

Disorders of the Olfactory & Gustatory Systems and their role in COVID-19, Parkinson's & Alzheimer's Disease

Author: Tara Borg Caruana

Supervisor: Professor Gary Hunter B.Sc.(Hons)(Liv.),Ph.D.(Warw.)

Abstract

The chemical senses of the body are more extensive than one may think. Although research has progressed on both the olfactory and especially gustatory systems, there is still a constant race to determine any new findings possible related to these systems. Even though these are two separate systems, they are dependent on each other. This review describes various disorders associated with both smell eg: anosmia and hyperosmia; and taste for example ageusia, and parageusia. The correlation between COVID-19, Alzheimer's & Parkinson's Disease with olfactory and gustatory disorders is also discussed.

Keywords: Olfactory system, gustatory system, COVID-19, Parkinson's and Alzheimer's Disease

Introduction

Olfactory disorders

Upon increasing age, the risks for olfactory disorders increase. Like in taste, all olfactory disorders are split into two categories: qualitative and quantitative disorders (1).

The disorders however can also be divided into their different points of origin (2), which are:

- i. Conductive: which is peripheral
- ii. Sensorineural: which is of central origin

Conductive disorders are caused by the inability of odorants to make their way to the olfactory epithelium and Olfactory

Receptors (refer to Figure 1). This is due to an anatomical barrier. Central disorders are caused due to a lack of processing of information by the olfactory receptors (OR), olfactory receptor neurons (ORN) or even by more central areas like the Central Nervous System as well as any central pathways leading to it (2).

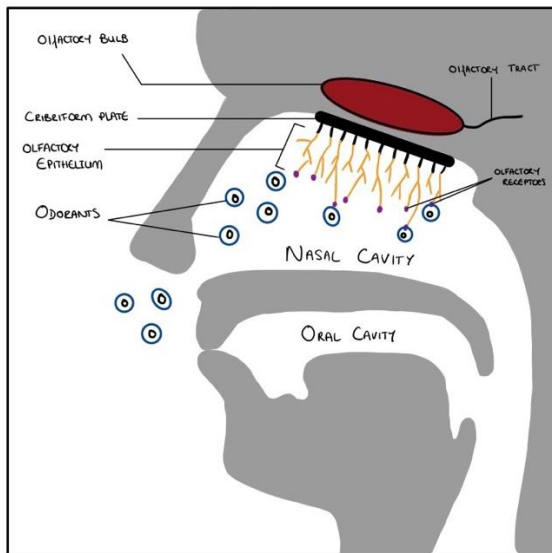


Figure 1: Diagram illustrating the Olfactory System in the human body and the initial phase of olfaction.

Quantitative Disorders

These two disorders are classified as Quantitative Disorders as they directly impact the amount a person smells and not the type of smell (1).

Anosmia is an olfactory disorder where there is a complete loss of smell. Hyposmia refers to a disorder where a person's smell decreases drastically but is still somewhat present although at a very suppressed level. Both these disorders can have quite a huge impact on a person's way of life as well as their health (3).

Many studies throughout the years have discussed and evaluated the relationship between anosmia and hyperosmia with eating disorders resulting in excessive weight loss. It is also a massive disadvantage to lose your sense of smell with respect to health risks. It can result in a person consuming food that is spoiled, rotten or even just consuming something which is not meant to be eaten (4). This can impose certain implications on the person's health such as gastrointestinal and digestive issues.

Hyperosmia is the least common of all quantitative disorders. This is when a person's ability to smell is intensified to the extreme and thus they smell excessively, contrary to hyposmia. In a past study, a link between hyperosmia caused by Lyme Disease was discovered (5).

Qualitative Disorders

These types of disorders affect the quality of smell i.e., they inhibit a person from correctly smelling something and being able to identify a particular odorant (1). The disorders are Parosmia and Phantosmia.

In Parosmia, a person has a dysfunction in the specificities of smell detection. The brain begins to identify it as an unpleasant smell (such as: rotting, burning, faecal or chemical smell), hence the odour is distorted (1). As of yet, there is still no cure for parosmia but there are medications that can help with the degree of severity of parosmia (6).

Parosmia can be divided into peripheral and central types but can also be a combination of both in certain cases (7). Some examples of central parosmia's are as follows:

- i. When pregnant women tend to have particular illusions on certain smells.
- ii. Hallucinations of odours (phantosmia) may occur in mental illnesses such as schizophrenia (7).

Examples of Peripheral Parosmia's include:

- i. Cacosmia is when a patient is constantly smelling bad odours. This can be due to epilepsy (6).
- ii. Essential parosmia is when a person continues to carry out the function of olfaction without any proper olfactory impression and like in cacosmia results in a distasteful odour (6).

Phantosmia is another type of hallucinative disorder where a person is convinced, they are smelling a particular odour without even taking a sniff of air. This usually is always caused by a tumour (6).

Taste Disorders

Taste disorders have quite adverse effects on one's overall health as well as their way of life. These types of disorders may lead to an even worse situation that can result in an eating disorder such as anorexia, which is caused by malnutrition (8). Taste disorders may also cause mental battles such as depression since the food tends to bring an element of joy to people's livelihoods thus when the element of taste is removed, as is the happiness that comes along with it.

Although it is widely known that loss of taste has such an impact on patients' lives, there is yet still no medication or any sort of treatment which can improve this dysfunction (8). The taste-related disorders

we will be discussing are Ageusia, Hypogeusia, Parageusia (dysgeusia) and Gustatory Hallucinations (Table 1).

Quantitative Disorders

Starting with Ageusia, which is when there is a complete loss of taste (9). Hypogeusia is when there is a partial loss of taste function resulting in a decreased overall ability to taste (10). As well as Hypergeusia, which is the exact opposite of hypogeusia. thus, instead of barely smelling anything at all, this disorder causes excessive smelling. This is due to elevated responsiveness to all types of tastants (9). These disorders are collectively referred to as Quantitative Disorders since they all influence directly the amount of taste perception and not the type of taste perception.

Qualitative Disorders

These types of disorders are called Qualitative as they directly impact the quality as well as the type of taste which is being perceived (10). Firstly, Parageusia is a disorder whereby a person has a very noticeable taste distortion and usually this results in them tasting certain foods that they used to enjoy before, as completely horrible now (10). This may also cause them to fixate more on certain foods which prior to this disorder they would not usually tend to go for due to the taste. Some people with parageusia have also noted a more prominent metallic taste in certain foods they eat.

The next disorder is phantogeusia which is when specifically, one starts to hallucinate certain tastes which realistically are not present. So for example: upon eating

something sour, the person with phantogeusia is convinced that they are tasting something sweet when in reality they are tasting the sour food but are just not mentally making the connection from mouth to the brain. This concept may be hard to understand as it is quite different from the other disorders as this stems mainly from a mental point of view and not as much from the taste bud aspect. It can also be defined as when somebody is tasting a specific taste which is happening during the absence of a tastant (9).

Dysgeusia is a more collective term that refers to both parageusia and phantogeusia (10).

Clinical Taste Disorders (primary symptom)	Causes
Ageusia (complete loss of taste)	<ul style="list-style-type: none"> • Nerve Lesion to the Lingual nerve & CN IX • Hypothyroidism • Crohn's Disease • Pernicious Anaemia • Excessive inflammation of the Olfactory Pathway
Hypogeusia (A greatly decreased ability to taste)	<ul style="list-style-type: none"> • Drug use • Zinc Deficiency
Parageusia (Distortion of taste)	<ul style="list-style-type: none"> • Medications • Chemotherapy • Pregnancy • Zinc Deficiency
Phantogeusia (Gustatory hallucinations)	<ul style="list-style-type: none"> • In the absence of food or drink • Occurs after taste loss due to viral Infection

Table 1: The relation of Taste Disorders to their causes. Table comparing the different types of taste disorders with their respective symptoms and causes. Ageusia is the rarest of all disorders. Adapted from Purves *et al.*, 2011.

Discussion

Effects of Inflammation and Viral Infections on Taste Function

Inflammation continues to be a major contributing element in all diseases associated with taste disorders. Inflammation which is caused by certain viral infections that tend to attack the upper region of the airway tract i.e. the larynx, as well as the upper region of the gastrointestinal tract such as the mouth and pharynx are heavily associated with the causes for taste dysfunction (8). Hepatitis B is another type of infection that specifically affects the gustatory system by increasing its sensitivity to different tastants. There are also diseases such as Lupus which is characterised as an auto-immune disease that also affects one's ability to taste (8).

Toll-like receptors (TLRs) secrete chemicals such as cytokines or interferons. These are secreted due to an inflammatory response that was stimulated by a foreign body i.e. a pathogen. Upon it entering the body, the pathogen is engulfed by cells that form part of our immune system. These are known as antigen-presenting cells, as they present an antigen on their cell surface which will in turn activate the TLR (8). Although the connection between TLR activation and taste dysfunction has been established, there are still many more discoveries to be done in order for this great suspicion to become concrete facts.

The Effects Of COVID-19, Parkinson's & Alzheimer's on taste and smell perception

COVID-19

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the virus that causes COVID-19, the coronavirus. A trend was noticed in patients who contracted this illness which has caused a worldwide pandemic. This trend was such of Olfactory and gustatory disorders. Some people reported symptoms such as anosmia only, and some complained of ageusia only however most of the people reported to have experienced both loss of taste as well as loss of smell (12)

Why is taste and smell lost? Although not much extensive research has been done in the past on why the sense of taste is lost, one thing is certain, which is that for the most part, our ability to taste is stemming from our capability of smelling different odours. Thus, the main pathological issue created by COVID-19 is more specific to the olfactory epithelium rather than solely to the taste buds in the mouth (13).

The mucus found in the nasal region is essential to trap odorant molecules which are then detected via the olfactory receptor neurons. In the case of COVID-19, once these viral cells enter the nasal cavity, they begin to interact with the ACE2 receptors found on the target cells within the mucous layer (14). This does not occur only in the nose but also in the mucous membrane in the oral cavity, which in this case is specifically found on the tongue. Thus, in both cases, SARS-CoV-2 uses the Angiotensin-converting enzyme 2 (ACE2) receptor to make its way into cells by binding to ACE2 using its spike proteins (12). Some researchers have also discovered that apart from SARS-CoV-2 requiring the ACE2 receptors on certain cells, it also needs the

protease, TMPRSS2 which aids in the binding of the spike protein, which is found on the COVID-19 cell surface, to the ACE2 receptor (13). Both the ACE2 receptor and the TMPRSS2 are found also in the throat and upper respiratory tract apart from the nose and mouth which further explains why apart from ageusia, and anosmia infected people also present with sore throats, severe coughing and shortness of breath.

Since this virus has only recently begun to transcend in the world of infectious diseases, more research is still yet to be done to justify any further relations between specific neurological pathways which may also be causing such olfactory and gustatory disorders.

Parkinson's & Alzheimer's Disease

Parkinson's Disease and Alzheimer's Disease are both neurodegenerative diseases. Parkinson's disease affects the dopaminergic neurons of the brain and affects problem-solving, speed of thinking, memory and mood (14). Whilst Alzheimer's disease is when there is atrophy of the brain and hence affects language, memory and thinking skills (15).

In Parkinson's Disease, the majority of the pathophysiology is occurring within the olfactory bulb as this is the final stage where the processing of olfactory information occurs, in fact, it is referred to as the 'Olfactory Thalamus' (16). In Parkinson's patients, only a few tend to report complete anosmia whilst many patients complain about hyposmia (thus a greatly reduced smelling function). Also, the ability for one to be able to differentiate between different odours as well as recognise an odour is

severely impacted in people with Parkinson's Disease. Severe loss of smell is also an early indication of Parkinson's disease thus it is generally used as a biomarker to diagnose the patient with Parkinson's. The exact cause of dysfunctional smell in Parkinson's Disease is still unknown but is thought to be caused by the changes in dopamine (a neurotransmitter) levels in the brain caused by this neurodegenerative disease (16 – 18).

Alzheimer's Disease is one of the most common diseases in the elderly when it comes specifically to neurodegenerative diseases. An identifiable marker of Alzheimer's is dementia. The first part of the brain which is impacted by this neurodegenerative disease is the olfactory system and hence this is also a biomarker for the diagnosis of Alzheimer's like in Parkinson's Disease as this symptom is presented very early on in the disease (15, 17).

Conclusion

From the cumulative information collected in the above literature review, it can be concluded that both sensations of smell and taste are vastly interlinked. This leads to certain issues when one of the systems starts to malfunction as due to the extensive and cohesiveness of the functionality of both systems, the other system will become dysfunctional too. Saying this, when discussing specific illnesses such as COVID-19, one can truly understand why when infected, smell and taste most of the time are lost simultaneously. This review also allows us to appreciate the importance of Olfaction and Gustation when diagnosing or noticing even more severe diseases such as

Alzheimer's and Parkinson's. Their dysfunction acts as biomarkers which are clear indications of these diseases. No matter how often overlooked, the Olfactory system and the Gustatory system have been shown to be essential functions in one's day-to-day life, which must be cared for and looked after because, unlike other disorders, most of the time, when taste or smell is lost, it proves to be very hard to regain that function. Medications aimed at improving taste or smell dysfunction are little to none and sometimes can also worsen the situation.

Declarations

Conflict of interest: N.A.

Ethical statement: N.A.

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