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.

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Did we forget the diffuse chemosensory system when studying COVID-19?

SARS-CoV-2 induces chemosensory disorder/dystonia. Eliezer et al. [1] reported the presence of a family of particular olfactory receptors that could be selectively altered by SARS-CoV-2, citing An and Liggett [2], who identified these receptors in central cortical neurons, vascular muscle, and epithelium of the lower airways.

This family of receptors resembles the diffuse chemosensory system (DCS), first described by Sbarbati et al. [3]. The DCS is an anatomical structure composed of solitary chemosensory/chemoreceptor cells (SCCs), which have phenotypic similarities to taste cells but are not aggregated into buds [4,5]. Molecules and receptors thought to be present only in the taste system have also been described in organs of the respiratory and gastrointestinal systems [6–8] such as nose [9], larynx [10], trachea [11–13], lungs [14], pharynx [10], and digestive system [15].

The SCCs located in different anatomical sites show some morphological differences, probably related to the multiple function that they perform in these sites in addition to their receptor function [8,16–18].

An involvement of the olfactory and gustatory systems by COVID-19 has already been demonstrated [19]. For the sense of smell, general dysfunction of the combined threshold, discrimination and identification scores, and individual scores of both discrimination and identification was detected. The gustatory dysfunction was general and particularly significant for sweet and bitter taste [19]. Generally, cellular localisation of SARS-CoV-2 in the nasal cavity, using the viral spike protein receptor angiotensin-converting enzyme 2 (ACE2) as a marker, has only been reported considering the most representative cell types of the olfactory or respiratory mucosa, neglecting the presence of SCCs in these epithelia [20]. There are currently no studies in the literature that analyse this aspect.

This deficiency may have repercussions on the understanding of the effects exerted by Covid-19 on epithelia, considering that epithelia are composed of heterogeneous cell populations, which with their different characteristics, properties, and functions contribute to creating a network of interconnected and cooperating cells. In this regard, different cell types have been shown to express bitter and sweet taste transduction pathways molecules and receptors in many peripheral sites, including respiratory and intestinal tissues [3,21–24]. Bitter and sweet receptors are G protein-coupled receptors (GPCRs), for which a role in the cellular entry mechanism of SARS-CoV-2 was already hypothesized [25].

Considering the COVID-19 symptoms, sputum [26,27] is indicative of both the body's immune reaction to SARS-CoV-2 and DCS activation [28,29]. The immune response leads to an increase in the production of mucus which, in the event of a strong immune reaction due, for example, to a viral attack, can degenerate into hypersecretion or dysfunction of the clearance system. DCS itself could contribute induce the immune response by triggering the mucus secretion to promote clearance [30] and/or by inducing dysfunction of the cilia motility [22]. Both hypersecretion and dysfunction of the clearance system could induce obstructive pulmonary diseases [31–33].

Furthermore, the paracrine action carried out by DCS [34] could also contribute to the development of interstitial pneumonia, through the recall of inflammatory cells and, therefore, of lymphocytes, in the interstitium. A type 2 immune response induced by DCS in the trachea has recently been hypothesized [35].

Descending in the gastrointestinal tract, DCS seems to play a fundamental role in the detection of ingested harmful drugs and toxins, thus initiating critical survival responses [36,37], responses consistent with the COVID-19 symptoms of diarrhoea, vomiting and abdominal pain [38,39].

The excessive activation of the immune system results in an immunosuppression effect, particularly in the more severe COVID-19 forms [26,27,39]. Could DCS activation play a role in this last effect? Could the strong reaction of both systems create destructive interference, inducing an aberrant response to COVID-19 and exacerbating symptoms? These aspects have not been taken into account in recent studies concerning SARS-CoV-2 infection, suggesting that the involvement of DCS in the mechanisms of this novel coronavirus infection is underestimated.

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Declaration of Competing Interest

The authors declare no conflict of interest.

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Sheila Veronese*, Flavia Merigo, Andrea Sbarbati
Department of Neuroscience, Biomedicine and Movement, University of Verona, 37134, Verona, Italy

* Corresponding author at: Department of Neuroscience, Biomedicine and Movement, University of Verona, 1 Sq. L.A. Scuro, Verona, 37134, Italy.
E-mail address: sheila.veronese@univr.it (S. Veronese).