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SARS-CoV-2 vaccination may help patients with persistent COVID-19 smell dysfunction

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Dear editor,

Olfactory dysfunction (OD) is recognized as a key symptom of coronavirus disease 2019 (COVID-19). Early olfactory loss is due to injury to the olfactory epithelium, with the initial insult to sustentacular cells leading to loss of function of the olfactory sensory neurons and loss of cilia on the neurons.[1,2] In most cases, neurons survive, sustentacular cells recover and olfaction improves in a few weeks following the COVID-19 infection.[2] According to psychophysical evaluations, OD may last more than 6 or 12 months in 1 to 10% of cases;[3-5] these patients are considered as having persistent hypo- or anosmia. The pathophysiological mechanisms underlying the persistence of OD in patients with a history of COVID-19 remain unclear and poorly investigated. From a physiological standpoint, the spread of the virus into the olfactory bulb leads to lesions of sustentacular cells: the cells expressing angiotensin-converting enzyme-2 (ACE2).[6] Olfactory neurons poorly express the virus receptor or not at all.[6] The regeneration of sustentacular cells occurs in few weeks[7] and is clinically associated with the recovery of smell within that period. Considering these findings, the persistence of OD in some patients raises many questions about the pathophysiological mechanisms of OD. In this letter, we aim to propose a potential hypothesis based on some recent clinical observations.

Since the development of vaccination in Western countries, we observed that some patients with persistent COVID-19 OD recovered in the weeks following the administration of vaccine against SARS-CoV-2. Although it is currently difficult to demonstrate potential association between vaccination and smell recovery, some findings may support that persistent OD could be due to the persistence of virus in the olfactory epithelium and region.

Firstly, our team found that patients with poor olfactory outcomes at 60 days post–COVID-19 reported lower levels of salivary and nasal immunoglobulin G (IgG) and IgG1, supporting a lower local immune response than in those who experienced rapid olfactory recovery.[8] The differences in immune response between patients with persistent OD and those without OD were supported by the study of de Melo et al.[9] In this study, authors observed, in a murine model, that SARS-CoV-2 induced acute anosmia and ageusia with both lasting as long as the virus remained in both the olfactory epithelium and bulb. Interestingly, they observed persistence of viral transcripts and of SARS-CoV-2–infected cells from olfactory mucosa sampling of patients with long-term persistence of anosmia.[9] However, olfactory region abnormalities were observed in imaging study several months after the onset of OD, which may support the persistence of inflammatory reaction in patients who did not report COVID-19 general symptoms.[10]

According to these findings and our clinical observations, we believe that the persistence of OD in COVID-19 patients could be related to the persistence of the virus in the olfactory region, which induces a chronic inflammatory reaction characterized by the destruction of re-infected cells throughout the recovery process, that is, neuroepithelium cells, sustentacular cells and olfactory neurons. Interestingly, it has been supported that inflammation may suppress regeneration of the olfactory stem cells.[11] In this way, we believe that the administration of vaccine may stimulate the local and systemic

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immune response against the virus, 'cleaning' the olfactory region from the remaining viruses, allowing the regeneration of stem cells. Future controlled studies are needed to compare the evolution of olfactory outcomes of patients with persistent OD according to the vaccine status of patients. Recent studies have shown that SARS-CoV-2 can be detected in immunologically privileged tissues, such as the testicles, without significant immune response.[12] Further studies are needed to test the hypothesis that the olfactory bulb could be considered as an additional anatomical region not exposed to a significant immune response, allowing for persistence of SARS-CoV-2.

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References

1. Vaira LA, Hopkins C, Sandison A, et al. Olfactory epithelium histopathological findings in long-term coronavirus disease 2019 related anosmia. *J Laryngol Otol*. 2020;134(12):1-5. doi:10.1017/S0022215120002455.
2. Brookes NRG, Fairley JW, Brookes GB. Acute olfactory dysfunction-a primary presentation of COVID-19 infection. *Ear Nose Throat J*. 2020;99(9):94-98. doi:10.1177/0145561320940119.
3. Boscolo-Rizzo P, Guida F, Polesel J, et al. Self-reported smell and taste recovery in coronavirus disease 2019 patients: a one-year prospective study. *Eur Arch Otorhinolaryngol*. 2021;7:1-6. doi:10.1007/s00405-021-06839-w.
4. Lechien JR, Chiesa-Estomba CM, Beckers E, et al. Prevalence and 6-month recovery of olfactory dysfunction: a multicentre study of 1363 COVID-19 patients. *J Intern Med*. 2021;290:451-461. doi:10.1111/joim.13209.
5. Petrocelli M, Cutrupi S, Salzano G, et al. Six-month smell and taste recovery rates in coronavirus disease 2019 patients: a prospective psychophysical study. *J Laryngol Otol*. 2021;135(5):436-441. doi:10.1017/S002221512100116X.
6. Lechien JR, Radulesco T, Calvo-Henriquez C, Chiesa-Estomba CM, et al. ACE2 & TMPRSS2 expressions in head & neck tissues: a systematic review. *Head Neck Pathol*. 2021;15(1):225-235. doi:10.1007/s12105-020-01212-5.
7. Anders JJ, Johnson JA. Transection of the rat olfactory nerve increases glial fibrillary acidic protein immunoreactivity from the olfactory bulb to the piriform cortex. *Glia*. 1990;3(1):17-25. doi:10.1002/glia.440030104.
8. Saussez S, Sharma S, Thiriard A, et al. Predictive factors of smell recovery in a clinical series of 288 coronavirus disease 2019 patients with olfactory dysfunction. *Eur J Neurol*. 2021. doi:10.1111/ene.14994.
9. de Melo GD, Lazarini F, Levallois S, et al. COVID-19-related anosmia is associated with viral persistence and inflammation in human olfactory epithelium and brain infection in hamsters. *Sci Transl Med*. 2021;13(596):eabf8396. doi:10.1126/scitranslmed.abf8396.
10. Güney B, Bacaksızlar Sarı F, Özdemir MY, Çullu N, Doğan E, Togan T. Changes in olfactory bulbus volume and olfactory sulcus depth in the chronic period after COVID-19 infection. *Acta Oto-Laryngologica*. 2021;141:786-790. doi:10.1080/00016489.2021.1946138.
11. Chen M, Reed RR, Lane AP. Chronic inflammation directs an olfactory stem cell functional switch from neuroregeneration to immune defense. *Cell Stem Cell*. 2019;25(4):501-e5.
12. Bhattacharya K, Mukhopadhyay LD, Goswami R, et al. SARS-CoV-2 infection and human semen: possible modes of contamination and transmission. *Middle East Fertil Soc J*. 2021;26(1):18. doi:10.1186/s43043-021-00063-6.