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Letter to the Editor

Does thickening or enhancement of the olfactory cleft on MRI explain anosmia/hyposmia in COVID-19 patients?

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We read with interest the article by Cetin *et al.* about a retrospective olfactory magnetic resonance imaging (MRI) study of 15 patients with anosmia (n=10) respectively hyposmia (n=5) ^[1]. It was found that eight patients had thickening in the olfactory cleft region and that nine patients showed enhancement of the olfactory cleft region ^[1]. One patient each had hyperintensities on diffusion-weighted imaging (DWI) imaging in the corpus callosum splenium, thalamus medio-dorsal nucleus, and mesencephalon respectively ^[1]. It was concluded that anosmia correlates with the MRI findings ^[1]. The study is appealing but carries limitations that raise concerns and should be discussed.

We disagree with the conclusion that MRI findings correlate with the sensory deficit ^[1]. Patient 14 (14yo male) had a DWI lesion in the corpus callosum but normal olfactory cleft ^[1]. The callosal lesion does not explain anosmia, which is why there is no relation between MRI and the sensory deficit in this patient. A further argument against a correlation is that no information was provided in how many patients anosmia was unilateral and in how many bilateral. In other words, was anosmia truly unilateral among the three patients with unilateral thickening of the olfactory cleft region and was anosmia bilateral among the five patients with bilateral thickening? Likewise, we should know whether enhancement of the cleft region correlated with the clinical presentation. In particular, did all five patients with bilateral enhancement also present with bilateral anosmia and the four patients with unilateral enhancement with unilateral anosmia? Final conclusions about a correlation between imaging and clinical presentation cannot be drawn as long as this fundamental information is not provided.

Regarding the three patients with cerebral DWI hyperintensities, we should be informed if they were further investigated for ischemic stroke or encephalitis. Both have been repeatedly reported as complications of SARS-CoV-2 infections ^[2, 3]. We should know if these three patients were further investigated for encephalitis by means of a lumbar puncture. Of particular interest is, whether there was pleocytosis in any of the three or whether the RT-PCR was positive for the virus in the CSF. Because DWI hyperintensity not necessarily means cytotoxic edema, we should know whether the DWI hyperintense lesions were hypo- hyper- or iso-intense on apparent diffusion coefficient (ADC) maps.

A pathophysiological mechanism to explain anosmia/hyposmia not considered is the binding of virus particles to olfactory receptors on the surface of the olfactory cells. If these receptors are blocked by the virus, no olfactory stimuli can be passed on to the brain at the olfactory epithelium. In this case, there may be also absence of MRI abnormalities, such as thickening, enhancement, or cytotoxic edema.

Patients 4 (27yo female) had hyperintensity of the medio-dorsal thalamic nucleus on diffusion-weighted imaging (DWI) and simultaneously thickening and enhancement of the olfactory cleft ^[1]. We should know which of these lesions was made responsible for anosmia.

Overall, the interesting study has limitations that call the results and their interpretation into question. Clarifying these weaknesses would strengthen the conclusions and could improve the study. Before explaining anosmia/hyposmia solely by olfactory MRI findings, alternative pathophysiological explanations should be considered and more detailed clinical information should be provided.

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