participant and used to exclude potential participants with conditions which might negatively affect chemosensory function [(5)] such as head trauma, chronic rhinosinusitis, neurological / endocrinological disorders, and previous nasal surgery. All participants were in good health, and reported no dysfunction of the senses of taste or smell.

Clinical examination

Detailed ENT examination was conducted on each participant. It included nasal endoscopy with a rigid endoscope (0°). None of the participants exhibited major nasal pathology.

Olfactory testing

Normosmia was verified by means of the "Sniffin' Sticks" test

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battery (Burghart, Wedel, Germany). The "Sniffin' Sticks" are a well established tool used to assess olfactory function [6]. Examination involves tests for phenyl ethyl alcohol odor thresholds, odor discrimination, and odor identification. They have been shown to have a test-retest reliability comparable to other established tests of olfactory function [7]. A score of more than 30 points is considered as normal, scores between 15 and 30 as hyposmic, and scores of less than 15 as indicating functional anosmia.

MRI

MRI was performed on a 1.5 Tesla scanner (Siemens Sonata®, Siemens Medical solutions, Erlangen, Germany). T1-weighted turbo spin echo sequences were obtained with a repetition time of 1900 ms and an echo time of 4.38 ms in both transverse and coronal planes. Slice thickness was 1.25 mm with a 0.4 mm intersectional gap, resulting in 80 slices for each subject. The acquisition matrix was 256x256 pixels, and the field of view was 280 mm. The images obtained were transferred as DICOM data to an IBM-compatible workstation. The nasal cavity area was measured in 5 coronal sections for each nasal cavity using the modified nasal segmentation system proposed by Damm et al. [8] in a previous study on olfactory function (Figure 1). Measurements were performed using the following 5 sections: 1) the external nasal valve area (in front of the head of the inferior turbinate); 2) the level of the head of the inferior turbinate, 3) the insertion of the middle turbinate in the lateral wall of the nose, 4) the middle of middle turbinate, and 5) the end of the inferior turbinate.

Horizontal division of the upper and lower nasal cavity was set at the axial level of the lower end of the middle turbinate. This division resulted in 3 measurements for each section (upper, lower, and total [upper+lower] segments) with a total of 14

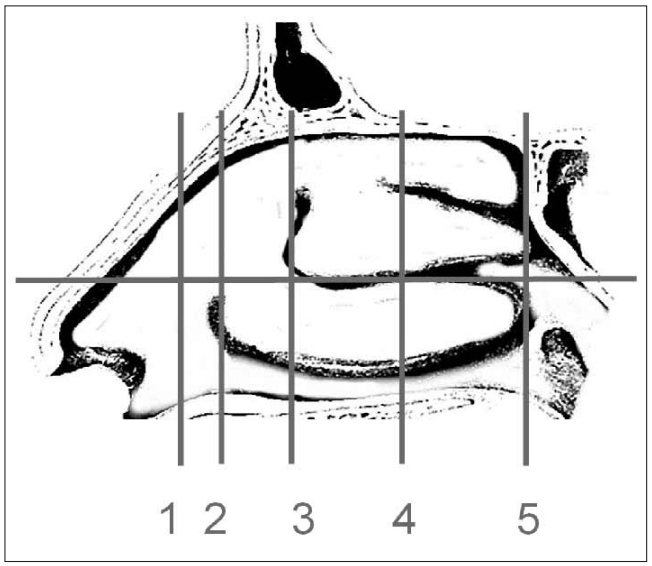

Figure 1. Schematic drawing of the lateral wall of the nasal cavity with the five measured cross sectional areas. The horizontal line divides the sections in upper and lower part.

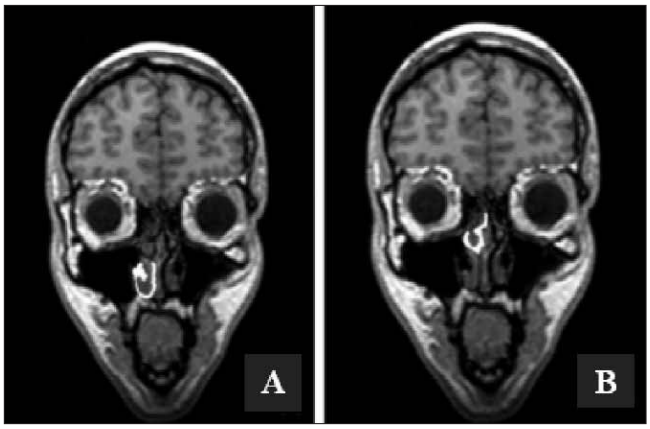

Figure 2. MRI coronal sections at the level of the middle of the middle turbinate. White areas represent measurements of slices on the right upper (A) and the lower right (B) part of the nasal cavity.

cross-sectional areas used for correlational analyses (the section at the upper part of the end of the inferior turbinate was not used, because it was too small to yield reliable values).

The sum of the four upper cross sectional areas was considered as "upper nasal cavity", the sum of the five lower cross sectional areas was considered as "lower nasal cavity". An analogous division was determined for the "anterior" and "posterior" parts of the nose using the sum of the first three and the last two areas mentioned above, respectively.

Measurements of nasal cross sectional areas were performed with Adobe Photoshop® 7.0 (Adobe Systems Incorporated, San Jose, CA, USA). The same examiner (IG) performed all of the MRI-based measurements without prior knowledge of the trigeminal sensitivity of the participant. The nasal cavity was outlined in the above-mentioned sections and the number of pixels in the delineated area was counted (Figure 2).

Chemosensory stimulation

Chemosensory stimuli were applied by means of a computer-controlled olfactometer, and based on air-dilution olfactometry (OM2S, Burghart, Wedel, Germany). This stimulator allows application of rectangular-shaped chemical stimuli with controlled stimulus duration and on-/off-set. Mechanical stimulation is avoided by embedding the odor in a constant flow of odorless, humidified air of controlled temperature (80% relative humidity, total flow 8 L/min, 36°C) [9].

Event Related Potentials (ERPs) in response to intranasal trigeminal stimulation with CO_2 and menthol

Trigeminal ERPs can be easily assessed in a clinical setting to enable complete chemosensory assessment of a subject [10]. ERPs were recorded at Fz, Cz, and Pz positions of the 10/20 system (referenced against linked earlobes [A1+A2]). Eye blinks were monitored via the Fp2 lead. The sampling frequency was 250 Hz; the pre-trigger period (used for baseline determination) was 500 ms with a recording time of 2048 ms per record (band pass 0.02-30 Hz). Recordings were additionally filtered off-line

(lowpass 15 Hz). ERPs were averaged after records contaminated by motor artifacts or blinks had been discarded. Following standardized procedures [9], the first positive peak of the chemosensory ERP was named P1, and the first negative peak N1. The N1 peak is followed by the late positive complex, the major peak of which was named P2 [11]. In addition to peak-to-peak amplitudes P1/N1 and N1/P2 (in order to obtain stable measures, independent of the baseline, averages were based on a limited number of single records), the post-stimulus latencies of N1, and P2 were analyzed. Analyses were performed using EPEvaluate software (Kobal, Erlangen, Germany).

Acquisition of trigeminal ERPs lasted approximately one hour. During this procedure subjects received white noise through headphones in order to mask the switching clicks of the stimulation device. To stabilize vigilance during ERP recordings, subjects performed a tracking task on a computer screen. The tracking task required participants to keep a small square shown on a computer monitor inside a larger moving square using a hand-held joystick.

Using a joystick, they had to keep a small square inside a larger one, which moved unpredictably [12]. Suprathreshold CO_2 stimulus concentration was 58% v/v and the menthol stimulus concentration used was 25% v/v. Stimulus duration was 250 ms. Each stimulus condition was presented 15 times in a randomized order. The interstimulus interval was approximately 20 s [9]. The side of nasal stimulation was chosen quasi-randomly. Thirty-two subjects (15 women, 17 men) received left-sided stimuli and 33 subjects (15 women, 18 men) received right-sided stimuli.

Recording of CO_2-detection thresholds

CO_2 detection thresholds were obtained using the same olfactometer mentioned above (stimulus duration 250 ms, total flow 8l/min). We employed a stepwise method of ascending limits of 10 different CO_2 concentrations starting at 15% v/v up to 37.5% v/v, if required. Every step increased concentration by 2.5% v/v and the subject was asked after each stimulus presentation whether they perceived the stimulus presentation in the nasal cavity.

Rhinomanometry

All subjects underwent assessment of their nasal airflow using active anterior rhinomanometry. A nasal resistance of 150 Pa was used for correlational analyses with other functional measurements.

Statistical analysis

For statistical analyses, SPSS® for Windows™ was used (Statistical Package for the Social Sciences, Version 12.0, SPSS Inc. Chicago, IL, USA). Descriptive statistics are presented within the text as means and associated standard deviations (SD). Comparison of the mean cross sectional areas between right and left sides and between sexes was performed using t-tests for paired and independent samples, respectively. Correlations between trigeminal function, rhinomanometry, and cross-sectional measurements of the nasal cavity were completed using Pearson statistics. In general, the level of significance was 0.05. For correlational analyses significance was set at 0.01 to avoid false positive results.

Table 1. Gender-related differences in the size of nasal cross-sectional areas were found in 6 of the 14 areas assessed. The asterisk indicates statistically significant differences ($p<0.05$).

	Right nasal cavity		Left nasal cavity	
	Mean	SD	Mean	SD
Insertion of middle turbinate				
Lower				
Female	1012.8(*)	366.1	1093.5(*)	371.1
Male	1278.9	446.7	1348.	399.4
External nasal valve area				
Lower				
Female	1163.6(*)	235.0		
Male	1364.9		327.9	
Total				
Female	1828.5(*)	366.9		
Male	2059.1	427.4		
Insertion of inferior turbinate				
Lower				
Female	1157.0(*)	302.3		
Male	1351.1	334.9		
Total				
Female	1848.1(*)	469.8		
Male	2109.3	489.7		

RESULTS

As expected, the comparison between sexes showed that men, in general, had larger nasal cavities than women (Table 1) [13]. Specifically, 6 sectional areas from a total of 14 were found to be significantly larger in men. Despite this, there were no significant correlations between CO_2 thresholds and size of the nasal cavity.

Suprathreshold stimulation with CO_2

A positive correlation was found between the amplitude N1/P2 of the trigeminal ERP and the upper external nasal valve section ($r = 0.39$, $p = 0.001$). The latencies of N1 and P2 exhibited negative correlations (on the left side) with the cross-sectional area of the posterior end of the inferior turbinate (lower part, N1: $r = -0.38$, $p = 0.002$ and total section, N1: $r = -0.36$, $p = 0.003$ and P2: $r = -0.34$, $p = 0.006$) indicating that responses appeared earlier when this area was larger.

Suprathreshold stimulation with menthol

The cross-sectional areas of the “upper nasal cavity” ($r = 0.37$)

and the "posterior nasal cavity" ($r = 0.37$) on the right side were positively correlated with the ERP amplitude N1/P2 induced by menthol stimulation at the recording position Pz, ($p = 0.03$). Positive correlations were also found between P1N1 amplitudes at position Cz on the right side for the area in the upper part of the nasal cavity at insertion of middle turbinate ($r = 0.43$, $p = 0.001$), and the area in the upper nasal cavity at the posterior end of the inferior turbinate ($r = 0.32$, $p = 0.010$). On the left side a correlation was found between amplitudes N1/P2 at Cz and the area of the upper part of the nose, at the middle of middle turbinate ($r = 0.34$, $p = 0.006$). Latencies of ERP to menthol were not significantly correlated with MRI measurements.

Rhinomanometry

The results were not significantly different between left and right side of the nose. No correlations were found between results from rhinomanometry and parameters describing the trigeminal ERP. However, rhinomanometric results were positively correlated with the size of the lower external nasal valve ($r = 0.48$, $p = 0.009$).

DISCUSSION

The present study indicates that suprathreshold trigeminal sensitivity depends on nasal anatomy. Sensitivity of healthy subjects to trigeminal stimuli increases with increasing size of the nasal cavity. Therefore, interindividual anatomical differences in the nose may influence intranasal trigeminal sensitivity. Considering the modulation of olfactory information by trigeminal input, the observed correlation between anatomical measurements and intranasal trigeminal function may also contribute to inter-individual differences in the perception of olfactory stimuli.

It was interesting to note that areas apparently related to trigeminal sensitivity were found at the anterior and posterior portions of the nasal cavity, and in the upper part of the nasal cavity, below the cribriform plate. No correlations between the size of the nasal cavity and trigeminal responsiveness were found for the inferior and middle meatus. Thus, it seems that there is a large overlap between intranasal areas related to trigeminal sensitivity and olfactory sensitivity. Specifically, previous work (e.g., [8,14]) has shown that areas under the cribriform plate and areas in the anterior portion of the nasal cavity are positively related to olfactory function. These data suggest there is similarity between the trigeminal and olfactory systems, which makes sense considering the intimate connection of the two sensory pathways [5,15,16] and their interactions [17].

Anatomical differences in trigeminal sensitivity may also relate to individual differences in the perception of nasal airflow. In turn, such differential perception of nasal airflow may relate to the perception of nasal "stuffiness", which may then play a role in the perceived necessity of nasal surgery. In addition, the present data clearly indicate that surgical interventions may potentially change intranasal trigeminal sensitivity. More research is needed to explore these relationships and possible interrelated functional consequences. It should be noted that although all MRI measurements were performed by the same examiner, precise outlining of the nasal cavities presents some difficulties when performed manually.

Interestingly, rhinomanometric results did not correlate with parameters of trigeminal ERP, although there were significant correlations between rhinomanometric results and the nasal size in the area of the nasal valve. These findings certainly reflect the variability of rhinomanometric results; however they cannot exclude that airflow and trigeminal sensitivity are unrelated.

CONCLUSIONS

The data suggest that nasal anatomy plays a significant role in interindividual differences in sensitivity to trigeminal stimuli.

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