

# Comment on "Analyzing various factors in the association between olfaction and perceived nasal patency" by Chao et al.\*

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## Dear Editor:

We read with pleasure the article by Chao et al. <sup>(1)</sup> that investigated the effects of olfactory stimuli on perceived nasal patency for participants with normative olfaction and participants with dysfunctional olfaction. We offer additional commentary on the extrapolated conclusions and we hope these perspectives provide insight into areas that may require further research and improvement.

Firstly, it is important to note that this study does not consider the effects of socioeconomic status (SES) and participants' lived environments on olfaction. Numerous studies indicate lower SES is correlated with significantly increased exposure to airborne pollutants throughout individuals' lived environments <sup>(2)</sup>. Exposure to airborne pollutants is also implicated in altering individuals' olfaction capabilities <sup>(3)</sup>. A study found that residents of Mexico City, who face high levels of ambient exposure to air pollution, had abnormal anatomic findings in the olfactory bulb and were outperformed in olfactory function testing when compared to lifelong residents of low-polluted towns <sup>(4)</sup>. Another study found that a population from the Mexican state of Tlaxcala, a region with lower pollution but still geographically comparable to Mexico City, could better discriminate between odors and could detect 2-phenyl ethanol at significantly lower concentrations when compared to a sample population from the highly air-polluted Mexico City <sup>(5)</sup>. This finding is especially significant when we consider that 2-phenyl ethanol was utilized as the olfactory-specific odor in Chao et al. and was a player in the study's conclusions. Without accounting for and controlling for the possible impact of pollutant exposures, data collected for participants in both the normosmic and dysfunctional olfaction groups in Chao et al. may be skewed and less generalizable than it is concluded to be.

Additionally, it was observed in the discussion of the exclusion criteria that the authors did not explicitly distinguish between the causative agent of olfactory loss for participants in the olfactory dysfunction group. Since this study aims to examine

the impact of olfactory stimuli on nasal patency, it is relevant to acknowledge that variable causes of olfactory impairment could result in varied sensitivity to certain scents, which may skew the results for this group. Studies have shown that olfactory dysfunction secondary to head trauma is a common condition and that anosmia may result in up to 21.6% of patients who experience traumatic brain injuries (TBI) <sup>(6)</sup>. While the recovery time for post-traumatic olfactory dysfunction often occurs within a couple of months of the injury, a case study found that recovery from trauma-related anosmia may occur years after the initial injury <sup>(7)</sup>. Another study on olfactory dysfunction after TBI showed that many patients developed anosmia, with only a small proportion regaining normal olfactory function, indicating the potential long-term impact of head trauma on the sense of smell <sup>(8)</sup>. Of the population that did improve following injury, many continued to have distorted olfactory perception, even after an eight-year recovery period. This finding is relevant when considering that within the exclusion criteria utilized by Chao et al., the source of olfactory impairment is not directly stated. Including the distinguishing cause of olfactory loss, whether congenital or acquired, may help prevent any skews from being present in results drawn within this group.

Overall, the authors conducted an extensive study examining the effects of olfactory stimulation on the perception of nasal patency. It is important to consider variables, such as SES, that may influence the environment in which individuals live and pollutants that they may be exposed to. Future studies should aim to control for potential confounding variables and ensure that the inclusion criteria provides a cohort that yields more generalizable results.

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## Authorship contribution

WB, PH, LVG: study design and conception, data collection, data

interpretation, drafting the article, and revising the article for important intellectual content. MJ: Data collection and revising the article for important intellectual content. IG: Statistical analysis and revising the article for important intellectual content. RS: Initial study proposal, data interpretation and revising the article for important intellectual content. BS, KT: Data interpretation,

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### Conflict of interest

The authors declare no conflict of interest.

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## Reply by Chao and Hummel

We would like to express our sincere appreciation for the valuable suggestion from DiPalma et al. and would like to respond to their comments. Firstly, we want to clarify that all participants in our study were investigated at a single location in Dresden, Germany. While we acknowledge that environmental factors can potentially impact baseline olfactory capability, it is important to note that our participants were exposed to similar environmental conditions. We understand DiPalma et al.'s argument regarding the potential influence of airborne pollution on odor discrimination and sensitivity. However, we want to emphasize that our study focused specifically on the sensation of nasal patency rather than the intensity or recognition of specific odors. Secondly, we agree that considering the etiologies of olfactory loss is an important factor to be addressed in future follow-up studies. However, for this pilot study, we did not have any specific hypotheses regarding the influence of various causes of olfactory loss on the interaction between the sensation of nasal patency and olfactory stimulation. Our primary aim was to examine the overall impact of olfactory loss on perceived airflow. It is worth noting that distorted olfactory perception, or parosmia, can occur not only in cases of traumatic brain injury but also in other conditions such as upper respiratory airway infections (especially COVID-19), sinonasal diseases, neurological / psychiatric disorders, exposure to toxic chemicals, or chemotherapy<sup>(1)</sup>. Since olfactory loss from all kinds of causes can potentially lead to parosmia and subsequent distortion of nasal patency sensation, it is not necessary to differentiate the specific etiology

in this current study. Instead, it is more appropriate to take into account the presence of parosmia, which can be challenging to recognize and quantify.

Furthermore, we would also like to highlight that investigating different etiologies targeting distinct levels of the olfactory system, from the olfactory mucosa to the olfactory bulbs and olfactory cortices in the brain, could serve as experimental controls to determine the location of interaction between the olfactory and trigeminal systems in terms of airflow perception. We encourage future research to address this issue and provide further insights into the sensation of nasal patency triggered by olfactory stimulation.

Once again, we extend our gratitude to DiPalma et al. for their input, which has enriched the discussion surrounding our study.

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