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Long-term Olfactory and Gustatory Dysfunction May Be Related to Neural Damage

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We appreciated the interest of Liu and Yu in our study[1] and would like to take this opportunity to comment on the pressing issue of persistent SARS-CoV-2–related chemosensory dysfunctions. Indeed, screening efforts following the first epidemic peak showed that a significant proportion of patients with COVID-19 might have mild or no symptoms at all: this evidence reinforces the diagnostic value of olfactory dysfunction (OD) and gustatory dysfunction (GD), especially as early complaints or in otherwise asymptomatic patients.[2] In fact, we previously demonstrated that OD and GD occurred as the first symptoms in 10% and 11% of cases, respectively.[3]

Moreover, in our prospective study, we observed that a significant proportion of patients complained of persistent OD and GD even after 2 negative nasopharyngeal swabs (NPSs). Similar results were reported by Yan et al.[4] However, in our cohort, patient number and follow-up time were insufficient to justify a correlation analysis. Still, we commented that resolution was not strictly related to NPS negativity. Evidently, the possibility of a false-negative result on reverse transcription polymerase chain reaction should also be taken into account, and only long-term follow-up will potentially give validity to such an observation.

As Liu and Yu correctly pointed out, OD and GD may be secondary to high nasal/oral viral load, leading to subsequent neural damage. In this view, while SARS-CoV-2 infection surely represents the index event leading to such neural impairment, it may not be strictly correlated to the recovery timing. Indeed, the OD/GD recovery rate may be more plainly related to the entity of the initial damage and rate of subsequent neural regeneration. In fact, 2 consecutive negative NPSs are likely to be indicative of an extremely low viral load or an absence of virus at all. The presence of sensorineural symptoms in these patients could demonstrate a poor correlation between viral load and neural damage in the recovery phase, differently from the onset period. This aspect supports the hypothesis that virus-induced neural impairment may last longer than the presence of the virus itself. In particular, Tsivgoulis et al[5] demonstrated that prolonged SARS-CoV-2–induced OD was significantly associated with lower olfactory bulb height bilaterally as compared with controls. This finding is consistent with the development of postinfection olfactory bulb atrophy, which possibly explains the persistent OD. Interestingly, this is supported by reports showing OD persistence after patient recovery and NPS negativity,[6] with objective impairment observable even at 6 months from the onset of symptoms.[7,8]

Finally, we believe that specific pathophysiologic studies are strongly warranted to definitely clarify this issue and ultimately optimize patient management.

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