Smell disorders and dysosmia

Disorders in olfaction are common, yet poorly understood. This article explains the mechanism of the olfactory system and the pathogenesis of dysosmia, along with current trends in management and treatment.

Disorders causing a decreased, absent or distorted sense of smell may induce a significant disability that can impact on an individual's health, safety and quality of life (Blomquist et al, 2004; Hummel and Nordin, 2005).

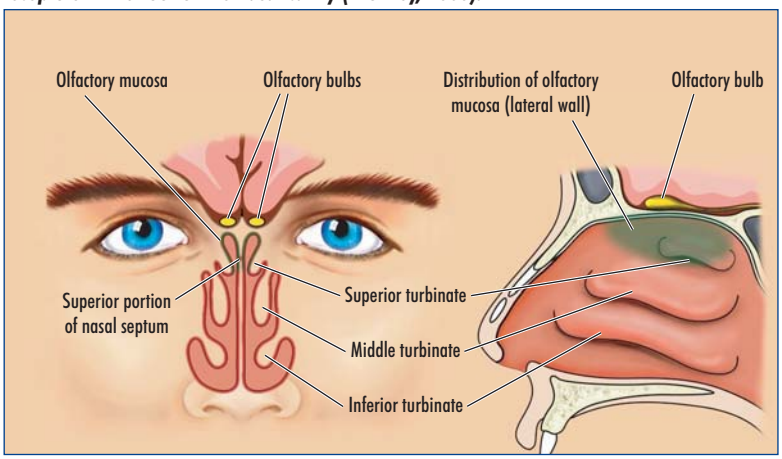
A normal sense of smell is termed normosmia. Deviation from the norm is described as anosmia (inability to detect odour), hyposmia (reduced ability to detect odour), and dysosmia (distorted detection of smell).

Dysosmia can be categorized as parosmia or troposmia (perceived distortion in the presence of a stimulus), or phantosmia (perception of an odour without a stimulus).

The term 'cacosmia' refers to detection of an unpleasant smell but since it is used inconsistently, both with and without the presence of a stimulus, it is better avoided (Leopold, 2002; Bonfils, 2005).

Dysosmia or olfactory distortion is a debilitating condition. Patients with parosmia typically perceive smell as 'foul', 'rotten', like 'sewage' or as 'burned' (Bonfils, 2005). Phantosmia, with the absence of an odorant stimulus in the environment, is often harder to tolerate than olfactory loss because of the constant unpleasant experience (Leopold, 2002).

Figure 1. Anatomy of the olfactory neural pathways, showing the distribution of olfactory receptors in the roof of the nasal cavity (Bromley, 2000).



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Over 30 years ago, it was estimated that more than 2 million adults in the United States were suffering from a smell or taste disorder. To date, few studies have investigated the real prevalence of olfactory disorders in the population. A survey from 1994 estimated a prevalence of 2.7 million adult Americans suffering from olfactory impairment alone (Hoffman et al, 1998). In another series of 750 patients with non-specific smell disorders, 10.4% were found to have a primary complaint of dysosmia (Deerms et al, 1991).

Anatomy and physiology of the smell pathway

The sense of smell is mediated through stimulation of smell receptors in olfactory mucosa. Olfactory mucosa occurs in the olfactory cleft in the superior part of each nasal cavity and in humans it covers the area of the cribiform plate, superior nasal septum and superior turbinate (*Figure 1*).

Dysosmia occurs whenever there is malfunction rather than complete loss of function within the olfactory pathways from mucosa to specific areas in the brain.

For a substance to be perceived as a smell, it must release volatile odorant molecules. Once these molecules reach the olfactory cleft, they interact and bind to olfactory nerve receptors within the olfactory neuroepithelium (Buck, 2000). Thus, the basis of odour perception is a chemical interaction between odorant molecules and receptors that is subsequently transformed into electrical signals to the brain.

A single olfactory receptor can recognize multiple odorant molecules and one odorant molecule can be recognized by several olfactory receptors. Different odorant molecules are recognized by a unique combination of receptors. Therefore, the odorant receptor 'family' is used in a combinatorial way such that the olfactory system can identify an enormous variety of odorant molecules (Malnic et al, 1999). Research has shown that humans can detect more than 10 000 different types of odour (Ressler et al, 1994).

Each olfactory receptor is a primary sensory bipolar neuron. An average nasal cavity contains about 100 million of these nerve cells that are regenerative throughout life and turnover within 30–60 days (Marshall, 2006). The axons of these regenerative bipolar cells penetrate the cribiform plate of the ethmoid bone as the first-order olfactory neuron to synapse with the second-order olfactory neurons located within the olfactory bulb. Here, they form bushy masses known as glomeruli (Menini et

al, 2004). Interestingly, studies have shown that olfactory bulb glial cells, known as olfactory ensheathing cells (OECs), are capable of assisting axonal regeneration of olfactory sensory neurons and can be used for repair of traumatic spinal cord injuries and neurodegenerative diseases (Mackay-Sim, 2005; Marshall, 2006).

From the olfactory bulb, projections of the second-order olfactory neurons travel to the olfactory cortex which is divided into five areas: the anterior olfactory nucleus, connecting the two olfactory bulbs through the anterior commissure; the olfactory tubercle; the piriform cortex, which is the main olfactory discrimination area; the cortical nucleus of the amygdala; and the entorhinal area, which projects into the hippocampus (Menini et al, 2004). The olfactory pathway does not involve a thalamic relay before its cortical projections. Relays from the olfactory tubercle and the piriform cortex are projected to other olfactory cortical regions and to the medial dorsal nucleus of the thalamus (*Figure 2*).

In addition to the main olfactory system, an accessory olfactory system, known as vomeronasal organ (VNO), or the accessory organ of Jacobson, is present inferiorly in the anterior nasal septum, deep to the nasal respiratory mucosa and next to the septal perichondrium. This bilateral membranous structure detects pheromones that may be important in sexual responses and neuroendocrine changes, although the significance in humans is circumstantial (Trinh and Storm, 2003).

Free trigeminal (fifth cranial) nerve endings are also found in the nasal mucosa. These are stimulated by aversive stimuli, such as ammonia, and are processed via separate pathways from the olfactory system. People who have lost their sense of smell therefore retain their ability to detect pungent odours even though they are unable to smell them.

Pathophysiology of dysosmia

There have been few publications on dysosmia since its recognition in the 1960s and the precise pathophysiology still remains unclear (Zilstorff, 1966).

The peripheral hypothesis

This presumes that there is an inability to create a complete 'picture' of an odorant because of a loss of functioning olfactory neurons based on the histological findings in patients with phantosmia (Leopold et al, 1991). Olfactory neurons would therefore transmit abnormal signals to the brain or there may be loss of inhibitory signals to normally functioning olfactory neurons. Ablation of abnormal olfactory mucosa has been associated with resolution of dysosmia (Leopold et al, 2002). Patients with unilateral phantosmia are reported to be able to eliminate the distortion by occluding the nostril or anaesthetizing the olfactory mucosa (Leopold, 2002). Furthermore, patients with dysosmia have some degree of olfactory intensity loss, hence suggesting some form of olfactory neuron dysfunction (Bonfils et al, 2005).

The central hypothesis

The integrative or interpretive centres in the brain are considered to perceive a distorted odour as a result of an area of hyper-functioning brain cells (Leopold and Myerrose, 1994). An example of this is the olfactory aura that occurs with some seizures, sometimes being preceded by a non-specific warning of impending symptoms (Leopold, 2000).

The central theory is supported by brain imaging using positron emission tomography (PET) scans in patients with phantosmia. Increased activity in specific areas of the brain decreased following excision of the corresponding olfactory epithelium (Leopold and Myerrose, 1994).

Clinical evaluation and investigations

History

The key question in dysosmia is whether or not an unpleasant smell can be detected by others since this will help differentiate infective sinus disorders from pathology of the olfactory mucosa or central connections and brain. The history should be focused towards the diagnostic possibilities such as sinus infection, viral illnesses, head trauma, illicit substance abuse, foreign body insertion and tumours of the nose or brain.

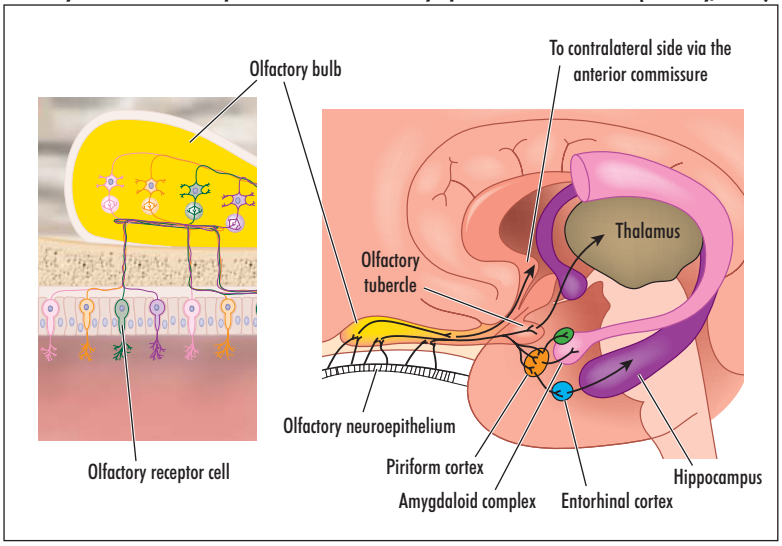
Examination

A detailed examination of the upper respiratory tract including flexible nasal endoscopy should be performed. Each side of the nose should be occluded in turn to see if the perception of distorted smell changes (Leopold, 2002). If central pathology is suspected, neurological examination will be necessary.

Investigations

An assessment of the sense of smell is required to estimate the degree of the smell disorder and also act as a baseline for future reference. The authors currently use

Figure 2. Simplified diagram of cortical regions thought to be involved in processing olfactory information as it passes from the olfactory epithelium to the brain (Bromley, 2000).



the University of Pennsylvania 40 item forced choice smell identification test (UPSIT; Sensonics Inc., Haddon Heights, NJ).

Scans of the sinuses and head are indicated for distortions of the sense of smell that persist after medical treatment. Pathology either in the sinuses or brain may well be revealed or excluded. Both magnetic resonance (MR) and computed tomography (CT) scans will provide helpful diagnostic information, but if CT alone is used then both sinus and intracranial brain settings should be requested.

Management of dysosmia

Rhinosinusitis should be treated with a combination of antibiotics and long-term topical steroids. Fungal sinusitis will require specific management.

Although some smell disorders may respond to a short systemic course of oral prednisolone, this has not been found to be effective in relieving dysosmia from the experience of the senior author.

Topical oxymetazoline HCl nasal drops have been reported to induce temporary relief of smell distortion, by inducing obstruction in the olfactory cleft from rhinitis medicamentosa (Leopold, 2002).

Surgical

Patients with dysosmia who are refractory to medical therapy may benefit from surgery. Dysosmia caused by chronic rhinosinusitis is managed by endoscopic sinus surgery only after medical therapy has failed to eradicate a source of infection. Although this presentation is unusual, it does occur with purulent maxillary sinusitis or with fungal infection.

In the absence of sinusitis, two specific surgical procedures have been described for treating dysosmia. Endoscopic excision of olfactory epithelium has been reported to relieve phantosmia in a small selective group of patients (Leopold et al, 2002).

Dysosmia has been treated by division of the olfactory fibres or removal of the olfactory bulbs via a bifrontal craniotomy. However, this approach will cause permanent anosmia and carries all of the risks associated with intracranial surgery (Kaufman et al, 1988; Markert et al, 1993).

KEY POINTS

- Olfaction involves a complex sensory mechanism involving various connections between the nasal mucosa and brain.
- Dysosmia is a perceived olfactory disorder with or without a stimulus.
- Dysosmia is caused by either an abnormality of the afferent olfactory neurons (peripheral hypothesis) or of the receptors in the brain (central hypothesis).
- Thorough history, examination and investigations are essential in attempting to ascertain a reversible pathological cause for dysosmia.
- Treatment may be medical or surgical, depending on whether an aetiological factor is ascertained.

Conclusions

Dysosmia is a common, yet poorly understood disorder that may be caused by an underlying condition. Its exact mechanism is unknown although theories have been postulated to suggest the disorder lies either at the nasal or cerebral end of the olfactory sensory system. A variety of medical and surgical therapies are available to treat the condition, which is best managed by clinicians with a subspecialty interest. Further studies are indicated in order to fully understand the condition and improve the long-term prognosis. BJHM

Conflict of interest: none.

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