Absent Blood Oxygen Level–Dependent Functional Magnetic Resonance Imaging Activation of the Orbitofrontal Cortex in a Patient With Persistent Cacosmia and Cacogeusia After COVID-19 Infection

Ismail Ibrahim Ismail, MSc; Khaled A. Gad, MD

A 25-year-old woman with no relevant medical history developed fever, generalized body pain, dry cough, anosmia, and ageusia in April 2020. She was diagnosed with coronavirus disease 2019 (COVID-19) by positive findings on polymerase chain reaction assay and positive findings on computed tomography of the chest. Her clinical course was uncomplicated, and she was treated conservatively. Anosmia and ageusia started to improve during the following month. However, during the recovery phase, she started to experience offensive odor (cacosmia) and taste (cacogeusia) with stimulation of these sensations. Ear, nose, and throat evaluation showed normal clinical and endoscopic nasal examination findings. Computed tomography findings of the paranasal sinuses were unremarkable. She was given oral and intranasal corticosteroids, in addition to multivitamins, zinc, and olfactory training. However, her symptoms persisted for 3 months, and she was referred to our neurology clinic for further evaluation. Findings of her neurological examination were normal.

Magnetic resonance imaging (MRI) of the brain revealed normal findings, including the olfactory bulbs and sulci, which showed no structural or signal abnormality (Figure 1A). A task-based functional MRI (fMRI) study was designed as alternating blocks of smell activation by a pleasant scent intervened with periods of rest. Blood oxygen level-dependent (BOLD) activation maps were generated and fused to T1-weighted multiplanar images. There was absent activation in the region of the orbitofrontal cortex (OFC), while the right uncus/piriform cortex demonstrated strong BOLD signal (Figure 1B and Figure 2).

Discussion
The association of COVID-19 with olfactory and gustatory dysfunction is evident and recognized among its cardinal symptoms, although smell seems to be more affected than taste. In a 2020 meta-analysis, alteration in smell (dysosmia, hyposmia, and anosmia) and taste (dysgeusia, hypogeusia, and ageusia) was estimated to affect 52.7% and 43.9%, respectively, of patients recovered from COVID-19 infection. While olfactory dysfunction in association with viral infection can be secondary to peripheral causes (eg, nasal congestion and rhinitis), COVID-19 is less commonly associated with these symptoms, and a central cause of olfactory processing is thought to be the underlying etiology, based on the potential neurotropic features of severe acute respiratory syndrome coronavirus 2.

Olfactory perception is a complex and sophisticated process that involves different parts of the brain. In normal individuals, several fMRI studies have shown an almost consistent pattern of BOLD activation of primary (eg, piriform cortex, amygdala, and entorhinal cortex) as well as secondary (eg, OFC, hypothalamus, and insula) olfactory areas. OFC contains the secondary and tertiary olfactory and gustatory cortex areas, where processing of this information occurs.

There is accumulating evidence of implication of OFC in patients with COVID-19 with olfactory dysfunction. A recent study reported hypometabolism of OFC using fluorodeoxyglucose positron emission tomography, while another report documented...
right OFC hyperintensity on brain MRI with frontal electroencephalography abnormalities in such patients. Moreover, Politi et al described transient cortical fluid-attenuated inversion recovery hyperintensity in the right gyrus rectus, suggesting that severe acute respiratory syndrome coronavirus 2 might invade the brain through the olfactory pathway and cause an olfactory dysfunction of sensorineural origin.

The utility of fMRI in patients with COVID-19 is not well established, and to our knowledge, this is the first published report using fMRI in a patient with persistent cacosmia and cacogeusia after COVID-19 infection. Given these findings, we could suggest central olfactory pathway impairment, mainly involving OFC, may be involved in the underlying etiology of persistence of olfactory and gustatory symptoms in patients after COVID-19 infection.

ARTICLE INFORMATION
Author Affiliations: Department of Neurology, Ibn Sina Hospital, Sabah Health Region, Kuwait (Ismail); Department of Radiology, Ibn Sina Hospital, Sabah Health Region, Kuwait (Gad); Diagnostic Radiology Department, Faculty of Medicine, Suez Canal University, Ismailia, Egypt (Gad).

Corresponding Author: Khaled A. Gad, MD, Department of Radiology, Ibn Sina Hospital, Gamal Abdel Nasser St, Sabah Health Region, Kuwait (khaledgad611@gmail.com).

Published Online: January 22, 2021. doi:10.1001/jamaneurol.2021.0009

Conflict of Interest Disclosures: None reported.
Additional Contributions: We thank the patient for granting permission to publish this information.

REFERENCES