Smell and taste in clinical neurology

Five new things

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Summary

Advancements in the field of smell and taste disorders have allowed easier and more reliable diagnosis with minimal effort and cost. Posttraumatic smell and taste disorders have shown a better prognosis than previously recognized. The recognition that many neurodegenerative disorders, such as amnesic mild cognitive impairment, Alzheimer disease, and premotor and idiopathic Parkinson disease have impaired smell loss is an important advancement in the clinical course of these disorders. Smell and taste abnormalities often lead to unexplained weight loss, decreased appetite, depression, and inability to smell smoke and recognize spoiled foods. Symptoms of dysosmia and dysgeusia have been more clinically defined and treated in the last 10 years, but treatment benefits are anecdotal. The morbidity and impaired quality of life in smell and taste disorders has been increasingly recognized and reported this last decade. Information on changes in food preparation has increased for those with impaired taste who do not enjoy eating.

In the last 30 years, clinical neurology has lagged behind neurologic advances in smell and taste disorders partly due to the sparse training in medical school and neurology residency. This is reflected in the standard neurologic examination, which states: “cranial nerves 2–12 are intact.” Cranial nerve 1 is rarely tested and uncommonly mentioned in “review of systems.” This review will update 5 new things in smell and taste in clinical neurology.

It is necessary to understand parts of the chemosensory system necessary for recognizing food we eat. The olfactory system, in addition to odor recognition, is necessary for registering food flavors (e.g., vanilla, chocolate). The taste system, which is made up of receptors on the tongue, palate, and pharynx, are necessary for identifying 5 tastes: sweet, sour, bitter, salt, and umami. Umami is the Japanese word for “savory or broth taste” and is represented by monosodium glutamate (MSG). The sensory portion of the trigeminal nerve recognizes texture, temperature, and spiciness of food. This information helps explain why taste and

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If head or facial injury is suspected, brain MRI with views of the olfactory system (cribriform plate, olfactory bulb and tracts, gyrus rectus, and medial temporal lobes) should be performed.

smell alteration causes impaired quality of life and why change in food preparation is an important treatment.

Update in smell and taste testing

One major advance in the last 25 years is development of standard smell and taste tests to help identify impairment. A validated smell test called The University of Pennsylvania Smell Identification Test or UPSIT is standardized for age and gender and available in different languages. A shorter version of this test is the Brief smell identification test (B-sit), which has 12 odors, and is less sensitive, but a good screening test. If the B-sit is abnormal, the UPSIT is recommended for more specificity.¹

Another validated smell test is called “Sniffin’ Sticks.” It consists of pen-shaped objects with an embedded odor at the top. It is standardized for age and gender, available in different languages, and unlike the UPSIT can measure smell threshold and can be used on many different patients. There are other validated smell tests available.¹ Taste testing requires administration by the physician or an assistant. It evaluates 4 tastes: sweet, sour, bitter, and salt. In the United States, whole mouth and localized tongue testing using a pipette is popular. Test solutions, using distilled or bottled water, are prepared for each taste in 4 different concentrations. The individual is told what tastes will be tested. Each solution is sampled, swished in the mouth, and spit out. The patient attempts to identify the taste.

Another test is called “The Taste Strip Test,” developed in Germany. It is made up of 4 sets of filter paper strips, each set having 4 concentrations of the 4 tastes. It is easy to perform and does not require mixing solutions.

Over 90% of individuals who complain of altered taste have a primary smell disorder.¹ This is because a normal olfactory system is necessary for recognizing food flavors. Patients do not distinguish between flavors and taste and use the term “taste” for any altered food enjoyment.

Asking the patient if they can recognize sweet, sour, and salt is a good way to determine that the taste system is intact. If the patient complains of altered taste, and smell testing is normal or mildly impaired, taste testing should always be performed.

Post-traumatic anosmia

Of all causes of smell and taste complaints in a smell and taste specialty clinic, 20% will be secondary to head trauma. This includes injury to the face, nasal structures, and any part of the skull.

Since head trauma is frequently associated with memory impairment, the injury may have been forgotten, so history from family or friends is necessary to verify this diagnosis. If head or facial injury is suspected, brain MRI with views of the olfactory system (cribriform plate,

Figure Brain injury at base of skull

Blunt force to the face, nose, and head causes the brain to move backward and forward. This causes a stretch injury to the olfactory nerves which are anchored to the cribriform plate. Frontal and temporal lobes become bruised from moving across the irregular base of skull.

olfactory bulb and tracts, gyrus rectus, and medial temporal lobes) should be performed. Eighty-three percent of individuals present with smell and or taste (impaired flavors) complaints within 1–5 days and 17% within 3 to 16 weeks of injury. The longer time period is often secondary to other injuries or memory impairment. Total smell loss occurs in 60%–80% of those tested and 20%–40% have mild to moderate smell loss.²

Four mechanisms are associated with smell loss in head trauma: 1) Injury to the face and nose, injuring the olfactory organ and nerves. 2) Injury to the skull without brain contusion. 3) Injury to the skull with brain contusion. 4) Any combination of 1–3. In direct facial and skull trauma, the brain is shifted back and forth due to acceleration and deceleration forces that can lead to contusions of the frontal and temporal poles and a shearing injury of the olfactory nerves traveling to and from the cribriform plate (figure). Studies show that occipital and side head trauma is more likely to cause olfactory impairment because of the protective effect of the frontal sinus and cartilage in frontal injuries.²

The prognosis of olfactory loss in head trauma has been traditionally considered dismal, but most studies lacked standardized smell and taste testing and did not account for subjective improvement. London et al.³ followed 106 cases of posttraumatic smell loss over 23 years, with careful smell testing and clinical evaluation. Of 69 patients with total smell loss, 44% made mild to moderate improvement, 11% returned to normal, and 45% did not improve. The important point was that 55% improved over time. This study has 3 important conclusions. First, the time between posttraumatic olfactory loss and baseline smell testing directly correlated with improvement. The longer the period, the better the improvement. The greatest smell improvement occurred within the first 6 to 9 months of injury, with subsequent improvement very slow or not at all. Secondly, lower olfactory loss at initial testing reflects a better prognosis. Individuals with mild to moderate smell loss are twice as

Table Smell testing in the diagnosis of neurodegenerative disorders

Clinical disorder	Olfactory testing (UPSIT)	Possible outcome
Amnesic mild cognitive impairment	30/40 or less and asymptomatic	This smell score plus impaired memory on neuropsychological testing plus decreased hippocampal volume on MRI leads to 82% likelihood of developing AD.
AD vs vascular or pseudodementia	30/40 or less	Strongly suggests AD; patients with vascular or pseudodementia usually have normal or mild smell loss: 34/40 or greater.
Premotor PD	30/40 or less	High correlation of developing PD in 4 years. Observe closely.
Atypical features of idiopathic PD	25/40 or less	Strongly suggests idiopathic PD; all other parkinsonian disorders have a much higher score: 29/40 or greater.

Abnormalities in all these disorders are frequently not recognized by the patient. This can lead to unexplained weight loss, decreased appetite, depression, and safety and nutritional concerns.

likely to improve to the normal range compared to severe smell loss. Finally, patients with age greater than 74 were less likely to improve than younger patients. Aging factors include changes in olfactory mucosa, sclerosis of the cribriform plate with compression of the olfactory nerves, and the frequent associated underlying neurodegenerative disorders like Alzheimer disease (AD) and Parkinson disease (PD) which impair smell.

Neurodegenerative disorders: Smell and taste impairment and value of smell testing

The earliest report of olfactory impairment in a neurodegenerative disorder was in 1975 in idiopathic PD, and in 1984 in AD. Since these reports, there have been many studies in other neurodegenerative disorders¹ (table).

Amnesic mild cognitive impairment Amnesic mild cognitive impairment (AMCI) is a memory disorder that lies between normal aging and dementia with minimal impairment in activities of daily living. Individuals with AMCI have a 60%–70% risk of developing dementia (usually AD) over a 5- to 7-year period. Smell testing has been studied in AMCI to determine if it can help predict who will develop dementia. A study in 2000 evaluated smell testing, using the UPSIT in AMCI and controls. The study showed that those who developed dementia were more likely to have an UPSIT score of <30/40 and no awareness of their loss (82% specificity). Other studies have shown that measuring MRI hippocampal volume, memory storage impairment on neuropsychological testing, and SPECT and FDG PET scanning is at best 86% specific for predicting dementia.⁴ If CSF for β -amyloid 42 and tau ratio is added to the prediction, specificity is increased to 90 plus percent.⁵ Substituting smell testing, and not performing SPECT, FDG-PET, and spinal fluid testing, results in 82% specificity, with a lower cost and morbidity to the individual. The abnormal smell test gives information about safety factors (inability to smell smoke, natural gas, identify spoiled foods, and impaired flavor recognition leading to weight loss, depression, and loss of appetite). Abnormal smell and memory in AMCI is not surprising, since pathology shows Alzheimer changes in the entorhinal and piriform cortex, important regions where short-term memory and smell is represented.

Alzheimer disease Smell impairment in AD has been recognized since 1984 and since then over 90% of individuals with AD have been found to have unrecognized smell impairment that begins in the AMCI stage or earlier and continues to progress with time (UPSIT <30/40).^{1,6} Pathologic studies have confirmed pathology (β -amyloid and tau) in the entorhinal and piriform cortex, the olfactory bulb, tract, and anterior olfactory nucleus. Smell testing can help separate the diagnosis of AD from vascular dementia and pseudodementia of depression which have normal or mild impairment.^{1,4}

Idiopathic Parkinson disease Smell loss in PD was first described in 1975, and did not correlate with medication or motor impairment but correlated with disease type. Tremor dominant

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type showed less smell loss than the rigid akinesia type. Like in AD, 90% of individuals with PD have unaware olfactory impairment (<25/40 on UPSIT) that does not progress. However, unlike in AD, maximal impairment is reached early on. The pathology is centered in the olfactory bulb and anterior olfactory nucleus. Later stages show involvement in the entorhinal region and piriform cortex, unlike in AD, where pathology is more central initially.^{1,6}

The premotor phase of PD has shown asymptomatic olfactory impairment. In a 2008 study,⁵ healthy volunteers underwent smell testing and were followed for 8 years. Thirty-five of 2,267 developed PD. Those with low smell scores 30/40 or less in the premotor phase developed PD within the first 3–4 years. Those developing PD later than 4 years did not correlate with olfactory loss.

Parkinson plus disorders Olfactory testing has been studied in Lewy body dementia, progressive supranuclear palsy, cortical basal degeneration, multiple system atrophy, and drug-induced and vascular parkinsonism. In a general neurology practice, these disorders may be misdiagnosed as idiopathic PD in 10%–20% of cases. Smell testing can help to separate these disorders from idiopathic PD. UPSIT scores in the above disorders are usually greater than 30/40, but scores of 25/40 or less are present in idiopathic PD.^{1,6} The AAN guidelines state, if a individual is suspected of having idiopathic PD and has a normal or mildly abnormal smell test, then another Parkinson disorder should be strongly suspected.

Update on dysosmia and dysgeusia

Dysosmia and dysgeusia are usually unpleasant (foul, sewage) smell and taste alterations causing severe impairment in quality of life. Both are classified into parosmia and parageusia, which refers to a triggered unpleasant smell or taste, or phantosmia and phantogeusia, which occur spontaneously without a trigger. One study evaluated 56 patients with parosmia. The duration was 3 months to 22 years with a median of 5 years. Seventy-five percent had diminished smell and 25% had total smell loss. Common triggers were tobacco, gasoline, coffee, and perfume. The causes were postviral (43%), chronic sinus disease (12%), cerebral trauma (10%), and idiopathic (35%). The mean time to develop was 1.5 months, but the range was immediate to 5 months.

Another article studied 116 patients with dysgeusia.⁷ Fifty percent were idiopathic, and others were due to dental material allergy, poor oral and dental hygiene, poorly controlled diabetes, decreased saliva (medication or salivary gland disorders), low zinc, low thyroid, and medications. These distorted sensations can suggest a seizure aura, arising from the medial temporal lobe. The difference is that olfactory or gustatory auras last under 2 minutes. Dysosmia and dysgeusia from olfactory disorders last 5 minutes to hours.¹

Suggested treatments of dysosmia (mostly anecdotal)

1. Reassurance: most cases resolve in 2 years or less.⁷
2. Nasal blockage with physiologic saline. Instill 5–10 cc (syringe) into each nostril in the head down position (4 times a day). When rising up, do not have the patient clear the nose, so the saline will block odors reaching the olfactory organ. If no benefit, discontinue after 1 week (helps in 25% of cases; personal experience).
3. Gabapentin 900 to 2,000 mg/day in divided doses with slow escalation over 3–4 weeks. In my 25 cases, 60% improved and 10% became asymptomatic. If successful, one or both

treatments should continue for 3 months. Periodically, taper one or both treatments every 3 weeks to see if symptoms return. If they do, return to the previous successful dose.

4. Surgical removal of olfactory epithelium in unilateral dysosmia has shown 90% success.^{7,8}

Suggested treatment of dysgeusia (mostly anecdotal)

1. Cepacol lozenges with benzocaine, 3–4 times a day (anesthesia of taste receptors).
2. Xylocaine mouth gel, 0.5%–1%, 3–4 times per day.
3. Zinc gluconate, 140 mg per day. Moderately helpful in 50% of cases⁷ (zinc necessary to regenerate taste buds and form saliva).
4. Gabapentin (900–2,000 mg/day) improved 4 personal cases.
5. Small ice cube in the mouth for 1 minute before meals.⁷ There is evidence that the gustatory nerve fibers are sensitive to temperature changes by thermosensitive ion channels. A channel called TRMP5, present in taste bud cells, confers a steep temperature dependence on taste perception processing. Taste and cold symptom interaction may be a reason for dysgeusia improvement.
6. Mirtazapine 15 mg at bedtime (one case reported).⁷

Morbidity of smell and taste impairment

In the last 15 years, there has been increased interest in the morbidity of taste and smell dysfunction. A study in 2001⁹ evaluated patients with impaired smell and found that 75% had impaired detection of spoiled foods, 61% could not detect gas leaks, 50% could not detect smoke, and 30% could not detect burnt food. Another study¹⁰ found decreased interest in cooking, eating less food variety, decreased appetite, and increased eating of sweeter and salty foods (worsened hypertension and diabetes). Another article¹¹ studied 176 smell and taste impaired patients; 21% gained weight (2.5 kg) (searching for better tasty foods); 11% had weight loss (5 kg); 35% invited fewer people for dinner; and 47% stopped going to restaurants. Sixty percent had no weight changes or altered food habits.

Depression occurs in 50% of patients. Many do not enjoy eating because of flavor loss. For others, their employment depends on normal smell (neonatal nurses, chefs, and firemen). Still others worry about inability to recognize their body odor and exposure to smoke. However, the basic tastes (sweet, sour, bitter, salt, and umami) and trigeminal function (texture, temperature, and spice) are preserved, the reason for success in changes in food preparation.⁸ For example, eating baked potatoes with butter or sour cream will have no flavor. Adding chunky, spicy salsa will give a spicy sensation, with increased texture. Regular baked chicken has no flavor. Adding Worcester sauce or chunky spiced salsa and a pinch of MSG can improve eating enjoyment. Marinating chicken in sweet and sour sauce or Italian dressing increases food enjoyment. There are many successful recipes, some tested and others provided by patients, that emphasize these principles.⁸

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Smell and taste: Five new things

- Improved smell and taste testing is reliable, easy to administer, and simplifies the diagnosis of smell and taste disorders.
- Prognosis of posttraumatic smell loss has been shown to be much better than previously considered.
- Smell testing can help in the diagnosis of neurodegenerative disorders such as amnesic mild cognitive impairment, AD, premotor and idiopathic PD, and Parkinson plus disorders.
- Dysosmia and dysgeusia have been better defined in the last 7 years and some successful studied and anecdotal treatments have been reported.
- The morbidity of smell and taste disorders has been increasingly recognized and more emphasis is being placed on changes in food preparation to overcome the number one disability: loss of eating enjoyment.

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DISCLOSURES

The author reports no disclosures relevant to the manuscript. Go to Neurology.org/cp for full disclosures.

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