Mucus transport in the olfactory cleft is significantly slower than in the nasal respiratory mucosa

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Dear Editor:

Intranasal mucociliary transport has been conventionally described as moving, essentially, in an anterior-to-posterior direction along the ciliated respiratory mucosa (RM) [1–3]. This mechanism is essential for clearing inhaled particles and pathogens and may be impaired in individuals with certain genetic conditions or infections [4]. However, little is known about mucus movement in the olfactory cleft (OC), a narrow area that poses technical challenges for observation and instrumentation. Understanding mucus movement in this region may provide insight into the location of olfactory epithelium, which is relevant for research, drug delivery, and surgical planning.

We explored whether intranasal application of methylene blue dye could reveal differential mucus movement over the OC compared with the RM. The saccharine test, an established but limited method of mucociliary assessment, has demonstrated normal mucociliary clearance from the inferior turbinate to the hypopharynx within 15 minutes [5]. However, previous observations have suggested that mucus movement tracked visually with methylene blue dye can cover approximately one-third of the nasal cavity length in around 2.5 minutes. Based on this, we hypothesized that regions with cells carrying non-motile cilia, such as the olfactory epithelium in the OC, would retain dye longer than the surrounding RM.

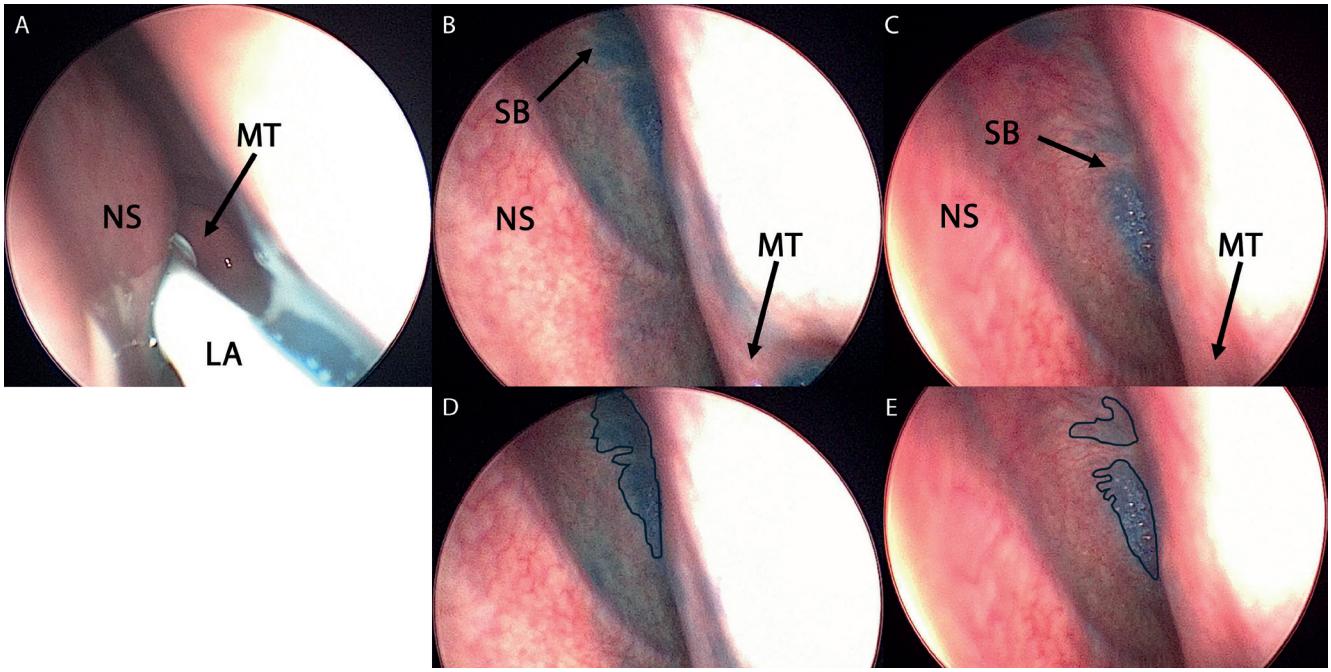
In this observation, four healthy adults with normal olfactory function (based on "Sniffin' Sticks" 16-item odor identification test, mean identification score = 15) and septal deviation (3 women, median age = 23.5), allowing lateralized endoscopic access, were seated upright with their head on a chin and forehead rest [6]. They received 2 sprays (0.13 ml each) of methylene blue (1 drop of dye in 10 ml water) via a long applicator pump atomizer. A 30° rigid nasal endoscope with Telepack (Karl Storz, Tuttlingen, Germany) guided and recorded dye placement. No decongestants were administered. Procedures were video recorded for at least five minutes after dye placement, exceeding durations previously documented for anterior RM. Dye retention and movement were visually assessed; no quantitative measurements were made.

Dye sprayed over the OC (limited by the skull base, anteriormost border of the middle turbinate, and the nasal septum, corresponding to a similar area where olfactory epithelium was found in a previous study [7]) persisted throughout the five-minute recordings. Although the area decreased in size, the original shape of the dye placement remained visible. This pattern suggests that clearance in this area may be slower than in adjacent areas. Differences in ciliary function (e.g., presence of non-motile cilia) or other regional mucosal properties could contribute to this pattern and warrant further investigation. While the movement in the OC was slower, it was not absent.

Limitations include the small sample size, inability to standardize spray volume due to instrument constraints, and subjective assessment of clearance. No biopsies were performed, and findings should therefore be interpreted as preliminary and observational.

Despite these limitations, this observation suggests a potential minimally invasive method for indicating regions of olfactory epithelium based on mucus transport. Such a method could provide a practical approach for studies requiring avoidance of olfactory regions or for surgical planning where preservation

Figure 1. Endoscopic visualization of methylene blue transport in the olfactory cleft.



A: Methylene blue dye placement in the olfactory cleft (OC). B-C: Dye in the OC at 1 minute 30 seconds (B) and at 5 minutes (C), demonstrating slower clearance over time. D-E: Outlined dye areas at 1 minute 30 seconds (D) and 5 minutes (E), highlighting persistent retention in the OC. NS: Nasal septum, MT: middle turbinate, LA: long applicator, SB: skull base.

of olfactory function is critical. Dye retention may offer a rapid and accessible alternative to approximate olfactory epithelial boundaries prior to tissue sampling.

Future work should focus on refining the methodology, standardizing spray volume and delivery device, evaluating movement markers in mucus with varying properties (volume and viscosity), recruiting additional participants, and measuring dye movement more objectively. Larger studies could determine whether intranasal dye retention consistently differentiates olfactory from respiratory regions confirmed with biopsy and validate its use as a mapping tool. Further, ex vivo studies using mucosal biopsies have the potential to analyze a higher number of specimen in parallel [8].

Conclusion

Prolonged retention of intranasal dye observed within the OC reflects region-specific mucus transport and may serve as a practical indicator of potential olfactory epithelium in the future. This approach holds promise for research applications, clinical assessment, and surgical planning in the nasal cavity. With further validation and methodological refinement, it may offer an observational approach to better understand and preserve olfactory function.

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Authorship contribution

AKH and TH conceived the observation. AKH and SB collected and analyzed the data. AKH drafted the manuscript. All authors revised and approved the final manuscript.

Conflict of interest

Since 2022 T.H. collaborated with the following companies: Sony, Tokyo, Japan; Smell and Taste Lab, Geneva, Switzerland; Takasago, Paris, France; Cyrano, Delray Beach, FL, USA; Cynexo, Trieste, Italy; Sentosphere, Paris, France; NOAR, Sao Paulo, Brazil; Baia Foods, Madrid, Spain; Burghart, Holm, Germany. The remaining authors declare no conflicts of interest.

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