

## CLINICAL LETTER

# Systematic MRI in persistent post-Covid-19 olfactory dysfunction should be reassessed

Ioana Brudasca MD<sup>1</sup> | Quentin Lisan MD, PhD<sup>2</sup> | Romain Tournegros MD<sup>1</sup> |  
 Moustafa Bensafi PhD<sup>3</sup> | Camille Ferdenzi PhD<sup>3</sup> | Arnaud Fournel PSM<sup>3</sup> |  
 Luna Denoix PSM<sup>1</sup> | Stéphane Tringali MD, PhD<sup>1,4</sup> | Maxime Fieux MD<sup>1,4,5,6</sup> 

<sup>1</sup>Service d'ORL, d'otoneurochirurgie et de chirurgie cervico-faciale, Centre Hospitalier Lyon Sud, Hospices Civils de Lyon, Pierre Bénite, France

<sup>2</sup>Service d'ORL et chirurgie cervico-faciale, Foch Hospital, Ecole de médecine, Université Versailles Saint-Quentin-en-Yvelines (Paris Saclay University), Suresnes, France

<sup>3</sup>Inserm U1028 - CNRS UMR 5292, Bron, France

<sup>4</sup>Université de Lyon, Université Lyon 1, Lyon, France

<sup>5</sup>Univ Paris Est Creteil, INSERM, IMRB, Créteil, France

<sup>6</sup>CNRS EMR 7000, Créteil, France

## Correspondence

Maxime Fieux, MD, Service d'ORL, d'otoneurochirurgie et de chirurgie cervico-faciale, Hospices Civils Lyon, Centre Hospitalier Lyon Sud, 165 Chemin du Grand Revoyet, 69310 Pierre-Bénite, France.

Email: [fieux.maxime@gmail.com](mailto:fieux.maxime@gmail.com)

## Abstract

**Background:** Magnetic resonance imaging (MRI) is the gold standard in the etiological assessment of a persistent olfactory dysfunction (OD). While the utility of imaging in COVID-19-related OD has yet to be established, MRI is recommended in all patients with persistent OD. The high prevalence of the latter after SARS-CoV-2 infection means evaluating this strategy is an important public health matter.

**Methods:** The main objective was to examine the impact of systematic MRI on the management of patients with OD. All adult patients consulting for persistent OD (>2 months) after primary SARS-COV-2 infection (PCR) between March 2020 and December 2021 were included ( $n = 67$ ). The secondary objective was to evaluate the relationship between the severity of the OD as measured by psychophysical testing (ETOC) and the volume of the olfactory bulb (OB) measured by MRI.

**Results:** All patients underwent MRI, and none led to a change in diagnosis or treatment. Among them, 82% (55/67) were considered normal by the radiologist on initial interpretation. There were no significant differences (visual analysis or OB volume) between groups (mild, moderate, and severe hyposmia).

**Conclusion:** Systematic MRI may be unnecessary in patients whose persistent OD began soon (a few days) after confirmed SARS-CoV-2 infection.

## KEYWORDS

imaging, olfaction, olfactory disorder

## 1 | INTRODUCTION

Magnetic resonance imaging (MRI) is the gold standard in the etiological assessment of persistent olfactory dysfunction (OD) (>2 months) and is recommended after a

SARS-CoV-2 infection.<sup>1</sup> Given the prevalence of persistent OD after SARS-CoV-2 infection (5%–11%), the relevance of time-consuming and expensive imaging exams remains to be determined, depending on whether they allow to improve the clinical management of patients or not.<sup>2</sup>

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The main objective of this study was therefore to examine the impact of systematic MRI on the management of patients with OD. The secondary objective was to evaluate the relationship between the severity of the OD as measured by psychophysical testing and the volume of the OB measured by MRI.

## 2 | METHODS

This was an observational study (between March 2020 and December 2021) including all adult patients with persistent OD (>2 months) confirmed by an abnormal European Test of Olfactory Capabilities (ETOC) score, after confirmed SARS-Cov-2 infection (by PCR). The ETOC<sup>3</sup> is a 16-step validated psychophysical test for OD. MRI was prescribed in accordance with national recommendations, and the volume of the olfactory bulb (OB) was measured semi-automatically in coronal T2 sections (Figure S1). Patients also had a routine nasofibroscope examination.

## 3 | RESULTS

The 67 patients included (characteristics in Table 1) were classified based on their ETOC score as having anosmia ( $n = 3$ ), severe hyposmia ( $n = 20$ ), moderate hyposmia ( $n = 32$ ), and mild hyposmia ( $n = 12$ ), and their characteristics are summarized in Table S1. The anosmic patients were excluded from analysis between groups because of the small sample size.

All patients (100%, 67/67) underwent MRI and none led to a change in diagnosis or treatment. Among them, 82% (55/67) were considered normal by the radiologist on initial interpretation. The pathological findings (isolated or combined) identified in 12/67 cases were: OB hypotrophy (7/12 patients), T2 hyperintensity in the OB (4/12 patients), T2 hypointensity in the OB (1/12), and uni- or bilateral edema of the OC (5/12 patients) with no difference between groups. Overall, the mean volumes of the right and left OBs were both 40 ( $\pm 10$ ) mm<sup>3</sup>. There were no significant differences in terms of visual analysis or OB volume between the groups of patients considered (mild, moderate, and severe hyposmia, Table 2).

## 4 | DISCUSSION

Among these 67 patients with confirmed SARS-CoV-2 infection, none of the MRI exams altered the initial diagnosis of persistent post-viral smell dysfunction. This suggests that systematic MRI may be unnecessary in patients whose persistent olfactory impairment began soon (a few days) after confirmed SARS-CoV-2 infection. Guidelines for the use of MRI should be based on clinical abnormalities and the likelihood of results leading to changes in treatment.

**TABLE 1** Demographic, epidemiological, and clinical characteristics of patients

Characteristics	Population ( $n = 67$ )
Female gender	77.6% (52/67)
Age (y)	44 ( $\pm 13$ )
Delay COVID-19 <sup>a</sup> – consultation (m)	7 ( $\pm 4$ )
Delay COVID-19 <sup>b</sup> diagnosis – smell disorder (d)	1 ( $\pm 3$ )
Delay Covid-19 diagnosis – MRI (m) <sup>c</sup>	8 ( $\pm 4$ )
Follow up (m)	11 ( $\pm 5$ )
Subjective olfactory dysfunction	
Total	49.2% (33/67)
Partial	47.8% (32/67)
Mild	3.0% (2/67)
Phantosmia	50.7% (34/67)
Parosmia	58.2% (39/67)
Nasal obstruction	12.0% (8/67)
Taste disorders	25.4% (17/67)
Trigeminal symptoms	20.9% (14/67)
Cognitive symptoms	32.8% (22/67)
Hygiene changes	59.7% (27/67)
Dietary changes	40.3% (27/67)
Quality of life alteration <sup>d</sup> :	
Mild	5.1% (3/67)
Moderate	74.6% (44/67)
Major	20.3% (12/67)

The values correspond to the proportions (numbers) for the categorical variables and the means (standard deviation) for the quantitative variables.

Abbreviations: d, days; m, months; MRI, magnetic resonance imaging; y, years.

<sup>a</sup>Delay between COVID-19 PCR or antigenic test diagnosis and ENT smell disorder-specialized consultation.

<sup>b</sup>Delay between COVID-19 PCR or antigenic test diagnosis and smell disorder symptoms.

<sup>c</sup>Delay between COVID-19 PCR or antigenic test diagnosis and MRI realization in months.

<sup>d</sup>Quality of life subgroups: major alteration (9–10/10), moderate alteration (5–8/10), and mild alteration (<5/10).

The delay between the onset of olfactory symptoms and the diagnosis of SARS-CoV-2 infection in these patients was 1 day ( $\pm 3$  days), a clear indication of their association. This is consistent with Saltagi et al.'s conclusions, that although MRI can be used to investigate OD, it is not cost-effective and is of questionable clinical value if no underlying mass or neurological disorder is suspected.<sup>4</sup> Whitcroft and Hummel suggest that MRI should be considered in patients with persistent OD, but point out that the utility of MRI in this context has yet to be established.<sup>1</sup>

MRI findings described in existing studies support some pathophysiological hypotheses for persistent OD in SARS-CoV-2 infection including: (i) transient edema of the OC; (ii) tropism of the SARS-CoV-2 virus for the olfactory epithelium (olfactory nerve thickening); and (iii) central

**TABLE 2** Magnetic resonance imaging (MRI) results according to European Test of Olfactory Capabilities (ETOC) smell disorder intensity subgroup

	Mild (n = 12)	Moderate (n = 32)	Severe (n = 20)	p-value
OB morphological abnormality	8.3% (1/12)	12.5% (4/32)	10.0% (2/20)	1.00
OB T2 hypersignal	9.1% (1/12)	9.4% (3/32)	0.0% (0/20)	0.38
OB T2 hyposignal	0.0% (0/12)	3.1% (1/32)	10.0% (2/20)	1.00
OC oedema	9.1% (1/12)	3.1% (1/32)	10.0% (2/20)	0.49
Volumetric measurements (mm <sup>3</sup> )				
Right OB (mm <sup>3</sup> )	50 (± 10)	40 (± 10)	40 (± 10)	0.58
Left OB (mm <sup>3</sup> )	40 (± 10)	40 (± 20)	50 (± 20)	0.81

The values correspond to the numbers (proportions) for the categorical variables and the means (standard deviation) for the quantitative variables. Abbreviations: OB, olfactory bulb; OC, olfactory cleft; VM, volumetric measure.

neural damage (concordance between MRI evidence of damage [FLAIR hypersignal of the OB or olfactory cortex signal abnormalities] and the persistence of OD); but the exact underlying viral mechanism at the root of the damage remains unclear. In this study, a decrease in OB volume was identified (40 mm<sup>3</sup> on average vs. 65–70 mm<sup>3</sup> in the literature<sup>5</sup>), but there was no significant difference in MRI findings between patients with mild, moderate, or severe hyposmia. These results are consistent with a systematic review of early (< 1 month) versus late MRI results in patients with COVID-19-related OD.<sup>6</sup> Authors found that morphological abnormalities, such as a decrease in OB volume, were frequently detected in later stages.

Although this study was retrospective, it is the largest to date reporting on the association between OB volume and persistent COVID-19 OD. The fact that the MRI matrix sizes and slice thicknesses (1 mm) could not be standardized is a limitation, but all OB volume analyses were performed with the same software.

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## CONFLICT OF INTEREST

All the authors have read and approved the paper's content. No authors have financial or personal conflicts to disclose. Neither the work nor any part of its essential substance, tables, or figures have been or will be published or submitted to another scientific journal or are being considered for publication elsewhere.

## DATA, MATERIALS, AND/OR CODE AVAILABILITY

The data sets used and/or analyzed in the present study are available from the corresponding author on reasonable

request. All methods were carried out in accordance with relevant guidelines and regulations.

## ORCID

Maxime Fieux MD  <https://orcid.org/0000-0001-8317-2286>

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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