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Distortion of Olfactory Perception: Diagnosis and Treatment

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Abstract

Clinically, olfaction can fail in any of three ways: (i) decreased sensitivity (hyposmia, anosmia) and two types of distortion (dysosmia); (ii) distorted quality of an odorant stimulation (troposmia); (iii) perceived odor when no odorant is present (phantosmia, hallucination). The distortions are usually much more upsetting to a person's quality of life than a simple loss. An ipsilatersal loss of olfactory sensitivity is often identified in the nostril with any type of olfactory distortion. The pathophysiology of a stimulated distortion (troposmia) is likely a decreased number of functioning olfactory primary neurons so that an incomplete characterization of the odorant is made. In phantosmia, two possible causations include an abnormal signal or inhibition from the primary olfactory neurons or peripheral olfactory or trigeminal signals that 'trigger' a central process. The clinician's goal is to carefully define the problem (e.g. taste versus smell, real versus perceived, one versus two nostrils), to perform the appropriate examination and testing and to provide therapy if possible. Treatment includes assurance with no active therapy (because many of these will naturally resolve), topical medications, systemic medications, anesthesia to parts of the nose and, rarely, referral for surgical excision of olfactory neurons. Endoscopic transnasal operations have the advantage of treating phantosmia and sometimes allowing a return of olfactory ability after the operation.

Introduction

The sense of smell provides people with valuable input from the chemical environment around them. When this input is decreased or distorted, disability and decreased quality of life are reported (Miwa *et al*., 2001). The purpose of this paper is to present a review of the current clinical understanding of olfactory distortions, how they can be evaluated and therapies to treat this debilitating condition. Unfortunately, research on humans with this condition is practically non-existent.

The human sense of smell generally fails in one of three ways (Leopold and Myerrose, 1994). One is an intensity reduction resulting in decreased olfactory sensitivity (hyposmia or anosmia). The other two are quality changes with a distortion of the perceived odor. One type of distortion occurs when inhaled odorants do not have the same 'smell' or 'odor' as remembered (troposmia, 'to twist or turn the sense of smell') (Leopold, 1995). The other type of distortion is the perception of an odor (usually unpleasant) when there is no odorant in the environment (phantosmia, hallucination). These distortions are usually much more disruptive to a person's life than a simple loss, because they are repeatedly being reminded of the problem.

The terms used to describe olfactory distortions have been confusing in the past, but generally the following terms are now used. 'Dysosmia' can be used to describe any distortion of the sense of smell. 'Troposmia' or 'parosmia' describes the perceived distortion when there is an odorant stimulus present. 'Phantosmia' (lasting longer than a few seconds) and 'olfactory hallucination' (lasting only a few seconds) describe the perception of an odor (usually unpleasant) when there is no odorant stimulus present. Care must be used with these terms, however, because *Dorland's Illustrated Medical Dictionary* (1988) defines 'parosmia' as 'Any disease or perversion of the sense of smell'. The 2000 edition of *Dorland's* actually equates 'parosmia' and 'dysosmia'. These definitions could potentially describe a simple olfactory loss or either type of distortion. Because of this, 'troposmia' will be used in this paper to describe a stimulated olfactory distortion. 'Cacosmia' is also a term sometimes used. It is the perception of a bad smell without an odorant stimulus, or an unpleasant phantosmia.

The etiology of the distorted perception in troposmia is not clear. Two general possibilities include a 'peripheral' theory where the loss of functioning olfactory neurons results in the inability to form a complete 'picture' of the odorant (Leopold *et al*., 1991) or a 'central' theory where the integrative or interpretive centers in the brain form a distorted odor (Leopold and Myerrose, 1994). Phantosmias (those unstimulated perceptions of odor that last longer than a few minutes) are also thought to have either peri-

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pheral or central causation, or a combination of the two. Peripherally, 'rogue' neurons that emit abnormal signals to the brain or a loss of inhibitory cells to normally functioning olfactory neurons could be at fault (Leopold *et al.*, 1991). Centrally an area of hyper-functioning brain cells could generate this odor perception (Leopold and Meyerrose, 1994). Clinically, it seems possible that a peripheral trigger from a chemosensory or even trigeminal stimulus could signal a central perception of odor (Leopold *et al.*, 2002). Most of the phantosmia patients we have seen can start the odor perception with a small nasal sniff or sneeze and they go to great lengths to avoid nasal air flow.

Careful evaluation of individuals with olfactory distortions suggests evidence for both of these theories. Peripheral causes are suggested by the finding that most individuals with distortions have an intensity loss along with the distortion. They will also say that the distortion was worse while the loss was occurring, such as the first few hours after head trauma or an upper respiratory infection loss. Phantosmia is almost always worse in the nostril with the least olfactory ability and those phantosmias that occur in only one nostril can be eliminated by occluding the air flow or anesthetizing the olfactory mucosa in that nostril. Finally, the olfactory histopathology of individuals with phantosmia shows a decreased number of neurons, a greater ratio of immature to mature neurons and disordered growth of olfactory axons (Leopold *et al*., 1991, 2002).

There is also evidence for central causes of olfactory distortion. There is a known olfactory aura that can sometimes accompany seizures. This typically lasts only a few seconds. Some individuals with phantosmias have commented that they can 'feel' a phantom odor coming before it actually arrives. Similarly, some of the people whose phantosmia has been cured by excision of olfactory epithelium have commented that there is still a 'feeling' that the bad smell is going to occur, yet it never does. Brain imaging using positron emission tomography (PET) scans of individuals with phantosmia has revealed increased activity in the contralateral frontal, insular and temporal regions, which decreased after excision of the olfactory epithelium from the nasal cavity involved (Leopold and Myerrose, 1994). Not enough patients have been PET scanned to know the significance of these activity areas.

Evidence that supports both peripheral and central causes of olfactory distortion includes observations on the natural history of the condition and its response to treatment. I have observed that approximately one quarter of individuals who have a single nostril phantosmia have a progression to involvement of the other nostril over a period of months to years. This could be explained by abnormally functioning primary olfactory neurons and their supporting cells in both nostrils or the ability of either nasal cavity to 'trigger' a central process. There has also been anecdotal improvement noted with treatment using anti-seizure and anti-depressant medications. These drugs may act on both peripheral and central neurons. There has been no published data on treatment of olfactory distortions with neurally active medications. This is informal information from other clinicians, my clinical experience and patient's reports.

Clinical evaluation: history

While obtaining a clinical history from someone with a complaint of olfactory distortion it is important to be sympathetic, since many of these individuals are anxious about their symptoms. Typically they have been given ineffective therapy or told to 'just live with it'. Because of analogies with psychiatric conditions, they may have been told that they have a mental illness. They may also have obtained information from the Internet or other sources that is inaccurate or misleading.

The initial task of the examiner is to define the complaint. Is it a true taste (salt, sour, bitter, sweet) complaint (as most will say) or is it an olfactory problem (as is more often the case)? Questions about food choices, coffee use, etc., will help here. Some patients truly have difficulty deciding whether it is a taste or smell problem. When this occurs, a metabolic problem that changes the aroma of body secretions needs to be ruled out, since these patients will often emit an odor (Leopold *et al*., 1990).

Whether the complaint is a decreased sense of smell, a distorted sense of smell or both needs to be determined. This may change after testing, but understanding the patient's perception of it is important for future counseling. If there is a distortion, is it only to inhaled odorants (troposmia) or does it exist when no odorants are in the environment (phantosmia)?

If it is a troposmia, two separate types of presentation are possible. In the first, all olfactory stimuli are reported to be uniquely different and identifiable and many or all are not what was remembered for that stimulus (e.g. rose smells like banana, banana smells like garbage, but potato smells like potato). In the second type there is a similar distortion to all odorants ('everything smells musty').

If it is a phantosmia, have the patient describe the quality of the odor perception. This will be helpful in the future management of this patient, such as after therapy. Typically they will use words like 'burned, foul, unpleasant, spoiled or rotten'. Often patients have difficulty with this naming task, and a better understanding of the patient's complaint can be determined by having him or her 'place' the odor to environments like outdoors, a factory, the garage, the kitchen, etc.

Antecedent events that precede the olfactory distortion have been described in the literature to include upper respiratory infection (viral?), head trauma, allergic rhinitis and chronic rhinosinusitis (Mott and Leopold, 1991; Duncan and Seiden, 1995; Apter *et al*., 1999; Quint *et al*., 2001). Whether they apply to stimulated or non-stimulated distortions is difficult to determine because of the imprecise words used (parosmia, dysosmia, etc.). In my experience,

patients with stimulated distortions (troposmias) usually have a history of something that might decrease the number of olfactory neurons, such as an upper respiratory infection, head trauma or aging. The distortions seem to occur during either neuron death or regeneration.

In contrast to this, we have noticed, as has Zilstorff, that most phantosmias present with no history of upper respiratory infection, head trauma or aging (idiopathic) (Zilstorff, 1966). The typical history for a phantosmia is that it begins spontaneously in a woman between 15 and 30 years of age with an episode of odor perception the individual thinks is real but others do not appreciate. This initial episode lasts ~5–20 min. It resolves spontaneously with no after effects. The next episode will occur the same way about 1 month later. Gradually over the next year the episodes become more frequent and last longer each time. The perception may be in one or both nostrils and may be blocked with occlusion of the nostril(s). Once the smell perception has started, it is usually not masked by foods and all foods have the flavor of the phantom smell. Typically the phantom smell resolves with sleep. Other activities that have been reported to stop the smell include Valsalva's maneuver, forced crying, intranasal instrumentation and gagging. After several months or years, these all become ineffective in stopping the phantom smell perception. Although there is nothing in the literature, I have found systemic corticosteroids to be ineffective in helping these people.

Psychiatric etiologies for olfactory distortion can exist with schizophrenia, alcoholic psychosis, depression and olfactory reference syndrome (similar to depression and treated with the same medications) (Leopold, 1995). Olfactory distortions have also been observed with epilepsy. These conditions should be ruled out if applicable and referral should be made to mental health professionals for diagnosis and care if suspected. Since olfactory distortions are a major factor in someone's life, it is expected that they will have responses to them, such as depression or anger. Appropriate care should be exercised to be alert to these 'secondary' effects of the distortion. Approximately half of my patients who have sought surgery for their distortions have at one time considered suicide because of the hopelessness of living a life where all food smelled like spoiled meat or worse.

Clinical evaluation: examination and testing

A standard head and neck examination should be performed, paying special attention to the chorda tympani nerve and middle ear, the nasal mucosa and airways and the tongue. The patient's general demeanor and psychiatric health should be assessed. Nasal endoscopy is indicated to examine the olfactory pathways in the nose. Unilateral and bilateral nasal occlusion can be done to assess changes in a distorted perception.

Testing should include uninasal olfactory testing with a standard test of identification and possibly threshold. Imaging of the brain and nasal cavity is necessary to rule out tumors, infections and obstructions. This can be done with contrast enhanced axial and coronal computerized tomography scans or magnetic resonance imaging scans. If a metabolic disorder is suspected, the patient should be referred for specialized metabolic testing of choline and other liver metabolisms (Leopold *et al.*, 1990).

Treatment for olfactory distortion: medical

Above all, individuals with olfactory distortion need to be reassured that they do not have a malignant disease or an infection. It may help to give them the name of the disorder and explain the neural etiology. If they also have olfactory loss it is necessary to council them regarding safety items like smoke detectors, avoiding explosive gases, explosive gas detectors and spoiled foods. Most patients will note a gradual decrease in the symptom with time, and this can occur over several years (Duncan and Seiden, 1995). Thus, 'watchful waiting' is an appropriate course to take.

For those individuals with olfactory distortions who are unwilling or unable to wait, there are several things to try. If perception of the distortion can be blocked with nasal occlusion, one of the easiest things to try is topical nasal saline drops. These can be placed in limitless quantity every few hours in the head-down-and-forward ('Mecca') position. Although this works less than half the time, and often for only short periods, it is harmless, has few adverse side effects, is inexpensive and may be just what the patient needs for a short respite from the awful smell. Alternatively, the daily use of Oxymetazoline HCl nasal drops to give the patient rhinitis medicamentosum has also been useful, and generally lasts longer. Both these therapies give a biological upper nasal block to the involved nostril(s) so air flow cannot reach the olfactory cleft.

Several medications, including sedatives, anti-depressants and anti-epileptic drugs, have been suggested to treat olfactory distortions (Zilstorff, 1966). I am not aware of any recent published trials using drugs to treat patients with olfactory distortions. Currently, Gabapentin is being used by several olfactory centers. Patients may or may not benefit from being on these drugs, and trials of therapy should be planned. Even if patients are helped, they may not be able to tolerate the side effects of the drug therapy, since the dose may need to be increased to achieve the desired effect.

Active pharmacologic disruption of the olfactory neurons has been proposed by Zilstorff (Zilstorff, 1966). The use of topical cocaine HCl can temporarily block most distortions by anesthetizing the neurons, and is useful in the diagnosis of these individuals. The drug is applied as a drop into the nostril of the supine patient while their neck is fully extended. Care must be exercised when using it, however, because undesired effects can occur. I have had patients with a temporary troposmia suddenly have a permanent phantosmia after use of topical cocaine. I have also had individuals

lose all their olfactory ability in one nostril after its application. Certainly, care must be exercised in deciding when to use topical cocaine and extensive informed consent must be obtained from the patient before its use. Beyond a single use, Zilstorff has suggested applications at several week intervals to achieve a reduction in the distortion. Because cocaine is an excellent vasoconstrictor, the effect may be to deprive the neuron of blood supply.

Treatment for olfactory distortion: surgical

The vast majority of individuals with olfactory distortions can be helped with the above therapies. Those who cannot may benefit from surgical therapies. Neurosurgical approaches using a bifrontal craniotomy to remove the olfactory bulbs or nerves have been reported (Kaufman *et al*., 1988; Markert *et al*., 1993). These procedures necessarily result in bilateral permanent anosmia and include the risks associated with a craniotomy.

To treat a patient's phantosmia and avoid a craniotomy, in 1988 I performed an excision of the olfactory epithelium as an endoscopic intranasal procedure (Leopold *et al*., 1991). Not only was this successful in eliminating the phantosmia, but the patient had her olfactory ability return. Based on this success, I have completed an additional 18 of these procedures on 10 patients over 13 years, with three patients requiring operations on both sides and five re-operations to completely excise the olfactory neurons. The indications for this endoscopic approach include a unilateral phantosmia that has been present for more than 2 years and can be eliminated with intranasal cocaine anesthesia of the ipsilateral olfactory mucosa. In a recent survey of the first eight patients (Leopold *et al*., 2002) all responded affirmatively to the question 'If you had it to do over again, would you have the surgery?'. One of the patients has a persistence of the phantom smell, but at a much lower intensity, and the remainder have complete resolution of the phantom smell.

The intent of the operation is to cut all the fila olfactoria and destroy all connections between the nasal cavity neurons and the olfactory bulb in the operated nostril. Patients are counseled about this pre-operatively and expect to loose all olfactory ability bilaterally. Long-term testing 1–11 years post-operatively in the studied patients shows the olfactory ability to be unchanged in 5/10 nostrils, improved in 2/10 and decreased in 3/10 compared with pre-operative levels. As an indication of how unstable the olfactory ability can be in these patients, in the non-operated nostril it was unchanged in 3/6, decreased in 1/6 and improved in 2/6. There were two cerebrospinal fluid leaks noted intra-operatively and these were patched successfully with mucoperiosteal grafts. There were no difficulties with visual changes, epiphora, meningitis or scarring resulting in chronic rhinosinusitis.

All of the olfactory cleft mucosa removed from these patients was specially processed to determine the changes that are present in this population. Olfactory epithelium and/or fascicles of the olfactory nerve were identified in all specimens. As reported in the introduction, the histological changes generally support peripheral neural damage, with large fascicles lacking neurons (Leopold *et al*., 2002).

Conclusion

By dealing with these very distressed patients with distorted olfactory ability, I have gained a great respect for the disability they have (Miwa *et al*., 2001). One needs to carefully talk with them to determine who can be helped and how to do it. The rare patient who needs surgical therapy should be evaluated in a center where expert care can be given and where the most can be learned about this debilitating problem by collecting information from many patients with the same condition.

There are still many things to learn about olfactory distortion. Further research should address the following questions.

What allows the return of olfactory ability after cutting all the fila olfactoria and can this information be used to treat individuals who loose their olfaction after head trauma or an upper respiratory infection? If the olfactory neuron does regenerate some of the time and if some of our patients regained olfactory ability after attempts to destroy it, does simultaneous regeneration have a possible benefit?

What causes the changes in olfactory ability in the contralateral nostril after surgery or cocainization of one nostril? Although the human olfactory system is thought to have ipsilateral innervation, are there efferent influences on function?

Can the information from ongoing studies of olfactory neurons be used to understand the cellular mechanics of these distorting neurons? Understanding the distorting process would be much easier if the basic mechanisms of coding were better understood.

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