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# The proper functioning of the sense of smell and its disturbances on the example of COVID-19 infection

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Abstract

COVD-19 disease causes a wide range of respiratory symptoms. One of them is the olfactory disorder, which is also associated with other viral infections. Impaired sense of smell is associated with damage to the respiratory epithelium. Sniffing problems lasting longer than a few days are reported by more than half of patients infected with SARSCov-2 virus. This problem affects the quality of life and may result, among other things, in eating disorders or an increase in exposure to harmful chemicals. The olfactory epithelium, containing receptor cells, is primarily responsible for the proper functioning of the sense of smell. Impaired smell in COVID 19 is associated with damage to the respiratory epithelium. The article is a review of the scientific literature, in which the issues related to the physiology and anatomical structure of the olfactory organ and the influence of SARSCov-2 virus infection on olfactory disorders were discussed.

**Key words:** COVID-19, SARSCov- 2, SARSCov- 2 infection, smell disturbances, olfactory disorders

## Introduction

SARSCov-2 coronavirus infection causes a number of heterogeneous respiratory symptoms of extremely varied severity. Ranging from mild symptoms to severe, where severe acute respiratory failure may develop. [3] Sniffing problems are symptoms that are increasingly reported in people infected with SARSCoV-2. About half of the patients suffer from an olfactory disorder. Smell disorders have a significant impact on the quality of life. It is related to the impaired ability to recognize the smells of food and the environment, which may result in malnutrition, weight disorders, food poisoning or depression. Equally important is the increase in exposure to hazardous chemicals. [15] Effective measures to prevent the spread of

SARS-CoV 2 virus are limited, so it is important to recognize the early symptoms of coronavirus disease. SARS-CoV infection mainly affects the lungs, it also causes fever, cough, and fatigue. However, there are other symptoms, such as loss of smell, which has been validated by clinicians and the public around the world. [7] This is confirmed by clinical trials conducted in the United States, Italy and Iran, where olfactory and taste disorders were strongly associated with COVID-19 infection. It has also been suggested to consider the loss of smell and taste as a subline marker or a possible early symptom of SARS-CoV 2 infection [9] There was also a correlation between the occurrence of olfactory disorders and an increase in mortality from COVID 19. Taking into account the frequency of smell disorders among COVID-19 patients, these symptoms were included in the official lists of symptoms of SARSCoV-2 infection around the world. [15].

Anatomy and physiology of smell

Human senses (sight, hearing, touch, taste) are well understood in most cases. On the other hand, the sense of smell, which is difficult to test, has still not been fully explored. Odor perception is a combination of an orthonosic odor, which is related to the sniffing of a smell of, for example, flowers or food, and a retronosic odor located in the oropharynx. It results from the flow of air through the nasopharynx during the act of swallowing or exhaling air through the nose. [3] Currently, it is believed that the smell is caused by numerous odor receptors, accumulated on the sensory cilia in the olfactory epithelium [7]. These receptors activate the appropriate olfactory centers and transmit a signal to the olfactory cortex in the brain. [2]. The nasal mucosa has an olfactory neuronepithelium which makes up 1.25% of the nasal mucosa and covers an area of 8 to 10 cm square. This surface consists of the ethmoid plate, the upper part of the nasal septum, and the middle and upper turbinates. There are approximately 10 million olfactory receptor cell dendrites in the olfactory bulb. The smell reaching the olfactory epithelium dissolves in the mucus layer and then, through a complex reaction, activates the olfactory receptors through complex reactions that require the presence of fragrance-binding proteins. [3] Sensory cilia are organelles supported by structures called microtubules, which protrude from outside the cell surface. They act as an antenna through which various environmental stimuli are received. The proper functioning of the sense of smell requires the proper structure and functioning of the olfactory cells. Hence, anosmia turns out to be a very common symptom of some types of ciliopathy, for example, Bardet-Biedl syndrome. [13]. One fragrance activates many types of receptors to varying degrees. The olfactory cells transmit chemical information that has the frequency of the emission of nerve impulses and send it to the olfactory glomeruli. This information is integrated and transmitted in the olfactory bulb. The olfactory bulb neurites pass into the olfactory pedicle to the primary olfactory cortex. The information processed in the cortex affects other areas of the brain, such as: the amygdala, the hypothalamus, the hippocampus, and the olfactory cortex. There are about 350 different genes in the human body coding for specific protein receptors. These receptors interact with selected groups of chemicals, leading to a complex process of identifying odors. Viral inflammation of the olfactory epithelium can change the structure of the cilia, which disturbs the perception of olfactory cells. [3] According to the OLFACAT study (OLFAction in Catalonia), loss of smell in the form of hyposmia or anosmia occurs in almost 20% of Europeans, where the overall population of European Union citizens is around 82 million. [12]. On the other hand, epidemiological data of olfactory disorders in the US adult population show that impaired smell is present at the level of 13.5% of the population. For comparison, in the same population, taste impairment occurs in 17.3%, while both dysfunctions are at the level of 2.2%. [6].

## The etiology of olfactory disorders

The main causes of acquired olfactory loss include upper respiratory tract infection such as rhinitis, inflammation of the paranasal sinuses by viruses: adenoviruses, rhinoviruses, coronaviruses, and influenza viruses. Other causes are traumatic brain injury or neurodegenerative diseases: Parkinson's disease, Alzheimer's disease, brain tumors. And also drugs, chemicals, radiation, and iatrogenic damage. [5] Loss of smell is a common occurrence in viral infections, especially in the common cold and acute inflammation of the paranasal sinuses. This symptom occurs on average in more than 60% of cases and usually heals itself after 3-7 days. However, there are cases of permanent post-viral loss of smell. [4] The loss of smell in upper respiratory tract infections is caused by a combination of many factors that prevent odor transmission. In mucositis as a result of a cytokine storm and neurodegeneration of the olfactory epithelium. [1].

## Covid-19-related olfactory disorders

First, the coronavirus infects the ciliary cells of the nasal epithelium, thereby causing the loss of cilia. Bjorn Afzelius detected the coronavirus in macaque ciliary cells. [7]. The same animals demonstrated the expression of SARS-CoV-2 in ciliated cells of the nasal epithelium. Coronaviruses enter the host cells via a spike (S) that binds to a specific receptor through a protease-dependent reaction. The SARS-CoV-2 virus uses the angiotensin converting enzyme 2 as the receptor and Transmembrane Serine Protease 2 (TMPRSS2) as the cellular protease. Protease and receptor expression has been described as the primary mechanism by which the coronavirus infects human nasal epithelial cells. [8,14]. There are currently two models that explain how the ciliated epithelial cells of the nasal epithelium are lost. The first is the amputation model in which the thistle is removed completely at the base, as is a sudden change in pH to remove the Chlamydomonas flagellum. Another model is the absorption model. Cilia can be gradually absorbed by the cytoplasm of the ciliary cell. [10]. Cilia loss is also seen in other viral infections. Tests using a transmission electron microscope have shown that shortened cilia regenerate during the patient's recovery, which results in the restoration of the sense of smell.

## Summary

Smell disorder is one of the most common symptoms of viral infections, including the SARS-CoV-2 virus. The physiological processes of the sense of smell mechanism and the structure of the anatomical structures responsible for the proper sense of smell are known. Attempts are currently underway to explain the causes of olfactory cell damage in the mechanism of SARS-CoV-2 infection. This will allow the search for effective treatments for chronic olfactory dysfunction in people who have undergone COVID-19. This will contribute to the improvement of the quality of life due to the restoration of the perception of smells and the improvement of the protective functions of the smell by faster reaction to chemical hazards.

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