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Anosmia and Hyposmia: Overview

Anosmi ve Hiposmi: Genel Bakış

Zeynel ÖZTÜRK[a,b], Nuray BAYAR MULUK[c], Oğuzhan OĞUZ[d], Sevilay AYNACI[e], Felicia MANOLE[f], Cemal CİNGİ[g]

[a]Baypark Hospital, Clinic of Otorhinolaryngology, Head and Neck Surgery, İstanbul, Türkiye
[b]Nişantaşı University Faculty of Medicine, Department of Otorhinolaryngology, Head and Neck Surgery, İstanbul, Türkiye
[c]Kırıkkale University Faculty of Medicine, Department of Otorhinolaryngology, Head and Neck Surgery, Kırıkkale, Türkiye
[d]Private Physician, İstanbul, Türkiye
[e]Eskişehir City Hospital, Clinic of Otorhinolaryngology, Head and Neck Surgery, Eskişehir, Türkiye
[f]University of Oradea Faculty of Medicine, Department of Otorhinolaryngology, Head and Neck Surgery, Oradea, Romania
[g]Eskişehir Osmangazi University Faculty of Medicine, Department of Otorhinolaryngology, Head and Neck Surgery, Eskişehir, Türkiye

ABSTRACT Approximately 95% to 99% of chemosensation is attributed to the sense of smell, whereas taste is responsible for the remaining chemosensation. One who suffers from anosmia is unable to detect smells. In addition to being acquired or congenital, it can be either transitory or permanent. Disorders in olfaction can be brought on through pathologic conditions at any level through the olfactory pathway. These disturbances can occur at multiple levels. Conductive or sensorineural deficiencies are two categories that can be used to categorize them. In diseases classed as conductive, also known as transport disorders, there is an interruption in transmitting an odorant stimulus to the olfactory neuroepithelium. Loss of sense of smell can be brought on by any mechanical obstruction that prevents scents from reaching the olfactory neurons. Several inflammatory processes can cause this obstruction, including uncomplicated infections that result in mucus plugs or nasal polyps. Some neurological causes have the potential to cause the disease. The more central brain structures are affected by the presence of sensorineural abnormalities. Tests of olfactory function have been created to give a valid measurement of olfactory dexterity. These smell tests examine the threshold of odor perception and odor identification. The butanol threshold test, the "University of Pennsylvania Smell Identification Test (UPSIT)," and the "Sniffin' Sticks" test are some of the tests included in this category. In this review, olfactory disorders are presented with a detailed literature survey.

Keywords: Olfactory disorders; anosmia; hyposmia; smell tests

ÖZET Kimyasal duyumun yaklaşık %95 ila %99'u koku duyusuna atfedilirken geri kalan kimyasal duyumdan tat sorumludur. Anosmisi olan kişi kokuları algılayamaz. Bu durum, kazanılmış veya doğuştan olabileceği gibi geçici veya kalıcı da olabilir. Koku alma bozuklukları, koku alma yolu boyunca herhangi bir seviyedeki patolojik koşullar nedeniyle ortaya çıkabilir. Bu bozukluklar birden fazla düzeyde ortaya çıkabilir. İletimsel veya sensörinöral eksiklikler, kullanılabilecek iki kategoridir. İletim bozuklukları olarak da bilinen, iletken olarak sınıflandırılan hastalıklarda, koku verici bir uyarının koku nöroepiteline iletilmesinde bir kesinti vardır. Kokuların koku alma nöronlarına ulaşmasını engelleyen herhangi bir mekanik engel, koku duyusunun kaybına neden olabilir. Mukus tıkaçları veya nazal poliplerle sonuçlanan komplikasyonsuz enfeksiyonlar da dahil olmak üzere çeşitli inflamatuvar süreçler bu tıkanmaya neden olabilir. Bazı nörolojik nedenler hastalığa neden olma potansiyeline sahiptir. Daha merkezi beyin yapıları sensörinöral anormalliklerin varlığından etkilenir. Koku alma becerisine ilişkin geçerli bir ölçüm sağlamak için koku fonksiyonu testleri oluşturulmuştur. Bu koku testleri, koku algılama ve koku tanımlama eşiğini inceler. Bütanol eşik testi, "Pennsylvania Üniversitesi Koku Tanımlama Testi (UPSIT)" ve "Sniffin' Sticks" testi bu kategoriye giren testlerden bazılarıdır. Bu derlemede koku alma bozuklukları ayrıntılı bir literatür taramasıyla birlikte sunulmaktadır.

Anahtar Kelimeler: Koku alma bozuklukları; anozmi; hipozmi; koku alma testleri

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Correspondence: Cemal CİNGİ
Eskişehir Osmangazi University Faculty of Medicine, Department of Otorhinolaryngology, Head and Neck Surgery, Eskişehir, Türkiye
E-mail: ccingi@gmail.com

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Approximately 95% to 99% of chemosensation is attributed to the sense of smell, whereas taste is responsible for the remaining chemosensation. One who suffers from anosmia is unable to detect smells or odors. In addition to being acquired or congenital, it can be either transitory or permanent. There are many different reasons for this. For instance, a loss of sense of smell can be brought on by any mechanical obstruction that prevents scents from reaching the olfactory neurons. Several inflammatory processes can cause this obstruction, including uncomplicated infections that result in mucus plugs or nasal polyps. Some neurological causes have the potential to cause the disease. Problems with the olfactory bulb's sensory nerves or any other part of the pathway that signals smell to the brain are examples of such problems. It would be good to have an understanding of how people sense smell to have a better understanding of this process.[1-5]

Various neurological factors can be responsible for the illness. Some examples include disturbances to the sensory nerves that make up the olfactory bulb or any other location along the path where the scent signal is transmitted to the brain.[5]

CLASSIFICATION OF OLFACTORY DYSFUNCTIONS

Pathologic activities at any level of the olfactory tract may cause disturbances in olfaction. These disturbances can occur at multiple levels. Conductive or sensorineural deficiencies are two categories that can be used to categorize them in a manner comparable to otologic dysfunction. The transmission of a smell stimulus to the olfactory neuroepithelium is interrupted in diseases classified as conductive, also known as transport disorders. The more central brain structures are affected by the presence of sensorineural abnormalities. Aging by passing years, sinonasal diseases, previous or present upper respiratory tract infections (URTIs), and various cranial traumas are the most common causes of primary olfactory deficits.[6,7] In general, older people are more likely to experience these symptoms.

DEFECTS IN THE CONDUCTION

Inflammatory processes cause the majority of olfactory abnormalities. There are many different kinds of rhinitis, such as allergic, acute, or toxic rhinitis (for example, caused by excessive cocaine usage). Chronic rhinitis produces mucosal disease that worsens with time and frequently reduces olfactory function, even though it is treated with intensive allergic, medicinal, and surgical interventions.[6-10]

Masses can obstruct the nasal cavity, depriving the olfactory epithelium of the ability to receive odorants. The most prevalent examples are nasal polyps, inverted papillomas, and any other type of nasal tumor.[6,7,9]

Developmental anomalies, such as encephaloceles and dermoid cysts may also cause blockage. Hyposmia is a condition that affects patients who have undergone laryngectomies or tracheotomies due to decreased or nonexistent nasal airflow. Due to a lack of early impulse for stimulation of the olfactory system, children who have tracheotomies and are cannulated at a very young age and for an extended period may continue to have issues with their ability to make sense of smell even after the cannulation has been removed.[6,7,9]

DEFECTS IN THE CENTRAL AND SENSORY NERVES

Central olfactory perception and transmission anomalies can be attributed to inflammatory and infectious processes. A viral URTI may cause a loss of smell by causing the olfactory neuroepithelium to be replaced by respiratory epithelium. However, investigations have shown that stem cells are still present, which may allow for the possibility of regenerating the olfactory epithelium. In such instances, regaining the sense of smell could take a few months to a few years, or it might never happen. Sarcoidosis, Wegener granulomatosis, multiple sclerosis (MS), and other diseases can all lead to a diminished sense of smell. Sarcoidosis is a disorder that impacts the systems of the brain. Chronic rhinosinusitis (CRS) seems to disrupt the neuroepithelium with irreversible loss of olfactory receptors through up-regulated apoptosis, challenging the long-held belief that the condition is primarily a conductive problem caused by mucosal edema and polyp growth. This is a condition that has been the subject of much speculation.[10]

Anosmia can be caused by head trauma, brain surgery, or subarachnoid hemorrhage, all of which have the potential to stretch, damage, or transect the fragile fila olfactory region of the brain, as well as

damage the brain parenchyma.[10] The findings of a study conducted by Bratt et al. revealed that among 182 patients who had suffered from moderate to severe traumatic brain injury (TBI), 13.7% were diagnosed with olfactory impairment. Additionally, 8.2% of the whole group was discovered to be suffering from anosmia. Olfactory impairment was shown to be associated with TBI in individuals who had suffered a fall, skull base fracture, or cortical contusion, according to the findings of the study.[11]

Using resting-state functional magnetic resonance imaging, Park et al. conducted a study in which they discovered that persons with traumatic anosmia exhibited a lower level of internetwork connectivity in the olfactory network than healthy controls.[12] On the other hand, the olfactory and whole-brain networks exhibited greater connectedness to the internetwork. Furthermore, individuals who suffered from traumatic anosmia exhibited decreased modularity and higher global efficiency in the whole-brain network, and these traits were found to be connected with the severity of the disease (10 of the patients).

Neuronal losses may be related to congenital disorders. Failing olfactory structure ontogenesis and hypogonadotropic hypogonadism are the two factors that contribute to the development of Kallmann syndrome, a form of congenital smell loss. According to the findings of one investigation, the vomeronasal organ was not present in patients diagnosed with Kallmann syndrome.[6]

Alterations in the endocrine system, such as hypothyroidism, hypoadrenalism, and diabetes mellitus, have the potential to influence olfactory function.[6]

The toxicity of medications administered systemically or inhaled (for example, aminoglycosides and formaldehyde) can contribute to olfactory impairment. Alcohol, nicotine, organic solvents, and the direct application of zinc salts are some of the many other medicinal substances and compounds that can change a person's sensitivity to smells.[13]

ETIOLOGY

Any problem that disrupts the system and leads to the perception of smell, whether mechanical or along the olfactory brain pathway, can cause anosmia.[14-16]

TABLE 1: Etiology of the olfactory disorders.

Olfactory disorders	Etiology
	Trauma to the head
	Neurodegenerative disease and aging
	Various congenital disorders
	Infective conditions
	COVID-19
	Various traumatic or obstructive disorders

It is estimated that between fifty percent and seventy percent of all cases of anosmia are caused by inflammatory and obstructive disorders.

Several conditions, including rhinitis, and nasal polyps are the most common causes of anosmia. Nasal and paranasal sinus illnesses are also contributing factors. Additionally, anosmia can be brought on by a combination of these disorders. Both mucosa inflammation and direct obstruction are variables that lead to the development of anosmia in patients suffering from these disorders.[1]

Etiology of the olfactory disorders are shown in Table 1.

TRAUMA TO THE HEAD

Trauma to the head is another major cause of anosmia. Trauma to the head can cause injury to the nose or sinuses, which can then lead to mechanical blockage and obstruction of the airway. Other methods in which an injury can produce anosmia include causing damage to the olfactory bulb, causing trauma or destruction to the olfactory axons at the cribriform plate, or directly injuring the olfactory regions of the cerebral cortex. It is possible for the trauma to the central nervous system (CNS) that causes anosmia to be either transitory or permanent, depending on the location and significance of the lesion. Olfactory neurons possess regeneration properties not shared by other CNS nerves. This one-of-a-kind capability is at the heart of significant research relevant to stem cells.[1]

NEURO-DEGENERATIVE DISEASE AND AGING

Anosmia is a condition that can develop due to these processes since they are related to the loss of smell. There is a correlation between normal aging and a re-

duction in the ability to detect smells. As people get older, they experience a decrease in the number of cells in the olfactory bulb and the surface area of the olfactory epithelium. Both of these factors are crucial for proper smell perception. It is noteworthy to note that there have been studies that have associated the impairment of the capacity to smell with neurodegenerative illnesses such as Alzheimer's disease, Parkinson's disease, and Lewy body dementia. These diseases are all examples of neurodegenerative conditions. There is an association between a lower capacity to perceive smell and an increased likelihood of acquiring neurodegenerative disorders, according to the findings of several research. It has been observed that anosmia has the most vital link with the eventual development of alpha-synucleinopathy, which encompasses conditions such as Parkinson's disease, diffuse Lewy body disease, and multisystem atrophy.[1]

VARIOUS CONGENITAL DISORDERS

Kallmann syndrome and Turner syndrome are two examples of congenital disorders recognized as related to anosmia.[1]

Infective Conditions

The presence of anosmia is considered to be one of the initial signs of a coronavirus disease-2019 (COVID-19) infection.[17] CRS is a disease that affects many people, and olfactory impairment affects as many as 83 percent of those with this condition. Therefore, it is thought that Type 2 inflammatory mediators at the level of the olfactory epithelium are implicated in the development of this olfactory loss. This is because olfactory dysfunction is mainly observed in those CRS patients who present with Type 2 eosinophilic inflammation. On the other hand, because extracting tissue from the olfactory epithelium is typically challenging, more knowledge should be given regarding the mechanisms responsible for inflammatory olfactory dysfunction. Even though this circumstance is not unique to COVID-19 infections and may be associated with all nose and sinus infections, there has been a rapid increase in interest in olfaction, and several research has been concentrating on the underlying mechanisms of olfactory dysfunction in inflammatory diseases.[17]

COVID-19

Both dysgeusia and anosmia are symptoms connected with the sickness caused by the COVID-19. Anosmia or hyposmia, in addition to dysgeusia, should raise suspicion of COVID-19 infection in patients who do not have other respiratory diseases, such as allergic rhinitis, acute rhinosinusitis, or CRS, according to the American Academy of Otolaryngology-Head and Neck Surgery. This recommendation is made for patients with no other respiratory diseases.[18-20] "New loss of taste or smell" is one of the symptoms that the Centers for Disease Control and Prevention has placed on its list of symptoms that may emerge between two and fourteen days after exposure to the COVID-19 virus, which is also known as severe acute respiratory syndrome-coronavirus-2. On the list of less common COVID-19 symptoms that the World Health Organization has prepared, a loss of taste or smell has also been included as a symptom.[21-23]

In a study conducted by Speth and et al. with 103 patients infected with COVID-19, the researchers found that the incidence of olfactory impairment was 61.2%. The condition was observed to manifest itself on the median infection day 3. The study's outcomes indicate a substantial connection between the degree of olfactory impairment and the degree of taste loss attained by the individual. An additional finding was that individuals who reported having olfactory impairment were more likely to have acute shortness of breath. According to the research findings, olfactory impairment was also considerably less prevalent in older age groups and significantly more prevalent in females.[23]

VARIOUS TRAUMATIC OR OBSTRUCTIVE DISORDERS

Several additional causes of anosmia exist. Some of these factors include olfactory dysfunction caused by toxic agents like tobacco, drugs, and vapors, olfactory dysfunction following a virus, facial trauma resulting in nasal or sinus deformity, neoplasms in the brain or nasal cavity that inhibit the proper functioning of the olfactory signal pathway, and subarachnoid hemorrhages. There is a possibility that olfactory groove meningioma will appear with gradually deteriorating olfactory impairment.[1,6,7]

Chronic illnesses such as diabetes mellitus and hypothyroidism are examples of prevalent conditions that can occasionally result in a diminished sense of smell or anosmia.[1]

Certain medications can sometimes cause olfactory abnormalities as an unintended consequence. This group includes a variety of pharmaceuticals, including beta-blockers, anti-thyroid meds, dihydropyridine, angiotensin-converting enzyme inhibitors, and intranasal zinc, among others.[1,7]

EVALUATION OF OLFACTORY PERCEPTION

When problems with smell and taste are the main symptoms of chemosensory dysfunction, it is crucial to quantify these issues. Determining how bad chemosensory dysfunction is the main reason for sensory testing.[6]

Several commercially accessible tests aim to streamline and standardize the sometimes tedious and complicated clinical examination process. It is a usual practice to check both nostrils simultaneously to save time. However, it is common practice to conduct unilateral testing to identify dysfunction in other sensory systems. If a problem with the olfactory system is found, it may be more effective to examine each nostril individually.[24]

To provide a reliable assessment of olfactory abilities, smell tests were developed. The identification and threshold of odor perception are investigated in these tests. Testing tools such as the butanol threshold test, the "University of Pennsylvania Smell Identification Test-Sensonics, Inc. www.sensonics.com," and the "Sniffin' Sticks test-Burghart Messtechnik GmbH www.burghart-mt.de" fall under this area. Research institutions have used odor recognition tests and measurements of brain electric potentials (sometimes called olfactory-evoked responses) to investigate aberrant olfactory function in neurological disorders.[6]

BUTANOL THRESHOLD TEST

Within the context of the butanol threshold test, a forced-choice test is utilized. One sniff bottle contains an aqueous concentration of butyl alcohol, and the other contains water. The patient is requested to identify the bottle with the odorant, and tests are performed on each nostril individually.[6,25]

After each erroneous response, the butanol concentration increases by three until the patient gets five correct replies or fails to identify the bottle containing 4% butanol correctly. After that, the butanol concentration increases by a factor of three.[6,25]

The concentration at which the patient correctly detects the butanol on 5 separate occasions is recorded as the detection threshold. The patient's threshold is compared to an average subject population by scoring.[6,26]

"UNIVERSITY OF PENNSYLVANIA SMELL IDENTIFICATION TEST: UPSIT"

Within the UPSIT, forty micro-encapsulated scents are presented in a scratch-and-sniff manner. Additionally, each odor has four response possibilities. The patient is the only one who takes the test and is instructed to guess if they cannot identify the item.[6,27]

Anosmic patients average a score either at or near chance (10/40 accurate). The scores and norms associated with age and gender are compared, and the results are examined. This exam's reliability is very high compared to other tests.[6,27]

A chart that compares scores to several patient populations is offered. These patient populations include patients who have MS, patients who have Korsakoff syndrome, and patients who are pretending to have anosmia. Those who fall into the latter category tend to achieve much lower scores on the examination than what would be expected by chance.[6,28]

"CROSS-CULTURAL SMELL IDENTIFICATION TEST"

A modification of the UPSIT that can be administered in just 5 minutes was suggested to obtain a speedy evaluation of olfactory function. After receiving comments on the familiarity of odors in several countries, including China, Colombia, France, Germany, Italy, Japan, Russia, and Sweden, the Cross-Cultural Smell Identification Test was designed with twelve items. The test was developed utilizing input from numerous nations.[6,29]

Bananas, chocolate, cinnamon, gasoline, lemon, onion, paint thinner, pineapple, rose, soap, smoke, and turpentine are some of the odorants in this compilation. Representatives from each country identi-

fied these odorants as having the highest consistency.[6,29]

This test is a suitable alternative for examining olfactory function in a clinical setting because it is quick and reliable. This is especially true in situations where time is limited.[6,29,30]

SNIFFIN' STICKS

To evaluate 1) Odor threshold through a single staircase method, 2) Odor discrimination with forced choice among three of sixteen different common odorants, and 3) Odor identification with multiple forced choice from four verbal items, this test utilizes a series of odor-dispensing devices that are similar to pens and can be reused. To provide an overall evaluation of olfactory function, a composite score is derived by combining the results of all three scores.[6,8]

CLINICAL SIGNIFICANCE

Elderly populations frequently experience a benign reduction in olfactory sensibility, which may manifest momentarily in intranasal inflammation or obstruction. This phenomenon is widespread among older populations. On the other hand, when doctors encounter irregularities in a clinical context, such as anosmia or hyposmia, it is necessary to conduct additional research into the underlying etiology being investigated. The first step in this approach involves gathering a detailed patient history and carrying out a comprehensive neurologic examination, which could include an assessment of the first cranial nerve.[31]

The olfactory function can be affected by a wide range of clinical conditions. Upper respiratory viral infections are the most prevalent cause of permanent anosmia and hyposmia.[32] Neurotropic viruses can potentially cause irreversible damage to the neural tissue of the olfactory system. This disease is a common reason for temporary anosmia, and it is regularly found in people of all ages. In sinusitis, nasal blockage can be caused by an inflamed nasal mucosa and increased mucus production. This condition is also one of the causes of incomplete anosmia.[33]

Recently, research has shown that anosmia is a significant early indicator of neurodegenerative disorders, including Parkinson's disease and Alzheimer's disease.[34,35] As a result, it is essential to evaluate the olfactory function when assessing neurodegenerative diseases. It is also possible for facial injuries to cause a loss of scent.[36] Facial trauma can sometimes result in a fracture of the cribriform plate and the discharge of cerebrospinal fluid. Fractures that involve injury to the cribriform plate are more likely to do this. Therefore, in these circumstances, we must perform comprehensive work to prevent infection of the brain and meninges.

Olfactory groove meningiomas and other intracranial masses can lead to secondary olfactory loss.[37] Research also indicates a significant link between olfactory dysfunction and schizophrenia.[38] Recent studies on olfactory triggers for migraine headaches and hyperemesis gravidarum during pregnancy suggest they may share a common mechanism related to allelic variations in dopaminergic receptors.[39] Additionally, some women have reported increased sensitivity to smells during pregnancy, although the scientific explanation remains limited.[40]

There was a decline in the olfactory sense reported by approximately 5 to 7 percent of patients who recovered from head trauma. Certain diabetic people also have problems with the functioning of their olfactory nerves. It is also possible for olfactory hallucinations to emerge in cases of psychosis or hippocampal injuries. When patients experience olfactory hallucinations, they characterize the odors as being unpleasant and peculiar.[31]

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

All authors contributed equally while this study preparing.

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