

Anosmia and dysgeusia as markers of severity and prognosis in COVID-19

It is currently known that the SARS-CoV-2 virus, the etiological agent of COVID-19, has a great neurotropism, infecting neural cells of the olfactory bulbs and surrounding areas, thus reaching the central nervous system, in addition to other pathways such as hematogenous, conditioning a wide range of neurological symptoms, including anosmia and dysgeusia.^[1]

However, there have been disparities in the results, since some study groups have reported that the presence of anosmia with or without dysgeusia is a factor of severity and poor prognosis, while other groups mention the opposite, its presence portends a good prognosis in patients, there have even been systematic reviews and meta-analyses in this regard.^[2-4]

Quantitative smell testing demonstrates that decreased smell function (hyposmia), but not always anosmia, is a major marker for SARS-CoV-2 infection and suggests the possibility that smell testing may help, in some cases, to identify COVID-19 patients in need of early treatment or quarantine.^[5]

Dysgeusia is a prevalent qualitative gustatory impairment that may affect food intake and quality of life. The facial (VII), glossopharyngeal (IX), and vagus (X) nerves are the three cranial nerves responsible for sensing taste. Typically, dysgeusia is considered a general term for all taste disorders. In addition, dysgeusia may be a symptom of underlying systemic conditions such as diabetes mellitus, chronic kidney disease, respiratory infections (currently includes COVID-19), and nutritional deficiencies.^[6]

With COVID-19, the rate of incidence of olfactory dysfunction in patients has been varied from 29.64% to 75.23% and the rate of incidence of taste dysfunction among people can be different from 20.46% to 68.95%.^[7]

We present a study in which we found that anosmia was associated with greater severity and poor prognosis, while dysgeusia was associated with less severity and better prognosis.^[8]

However, what could be the factors that influence these symptoms to have a positive or negative correlation in severity and prognosis?

The answer probably has several aspects associated with the ecological triad.

Host Factors

It is mentioned that patients who have risk factors such as obesity, diabetes, or hypertension, as well as primary or secondary immunosuppression, could suffer more severe conditions and favor greater neurotropism; It has also been shown that there are other receptors in the brain in addition to angiotensin-converting enzyme 2 (ACE2) that can act to facilitate the neuroinvasion of SARS-CoV-2, such as the Basigin (BSG), neuropilin-1 (NRP1), transmembrane serine protease 11A (TMPRSS11A), and furin receptors, but the amount of them varies from one individual to another. Other studies that have worked with single-cell sequencing revealed that ACE2 is expressed in supporting cells, stem cells, and perivascular cells, rather than in neurons. These findings suggest that CoV-2 infection of nonneuronal cell types causes anosmia and related disorders in odor perception in COVID-19 patients.^[9,10]

Agent Factors (SARS-CoV-2)

Per se, this betacoronavirus has a great affinity for the central nervous system in such a way that it is considered neurotropic, neuroinvasive, and neurovirulent, however, some variants have a greater capacity than others, highlighted in this area the ancestral variant D614G, followed by the Delta variant (B.1.617.2) and finally by Omicron BA1 (B.1.1.529), the latter presenting the least neurotropism *in vitro* and *in vivo* studies.^[11]

Environmental Factors

It is mentioned that some geographical regions have favored greater severity and involvement with subsequently increased neurotropism than other regions; Asian regions initially did not report neurological symptoms such as anosmia or dysgeusia, these appeared as the pandemic was conquering European and later American regions with the following globalization of these symptoms; Although other regions such as Iran reported these alterations since the beginning of the pandemic. Sudden onset of olfactory dysfunction was reported in 76.24% of the participations and persistent anosmia in 60.90% since the start of the COVID-19

epidemic. In addition, 80.38% of participants reported concomitant olfactory and gustatory dysfunctions. Factors such as temperature, humidity, and air quality have been identified as facilitators of the transmission of SARS-CoV-2.^[12,13]

We consider that the conjunction of these factors as a whole is what predisposes to greater or lesser severity of the disease and therefore of neurotropism, and according to these characteristics, symptoms such as anosmia or dysgeusia, among others, can behave as good or bad prognosis in different populations. In the same way, there are racial, genetic, and geographical variations that predispose some populations to have these more entrenched characteristics and that, having a higher incidence of these symptoms, act as severity factors.

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