Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Reply to "MRI Evaluation of the Olfactory Clefts in Patients with SARS-CoV-2 Infection Revealed an Unexpected Mechanism for Olfactory Function Loss"

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We read with great interest the letter by Eliezer and Hautefort discussing our recent report in *Academic Radiology* of magnetic resonance imaging (MRI) findings in a patient with coronavirus disease-2019 (Covid-19) and enumerating the possible mechanisms of SARS-CoV-2-induced anosmia (1).

Our report (2) along with a similar report from Eliezer et al. (3) were the first MRI studies of olfactory bulb in anosmia of Covid-19, revealing normal olfactory bulb size and signal intensity despite a complete loss of olfaction. In their letter, Eliezer et al. state that "However, we were confused by their interpretation of the MRI since a bilateral obstruction of the olfactory clefts, below the olfactory bulbs, is observed, as has been described in our first report." We performed the MRI in a healthy young man with persistent isolated anosmia lasting for 6 weeks without any sinonasal symptoms. In addition to revealing no significant change in the olfactory bulb size and signal intensity, the MRI revealed no sinonasal mucosal abnormality and patent olfactory clefts, which is consistent with the clinical absence of sinonasal symptoms, and indicates a sensorineural mechanism for anosmia in our patient. Finding of bilateral obstruction of olfactory clefts by Eliezer et al. suggests that a conductive mechanism may have (also) been responsible for anosmia of Covid-19 in their patient.

We agree with the authors that differential gene expression in the olfactory epithelium and olfactory neurons may have important pathophysiological implications in anosmia of Covid-19. Nonetheless, there are various subtypes of respiratory epithelial cells including basal cells, ciliated cells, brush/microvillar, and secretory goblet cells, which may act as the entry sites for SARS-Cov-2 (4). SARS-CoV-2 engages angiotensin-converting enzyme 2 (ACE2) as the entry receptor and employs the cellular serine protease TMPRSS2 for S protein priming (5). The olfactory sensory neurons do not express ACE2 and TMPRSS2, which is in contrast to nasal respiratory epithelium, stem cells and olfactory epithelial support cells (6). Indeed, recent studies have shown that expression of ACE2 and TMPRSS2 on non-neuronal cells may act as viral reservoir and be responsible for SARS-Cov2 entry (6), which may result in anosmia.

In the apparent absence of anatomical changes on MRI and to assess a putative loss of neuronal function in anosmia of Covid-19, we performed ^{18}FDG PET/CT scan in a patient with isolated anosmia under neutral olfactory condition, which revealed hypoactivity of the left orbitofrontal cortex, thus suggesting a probable neuroinvasive mechanism for anosmia of Covid-19 (7). Further basic, clinical, imaging, and functional studies are needed to fully elucidate the underlying mechanisms for SARS-Cov-2-induced anosmia.

AUTHOR CONTRIBUTION

M.K. has performed the literature search, and M.K. and S.H. have written the article.

DECLARATION OF COMPETING INTEREST

M.K. and S.H. report no conflict of interest or funding sources.

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