Odor perception depends on airflow, odor solubility and intranasal application site*

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To the Editor:

Odorants are sensed by olfactory receptor neurons in the olfactory epithelium. Odor molecules pass through the nasal cavity and dissolve in the mucus of the olfactory epithelium which is located on the superior portion of the cavity. There they bind to olfactory receptors on the dendrites of the olfactory receptor neurons [(1)]. Therefore, among many other parameters, the number of odorant molecules that reach the olfactory receptors, strength of airflow, solubility of odorant and the location of the site of odor stimulation may significantly influence olfactory perception. In addition, these factors are of significance when designing olfactory measurements [(2)], which require temporally and quantitatively precise delivery of odor stimuli and therefore necessitate an appropriate olfactometer, a device that delivers odors with a defined concentration at a defined flow rate to a participant [(3,4)]. Therefore, the analysis of the impact of airflow, solubility and application site provides not only a deeper understanding of olfactory perception, but also practical references for designing olfactory experiments and choosing appropriate for stimulation parameters.

The present study aimed to quantitatively explore the influence of airflow on odor presentation, solubility of the odorants and intranasal application site on odor intensity and pleasantness. Odors were delivered with computer.-controlled olfactometer [(5,6)]. The impact of different airflows (2 L/min and 4 L/min) and solubilities (L-carvone as an odorant with high solubility in water [367 mg/L water] and farnesol with low solubility [1.7 mg/L water]) were compared in experiment A (stimulus duration 2 s). Experiment B was designed to explore the effect of the site of stimulus presentation, whether it was more or less distant from the olfactory cleft. One stimulus presentation site was at the naris, at the entrance to the nose (with stimuli being released through a Teflon® tubing the opening of which was placed approximately 1 cm into the nasal cavity beyond the nasal valve). The other stimulus presentation site was approximately 6 cm deep inside the nasal cavity with the opening of the tubing at the level of the insertion of the middle turbinate. The outer diameter of the tubing was 4 mm, the inner diameter 2 mm (total airflow 8 l/min; stimulus duration 250 ms). The tubing was placed under endoscopic control. It was kept in place through a frame similar to lens-less glasses [(7)]. The ancillary experiment C was designed to explore the effect of trigeminal activation and lateralization of L-carvone and farnesol, using the principles of odor lateralization [(8)].

We found that: for experiment A, the repeated measurement analysis showed that Flow ($F=110.9$, $P<0.001$) and Odor ($F=21.0$, $P<0.001$) had significant effects on intensity. Specifically, the intensity of stimuli presented at 4 L/min was higher than during the 2 L/min condition, and intensity of L-carvone were higher than those for farnesol (Table 1 and Figure 1). No significant interaction was found between Odor and Flow on intensity ($F=0.9$, $P=0.35$). Additionally, Flow ($F=6.2$, $P=0.017$) had a significant effect on pleasantness, with odors being rated as more pleasant at 2 L/min than at 4 L/min. No significant effect was found for Odor ($F=0.11$, $P=0.74$), and there was no interactive effect between Odor and Flow on pleasantness ($F=0.12$, $P=0.73$).

For experiment B (descriptive statistics of intensity and pleasantness ratings listed in Table 2), there was no significant difference between Nostril and Turbinate on intensity nor pleasantness. (Table 2 and Figure 2). Experiment C performed in 6 healthy, normosmic subjects (2 men, 4 women; age range 24-33 years) showed that neither L-carvone (lateralization score from a total of 10 lateralization trials per subject: 5.83±2.17) nor farnesol (lateralization score: 5.17±2.17) had significant trigeminal activity (10 means the stimulus can be perfectly lateralized. and 5 means random perfomance), and the two odors were not different in

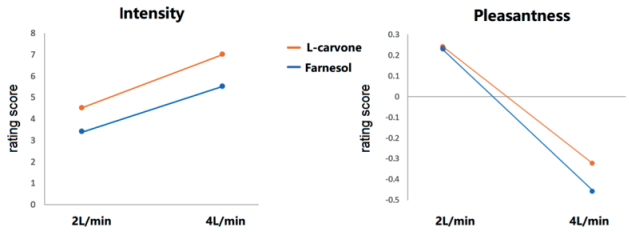

Figure 1. The effect of odors and flow on average odor intensity and pleasantness.

For experiment B (descriptive statistics of intensity and pleasantness ratings listed in Table 2), there was no significant difference between Nostril and Turbinate on intensity nor pleasantness. (Table 2 and Figure 2). For the complained side effects, there were 5 in Nostril condition and 17 in Turbinate condition.

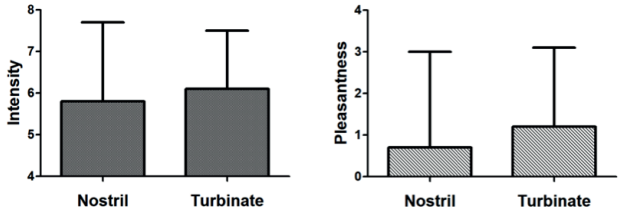

Figure 2. Average intensity (left) and pleasantness ratings (right) separately for the two sites of stimulus administration, nostril and middle turbinate (means ± standard deviations).

terms of lateralization scores (t=2.57, P=0.53).

Consistent with previous studies, we found that intensity ratings increased with an increase of airflow and solubility. However, different from our predictions, there was no interaction between factors "airflow" and "solubility". This was also contrary to results by Sobel et al. who showed that an increase in intensity would be less pronounced in odorants with low solubility compared to highly soluble odorants because of their different sorption patterns to the nasal epithelium [9]. However, it should be recognized that the observations by Sobel et al. were based on flow changes during the nasal cycle which may have been more pronounced than the currently used flows of 2 and 4 L/min. Future studies using more extreme differences between flow rates may be needed to further explore the interactive effect between nasal airflow and odorant solubility. Still, it can be stated that an increase of the nasal airflow by 100% had no significant effect on odor intensity in relation to the solubility of odorants.

We also explored the influence of airflow and solubility on odor pleasantness. Both L-carvone and farnesol were largely rated as "neutral" by the subjects, and there was no significant difference between these two odors. "High flow" significantly decreased

Table 1. Intensity and pleasantness ratings of odors for different airflows, separately for the left and right sides (means ± standard deviations).

	L-Carvone		Farnesol	
	2L/min	4L/min	2L/min	4L/min
Intensity	4.5±1.9	7.0±1.5	3.4±1.9	5.5±2.5
Pleasantness	0.2±1.3	-0.3±2.0	0.2±1.3	-0.5±1.8

Table 2. Intensity and pleasantness separately for the sites of stimulation (means ± standard deviations).

	Nostril	Turbinate	t	P
Intensity	5.8±1.4	6.1±1.9	0.923	0.363
Pleasantness	0.7±2.3	1.3±1.9	1.777	0.085

the pleasantness and shifted it from the neutral/pleasant side to the unpleasant side. Importantly, the observed differences cannot be attributed to changes in trigeminal activation as shown within a lateralization paradigm. Here it can be assumed that the unpleasant nature of the odors came out more clearly at a higher intensity. Similar to odor intensity, however, the change in airflow did not produce significantly differential judgments in relation to the solubility of the odors.

Previous research suggested that only approximately 15% of the airflow reaches the olfactory epithelium during normal breathing [10]. Therefore, higher odor intensities may be achieved by a more direct application of the odor to the olfactory epithelium. However, the current results showed that in the case of the odor release at the level of the head of the middle turbinate, odor intensity increased only minimally, and there was no significant difference between the odor release at sites that were anatomically closer or more distant from the olfactory epithelium. The reason for this surprising effect may be that the stimulus concentration might have been too high. The assumption then would be that such an effect would only be visible at lower concentrations or at threshold levels. Similarly, there was no significant difference in pleasantness ratings between the two application conditions.

In conclusion, the present study suggests that a change of the position of intranasal odor release has no major effect on the perception of odors presented at higher suprathreshold levels. However, intranasal airflow affected intensity and pleasantness, confirming previous studies.

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Authorship contribution

BC: conception and design, acquisition of data, analysis and interpretation of data; drafted the article. AP: conception and

design, acquisition of data. PN: interpretation of data; revised the manuscript critically for important intellectual content. TH: conception and design, acquisition of data, analysis and interpretation of data; revised the manuscript critically for important intellectual content. All authors gave final approval of the version to be published.

Conflict of interest

The authors have no conflicts of interest to declare.

Statement of Ethics

This study was conducted in accordance with the guidelines of the Declaration of Helsinki, the retrospective protocol was approved by the Ethics Committee at the TU Dresden (protocol number EK297082014).

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