Review Article

Nutrition and taste and smell dysfunction

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Abstract
Food selection plays a pivotal role in maintaining adequate nutrient intake, thus elucidating drivers of food choice is a meaningful strategy to maintain health and manage disease. Taste and smell are key determinants of food choice and warrant careful consideration. In this review, we first discuss how sensory stimulation influences food selection and metabolism. We then review the evidence regarding the relationship between taste and smell dysfunction and food preferences and selection, with attention given to contexts of certain chronic diseases. We conclude with brief recommendations for the management of chemosensory disorders. While sensory abilities influence food selection, the effect of taste and smell dysfunction on long-term consumption patterns and health status must be considered in light of environment, exposure, and culture.

Introduction

Of the many interacting influences on food selection, sensory inputs are often the primary driver.† Sensory signals also affect the metabolism of ingested nutrients. Through these functions, the chemical senses (taste, smell and chemical irritation) play a role at all stages along the continuum from health to disease. Concurrently, the function of these sensory systems is modified by an individual’s health status. The sensory properties of foods interact with the sensory capabilities of consumers to generate sensations that are measured by their detectability, intensity, quality, duration, and hedonic valence. The first four dimensions are the substrate for hedonic judgements and the latter exerts the most important influence on food choice under conditions of an available, varied diet.

Sensory influences on diet selection

In addition to serving as a warning system for potentially toxic substances, sensory systems may also have evolved as
a way to detect energy and key nutrients. Here, we review evidence surrounding the chemosensory detection of the macronutrients (carbohydrates, protein, and fat) and sodium, and their relation to nutrient and food selection.

Dietary carbohydrates are often consumed in the form of starch and sugars. Although increasing evidence indicates complex carbohydrates may be detected by the taste system, sweetness is the sensory attribute most commonly associated with carbohydrates, and for which the most data are available. Sensitivity to sweetness is present in utero and influences sucking behavior in pre-term infants. Despite the biological predisposition for sweet taste, the preference for and intake of sweetened foods depends heavily on culture. Exposure, more than functional dimensions of sensory abilities such as threshold sensitivity or perceived intensity ratings, is related to sweet preferences. For example, frequent exposure to sweetened soft drinks increases the preferred sucrose concentrations among individuals who originally preferred lower concentrations. However, relationships between exposure to selected sugary foods and acceptance cannot be generalized to all sweetened foods. Exposure to sugar-sweetened water during the first six months after birth is associated with greater intake of sweetened water at six months of age, but not with consumption of sugar-sweetened fruit drinks at two years of age. Other studies have failed to find significant associations between intake of sweet foods and hedonic ratings of a test item. Overall, the sweetness of some carbohydrate sources promotes intake of these compounds and foods that contain them, but there is no biological determinism that overpowers dietary experience and cultural norms.

Intact proteins are generally weak chemosensory stimuli. Their constituent amino acids as well as short peptides have varied taste qualities. Umami, best exemplified by mono-sodium glutamate, is considered by many as a basic or primary taste quality. The quality is sub-served by a unique receptor and is not replicated by other "primary" taste sensations. Although protein hydrolysates are generally regarded as unpalatable, their acceptance is heightened in populations with low or marginal protein status, suggesting the presence of a body response. However, other "primary" taste sensations such as savory taste modulate food preferences more than sweet taste. Furthermore, preference for high protein foods decreases more following consumption of a savory meal rather than a sweet meal. Together with sensory explanations for a protein-specific appetite, others have proposed that protein is the primary physiological signal driving total energy intake, a theory derived from observations of low variability in protein intake cross-culturally and within cultures over time. This view is termed the "protein leveraging hypothesis." It is postulated that diets low in protein would be consumed in larger quantity to achieve a needed level of protein intake, and diets high in protein would be ingested in lower quantities as protein needs would be met more easily. However, several studies have directly tested this hypothesis and have not provided consistent support. Although some have demonstrated a change in energy intake in response to altered dietary protein, none has consistently shown a convergence towards an optimal level of protein intake when presented both higher and lower protein diets. The taste of protein, i.e., amino acids and peptides, may serve more as a hedonic modifier than a fundamental controller of ingestive behavior.

Although increasing evidence suggests that fat is detectable via gustation as well as other sensory systems, data supporting a role for fat taste on dietary behavior is mixed. The primary form of fat in the diet is triacylglycerol, a large molecule without documented efficacy as a taste stimulus. However, its constituent fatty acids are potent olfactory stimuli and effective, albeit more subtle, taste signals. Their chemosensory properties are generally unpleasant, and foods containing high quantities are rejected (except in selected cases where a liking develops through dietary exposure and cultural norms, e.g., appeal of strong cheeses). Thus, the food industry expends considerable effort to ensure fatty acids remain below detection levels so products are viewed favorably. In this regard, fat taste is a powerful determinant of intake. Early hypotheses held that the increasing fat content of breast milk over a feed was a cue used by nursing infants to terminate a feed. Evidence related to this view is mixed, but generally negative. High fat foods are often viewed as desirable by consumers, but this is likely attributable to non-olfactory and gustatory properties. Rather, the contribution of triacylglycerols to the mouthfeel of foods (e.g., lubricity, creaminess) are primarily responsible for hedonic appeal. Some have suggested an association between low fat detection, high intake of fatty foods, and elevated BMI or disinhibited eating behavior. However, findings from a recent meta-analysis do not support a relationship between fat detection or intensity ratings and body weight.

Taste sensitivity to salt develops at approximately 4–6 months of age and generally elicits a positive response. However, children quickly learn cultural norms regarding where sodium is appropriate in the diet. Indeed, a twin study demonstrated that environment was more influential than genetics on salt taste. Others have reported that dietary intake influences salt preferences, as reduced sodium intake lowered salt preferences independent of changes to salt taste detection. Earlier work indicated increased or decreased dietary salt is associated with higher and lower preferred salt concentrations in foods, respectively.

Salt taste has been proposed as a mechanism to regulate physiological needs for sodium. Sodium depletion increases salt sensitivity and preference for salty foods. However, the association is not symmetrical: high levels of sodium consumption do not blunt preferences, and may even augment them. Exercise may also alter sensory perception and preference for sodium. However, a more recent placebo-controlled cross-over study failed to show an effect of encapsulated sodium or potassium supplementation on salt detection thresholds, or desire to eat salty foods. Given the health concerns related to sodium intake, resolution of this mixed literature warrants further study. Taken together, current evidence suggests salt preferences are primarily determined by exposure, rather than innate sensory abilities.
Impacts of sensory stimulation on physiology

In addition to influencing food choice, sensory stimulation also affects food digestion, and the absorption and metabolism of nutrients through the elicitation of cephalic phase responses. These are vagally-mediated physiological responses to sensory stimulation. Cephalic phase responses include, but are not limited to, saliva flow and composition, gut motor activity and enzyme release, endocrine and exocrine secretions, thermogenesis, as well as cardiovascular and renal effects. These responses generally mimic those occurring as food is processed in the GI tract, but they occur within minutes of food exposure, are of short duration, and of low magnitude. They are viewed more as the triggers that initiate and modulate the actual digestion, nutrient absorption, and ultimately metabolism of foods.

The functionality of cephalic phase responses in digestion was demonstrated over 100 years ago by Pavlov when he observed that sham feeding improved digestion during intragastric intubation in dogs. Numerous examples of functional cephalic phase responses have also been documented in humans at all sites within the GI tract. Visual cues to sour foods, chewing, and sour taste stimulate saliva release. Gastric motility and acid secretion is enhanced by palatable foods compared to less preferred items. Pharmacological inhibition of the first (cephalic) phase insulin response leads to higher and more prolonged post-prandial glucose concentrations. Likewise, administration of insulin during the pre-absorptive period results in improved glucose control in obese subjects. Similarly, oral fat exposure alone is sufficient to alter plasma triacylglycerol levels in healthy humans, independent of cognitive or sensory influences. A dose-response relationship between the molarity of an oropharyngeal and laryngeal misting solution and urine volume and osmolality of human volunteers has been observed. Others have demonstrated that sensory stimulation is sufficient to decrease cardiac output, heart rate, and blood pressure and increase thermogenesis.

Smell and taste dysfunction

Taste and smell disorders can range from complete loss of function (ageusia and anosmia, respectively) to degrees of loss (hypogeusia and hyposmia, respectively). In some cases, individuals also experience inappropriate sensations for a given stimulus, termed dysgeusia (taste) and dysosmia (smell). Although the majority of individuals with chemosensory complaints identify both taste and smell loss, olfactory dysfunction is primarily responsible for most complaints. Due to variability in defining and evaluating taste and smell function, estimates of chemosensory dysfunction differ widely. A recent cross-sectional analysis of NHANES data reported taste quality and smell confusion in approximately 26.3 million (17.3%) and 20.5 million (13.5%) adults over 40 in the United States, respectively. Other studies have suggested an incidence of severe olfactory miscoding at 2.7%–3.8% and severe gustatory miscoding at 14.8%. However, in clinical populations, the incidence of olfactory disorders is much higher than that of gustatory disorders. The incidence of chemosensory disorders has been associated with ethnicity (smell and taste) and gender (smell only). The majority of taste and smell disorders are attributable to upper respiratory tract infections (19%–26%), head trauma (14%–18%) and nasal and paranasal sinus disease (15%–21%). However, many (22%) also have no identifiable cause or are considered idiopathic.

Despite the common observation that sensory properties influence food choice, evidence supporting an association between taste and smell function and nutritional status is limited. Most individuals with taste and smell dysfunction report a loss of appetite, but maintain adequate dietary intake. Although dysgeusic patients commonly report distorted tastes for common foods such as meats, fresh fruits, coffee, eggs, and carbonated beverages, their overall nutrient intake is not necessarily altered. Others have noted no association between olfactory function and fruit and vegetable intake. However, certain eating behaviors may be altered in some cases of chemosensory dysfunction, such as increased seasoning and sugar use in anosmic individuals. Changes in related culinary practices, such increased salt, sugar, and fat use, could complicate issues with hypertension, diabetes and cardiovascular disease, respectively. More generally, some individuals with chemosensory disorders increase food intake to compensate for decreased sensory stimulation and gain weight, while other patients decrease food intake due to lower food appeal, resulting in weight loss. Either response occurs in only a small subset of patients.

As with physical health status, limited data support a significant impact of chemosensory function on mental health. While decreased chemosensory function may affect the quality of life, there is no clear relationship between olfactory function and psychiatric disorders. A recent systematic review of the literature relating olfactory function and depression found inconsistent evidence for altered smell detection, sensitivity, and identification; despite concluding that the majority of studies found differences in some indicator of olfactory function, the nature of the disruption was inconsistent. Large variability in measurement and definition of olfactory function was noted as a significant limitation. Although the majority of individuals with chemosensory dysfunction cope appropriately, there are some reports of concerning mental health consequences for a meaningful minority.

Chemosensory function and aging

While dysfunction in chemosensory abilities is commonly associated with elderly populations, questions remain regarding the independent effect of age on taste and smell. Differences in chemosensory abilities in elderly populations are often difficult to attribute solely to sensory function, as many age-associated factors such as overall health status, denture use, education, medication use, and other environmental insults can influence taste and smell responses. In studies that have observed differences, the effect varies widely among individuals and stimuli. Furthermore, the size of detected differences in the elderly may be clinically irrelevant in terms of influencing food choice or health status. After adjusting for potential
confounders, recent cross-sectional studies have failed to find a significant relationship between olfactory abilities and nutritional status in the elderly. In light of the variety of etiologies contributing to chemosensory dysfunction and nature of the complaints in the elderly, current evidence does not support a universal strategy (e.g., flavor fortification, treatment with zinc) to improve nutritional status through sensory-related interventions.

**Chemosensory abnormalities associated with chronic diseases**

Alterations in taste and smell function may also occur as a consequence of other disorders. Due to specific dietary needs in many of these conditions, taste and smell function have been proposed as a strategy to influence food intake.

**Cancer**

Because maintaining adequate energy and nutrient intake in cancer patients is important for effective treatment, strategies to increase dietary compliance are needed. In untreated cancer patients receiving palliative care, 86% report some sort of chemosensory complaint. The nature of complaints among cancer patients is highly variable, as dysgeusia, dysosmia, and heightened and diminished sensitivity to specific taste qualities or odors have all been reported. Although earlier studies failed to find an association between chemosensory complaints and appetite, food preferences, and body weight, more recent research has associated chemosensory function with lower energy intake, appetite, BMI, quality of life, and protein intake in cancer patients.

Chemosensory dysfunction is frequently associated with anti-cancer therapies. Radiation therapy reduces the number of taste buds, and tongue exposure is related to taste impairment. Patients undergoing radiation therapy exhibit diminished taste sensitivity relative to pretreatment levels. Although some report that taste sensitivity recovers to baseline levels following radiation therapy, others continue to observe alterations six months post-treatment.

Chemotherapy treatment also commonly induces changes in sensory function, with 56%–76% of patients reporting dysgeusia or some form of taste alterations. Dysgeusia incidence may be related to cancer type. Cyclical effects of chemotherapy on taste function, as demonstrated by quality-specific decreases in taste identification abilities, liking, and appetite in early, but not later, treatment cycles, have also been observed. While the nature of gustatory disturbances in cancer patients are incompletely characterized, recent evidence suggests that taste alterations during chemotherapy may be related to specific macronutrients (e.g., protein) rather than specific tastes. Diminished olfactory sensitivity has also been reported in patients undergoing chemotherapy treatment. Changes induced by chemotherapy treatment are often transitory and recover within six months post-treatment. Alterations in chemosensory function in cancer patients undergoing chemotherapy can impact food preferences and practical and social aspects of everyday life. Practitioners are advised to inform patients of potential alterations to their taste and smell perception prior to chemotherapy treatment.

**Hypertension**

Associations between sodium intake and blood pressure have prompted investigations of the relationship between salt taste, salt intake and blood pressure. Although some have proposed that decreased salt taste sensitivity would lead to high salt use, it could also be argued that decreased salt taste leads to lower salt use due to lack of reward value. Additionally, higher salt sensitivity could lead to reduced intake, as less would be more impactful, or greater intake, as it would be more rewarding. Because of a lack of clear evidence, such claims are descriptive rather than mechanistic. The preponderance of evidence does not support any difference in sodium chloride sensitivity or liking between normotensive and hypertensive patients. Examination of individuals classified as “salt sensitive” or “insensitive” has also failed to reveal meaningful differences of salt taste sensitivity, intensity perception, or liking. It should be noted that hypertensive drug treatment regimens may alter taste. In such cases, alternate medications should be considered.

**Hypothyroidism**

Taste and smell function are commonly altered in hypothyroidism, with reports of both dysgeusia (50% of patients) and dysosmia (39% of patients). The nature of taste disruption in hypothyroidism may be quality-specific, as decreased taste function has been detected for bitterness and sweetness, but not other qualities. Others have reported that only bitterness is altered. Lower odor threshold, discrimination, and identification scores have also been reported in patients with hypothyroidism. The mechanisms responsible for taste and smell alterations in hypothyroidism are unclear, but may involve changes in secretions in the nasal cavity, alterations of the olfactory epithelium or olfactory bulb function, or neural conductivity. Pharmacological treatment often resolves chemosensory disturbance in patients with hypothyroidism. Individuals with hyperthyroidism may also experience quality-specific taste alterations, as hyperthyroid patients report lower salty and bitter intensities.

**Obesity**

Relationships between sweet and fat detection and body weight have been explored in populations that are lean and obese to elucidate the concomitant rise in the availability of palatable, energy-dense foods and obesity. However, the evidence base does not support systematic differences in taste sensitivity and preferences among people who are lean or have high percent body fat. Very limited data suggest a higher prevalence of olfactory impairment in extremely overweight individuals. Although some evidence indicates a difference in high-fat food preference in obese populations, other studies have failed to find a relationship. Furthermore, a prospective study reported no difference in hedonic responses based on body...
Increased sweet taste sensitivity. Evidence supporting a relationship between weight loss due to energy restriction and taste function are mixed, as weight loss interventions have resulted in no change, impairment, and improvement of sweet taste abilities. 

**Diabetes**

Decreased sweet taste sensitivity is the most consistently reported chemosensory disturbance in diabetic patients. Chemosensory dysfunction has been reported in over 60% of diabetes patients and is likely related with associated comorbidities and complications. Studies comparing taste and smell function of uncomplicated diabetic patients and healthy controls have failed to detect significant differences in sensory abilities. Furthermore, others have found positive relationships between the degree of neuropathy and severity of gustatory symptoms, taste function, and olfactory function. Disease duration and the presence of additional complications is also associated with chemosensory dysfunction in diabetic patients. Taken together, the evidence suggests that reported changes in sweet taste function in diabetic patients are likely due to peripheral neuropathy rather than defects of glucoreception.

**Strategies for management of chemosensory disorders**

As there is no single cause of chemosensory dysfunction, recommendations must be adapted to individual circumstances. In some cases, surgery or steroids may be appropriate for treatment of olfactory disorders. In other cases, taste and smell function recover spontaneously or when the medical disorder responsible for the disturbance is resolved. To determine the impact of chemosensory function on overall health, practitioners are first advised to understand how an individual’s dietary intake is affected by their patient’s taste and smell dysfunction, as the evidence does not currently support a single management strategy.

As current evidence does not support a role of nutrient deficiency in the majority of chemosensory disorders, dietary supplementation is not typically recommended as a treatment strategy. Although nutrient deficiencies may play a role in some chemosensory disorders, they are rare and often not the primary cause. The use of zinc supplementation, for example, has generally had limited efficacy. Although other micronutrients (e.g., vitamin A, B vitamins, vitamin E, copper, iodine, and iron) have been associated with chemosensory function, the overall evidence does not support the use of supplements to treat taste and smell disorders. Selective flavor fortification may be a useful strategy for a subset of individuals with diminished taste and smell function, but its effectiveness is limited in aguesic or anosmic patients, or in those cases where sensory function is not the underlying cause of altered food intake. Other strategies have been proposed to alter taste perception in specific medical conditions, such as the use of plastic utensils, chewing slowly, and ice chips in cancer patients. Emphasizing spiciness or non-chemosensory food attributes such as appearance or texture provide additional avenues for management.

**Conclusion**

Taste and smell function play an important role in diet selection and metabolism. However, the effect of sensory function on habitual food intake and ultimately health status must be considered within the context of several other factors such as environment, exposure, and culture. Consequently, dietary management of patients with chemosensory complaints should be individualized.

**References**

1. Woods SC. The eating paradox: how we tolerate food. Psychol Rev. 1991;98(4):488–505.
2. Mattes RM. Nutrition and the chemical senses. In: Shils ME, Shike M, Ross AC, Caballero B, Cousins RJ, eds. Modern Nutrition in Health and Disease. 10th ed. Baltimore: Williams & Wilkins; 2005:695–706.
3. Lo JYQ, Lacy KE, McBride RL, RSJ D. Evidence supporting oral sensitivity to complex carbohydrates independent of sweet taste sensitivity in humans. PLoS One. 2017;12:e0188784.
4. Tatzer E, Schubert MT, Timischl W, Simbruner G. Discrimination of taste and preference for sweet in premature babies. Early Hum Dev. 1985;12(1):23–30.
5. Maone TR, Mattes RD, Bernbaum JC, Beauchamp GK. A new method for delivering a taste without fluids to preterm and term infants. Dev Psychobiol. 1990;23(2):179–191.
6. Mennella JA, Pepino MY, Reed DR. Genetic and environmental determinants of bitter perception and sweet preferences. Pediatrics. 2005;115:e216–222.
7. Pepino MY, Mennella JA. Factors contributing to individual differences in sucrose preference. Chem Senses. 2005;30(suppl 1):i319–320.
8. Sartor F, Donaldson LF, Markland DA, Loveday H, Jackson MJ, Kubis H-P. Taste perception and implicit attitude toward sweet related to body mass index and soft drink supplementation. Appetite. 2011;57(1):237–246.
9. Beauchamp GK, Moran M. Acceptance of sweet and salty tastes in 2-year-old children. Appetite. 1984;5(4):291–305.
10. Pangborn RM, Giovanni ME. Dietary intake of sweet foods and of dairy fats and resultant gustatory responses to sugar in lemonade and to fat in milk. Appetite. 1984;5(4):317–327.
11. Birch GG, Kemp SE. Apparent specific volumes and tastes of amino-acids. Chem Senses. 1989;14(2):249–258.
12. Murphy C, Withee J. Age and biochemical status predict preference for casein hydrolysate. J Gerontol. 1987;42(1):73–77.
13. Vazquez M, Pearson PB, Beauchamp GK. Flavor preferences in malnourished Mexican infants. Physiol Behav. 1982;28(3):513–519.
14. Griffioen-Roose S, Mars M, Siebelink E, Finlayson G, Tomé D, de Graaf C. Protein status elicits compensatory changes in food intake and food preferences. Am J Clin Nutr. 2012;95(1):32–38.
15. Griffioen-Roose S, Finlayson G, Mars M, Blundell JE, de Graaf C. Measuring food reward and the transfer effect of sensory specific satiety. Appetite. 2010;55(3):648–655.
sample of the US population: a cross-sectional study. *BMJ Open*. 2016;6(11):e013246.
63. Schubert CR, Cruickshanks KJ, Fischer ME, et al. Olfactory impairment in an adult population: the Beaver Dam Offspring Study. *Chem Senses*. 2012;37:325–334.
64. Boesveldt S, Lindau ST, McClinck MK, Hummel T, Lundstrom JN, Lindstrom JN. Gustatory and olfactory dysfunction in older adults: a national probability study. *Rhinology*. 2011;49:324–330.
65. Mott AE, Leopold DA. Disorders in taste and smell. *Med Clin North Am*. 1991;75(6):1321–1353.
66. Ferris AM, Schlitzer JL, Schierberl MJ, et al. Anosmia and nutritional status. *Nutr Res*. 1985;5(2):149–156.
67. Lee J, Tucker RM, Tan SY, Running CA, Jones JB, Mattes RD. Nutritional implications of taste and smell dysfunction. In: Doty RL, ed. *Handbook of Olfaction and Gustation*. John Wiley & Sons, Inc; 2015:829–864.
68. Markley EJ, Mattes-Kulig DA, Henkin RI. A classification of dysgeusia. *J Am Diet Assoc*. 1983;83(5):578–580.
69. Mattes RD, Cowart BJ. Dietary assessment of patients with chemosensory disorders. *J Am Diet Assoc*. 1994;94(1):50–56.
70. Scinski A, Wrobel E, Korkosz A, et al. Depressive symptoms and olfactory function in older adults. *Psychiatry Clin Neurosci*. 2008;62(4):450–456.
71. Pause BM, Miranda A, Göder R, Aldenhoff JB, Ferstl R. Reduced olfactory performance in patients with major depression. *J Psychiatr Res*. 2001;35:271–277.
72. Lombion-Pouthier S, Vandel P, Nezelof S, Haffen E, Millot JL. Odor perception in patients with mood disorders. *J Affect Disord*. 2006;90(2–3):187–191.
73. Taalman H, Wallace C, Milev R. Olfactory function and depression: a systematic review. *Front Psychiatry*. 2017;8:190.
74. Croy I, Nordin S, Hummel T. Olfactory disorders and quality of life—an updated review. *Chem Senses*. 2014;39(3):185–194.
75. Song X, Giacalone D, Bølling Johansen SM, Frøst MB, Toussaint N, de Roon M, van Campen JP, Kremer S, Jin S-Y, Jeong HS, Lee JW, Kwon KR, Rha K-S, Kim YM. Effects of depression on food preferences among older adults. *Trends Food Sci Technol*. 2016;53:49–59.
76. Mattes RD. The chemical senses and nutrition in aging: challenging old assumptions. *J Am Diet Assoc*. 2002;102(2):192–196.
77. Jin SY, Jeong HS, Lee JW, Kwon KR, Rha KS, Kim YM. Effects of nutritional status and cognitive ability on olfactory function in geriatric patients. *Auris Nasus Larynx*. 2016;43(1):56–61.
78. Toussaint N, de Roos M, van Campen JP, Kremer S, Boesveldt S. Loss of olfactory function and nutritional status in vital older adults and geriatric patients. *Chem Senses*. 2015;40(3):197–203.
79. Ottery FD. Definition of standardized nutritional assessment and interventional pathways in oncology. *Nutrition*. 1996;12(1 suppl):S51–S59.
80. Hutton JL, Baracos VE, Wismer WV. Chemosensory dysfunction is a primary factor in the evolution of declining nutritional status and quality of life in patients with advanced cancer. *J Pain Symptom Manage*. 2007;33:156–165.
81. Hovan AJ, Williams PM, Stevenson-Moore P, et al. A systematic review of dysgeusia induced by cancer therapies. *Support Care Cancer*. 2010;18(8):1081–1087.
82. Boer CC, Correa ME, Miranda EC, de Souza CA. Taste disorders and oral evaluation in patients undergoing allogeneic hematopoietic SCT. *Bone Marrow Transpl*. 2010;45:705–711.
83. Bovio G, Montagna G, Bariani C, Biaardi P. Upper gastrointestinal symptoms in patients with advanced cancer: relationship to nutritional and performance status. *Support Care Cancer*. 2009;17:1317–1324.
84. Trant AS, Serin J, Douglass HO. Is taste related to anorexia in cancer patients? *Am J Clin Nutr*. 1982;36(1):45–58.
85. Carson JA, Gormican A. Taste acuity and food attitudes of selected patients with cancer. *J Am Diet Assoc*. 1977;70(4):361–365.
86. Boltong A, Aranda S, Keast R, et al. A prospective cohort study of the effects of adjuvant breast cancer chemotherapy on taste function, food liking, appetite and associated nutritional outcomes. *Plast Reconstr Surg*. 2014;9(7):103512.
87. Yamashita H, Nakagawa K, Tago M, et al. Taste dysfunction in patients receiving radiotherapy. *Head Neck J Sci Spec*. 2006;28(6):508–516.
88. Yamashita H, Nakagawa K, Nakamura N, et al. Relation between acute and late irradiation impairment of four basic tastes and irradiated tongue volume in patients with head-and-neck cancer. *Int J Radiat Oncol Biol Phys*. 2006;66(5):1422–1429.
89. Sandow PL, Hejrat-Yazdi M, Heft MW. Taste loss and recovery following radiation therapy. *J Dent Res*. 2006;85(7):608–611.
90. Epstein JB, Robertson M, Emerton S, Phillips N, Stevenson-Moore P. Quality of life and oral function in patients treated with radiation therapy for head and neck cancer. *Head Neck*. 2001;23(5):389–394.
91. Zabernigg A, Camper EM, Giesinger JM, et al. Taste alterations in cancer patients receiving chemotherapy: a neglected side effect. *Oncologist*. 2010;15:913–920.
92. Ponticelli E, Clari M, Frigerio S, et al. Dysgeusia and health-related quality of life of cancer patients receiving chemotherapy: a cross-sectional study. *Eur J Cancer Care*. 2017;26(2):e12633–n/a.
93. de Vries YC, Winkels RM, van den Berg MGA, et al. Altered food preferences and chemosensory perception during chemotherapy in breast cancer patients: a longitudinal comparison with healthy controls. *Food Qual Prefer*. 2018;63:135–143.
94. Waliczek-Dworschak U, Guzdziol V, Mitzschke C, Froehner M, Hummel T. Testicular cancer patients undergoing cisplatin based chemotherapy exhibit temporary olfactory threshold scores changes. *Eur Arch Otorhinolaryngol*. 2017;274(7):2813–2818.
95. de Vries YC, Helmich E, Karsten MD, Boesveldt S, Winkels RM, van Laarhoven HW. The impact of chemosensory and food-related changes in patients with advanced oesophago gastric cancer treated with capecitabine and oxaliplatin: a qualitative study. *Support Care Cancer*. 2016;24(7):3119–3126.
96. Wickham RS, Rehwaldt M, Kefer C, et al. Taste changes experienced by patients receiving chemotherapy. *Oncol Nurs Forum*. 1999;26(4):679–706.
97. Roura E, Foster S, Winklebach A, et al. Taste and hypertension in humans: targeting cardiovascular disease. *Curr Pharm Des*. 2016;22(15):2290–2305.
98. Mattes RD. Salt taste and hypertension: a critical review of the literature. *J Chronic Dis*. 1984;37:195–208.
99. Mattes RD, Falkner B. Salt taste and salt sensitivity in black adolescents. *Chem Senses*. 1989;14(5):673–679.
100. Mattes RD, Westby E, De Cabo R, Falkner B. Dietary compliance among salt-sensitive and salt-insensitive normotensive adults. *Am J Med Sci*. 1999;317(5):287–294.
101. Kirsten VR, Wagner MB. Salt taste sensitivity thresholds in adolescents: are there any relationships with body composition and blood pressure levels? *Appetite*. 2014;81:89–92.
102. Doty RL, Philip S, Reddy K, Kerr KL. Influences of antihypertensive and antihyperlipidemic drugs on the senses of taste and smell: a review. *J Hypertens*. 2003;21(10):1805–1813.
103. McConnell RJ, Menendez CE, Smith FR, Henkin RJ, Rivlin RS. Defects of taste and smell in patients with hypothyroidism. *Am J Med*. 1975;59(3):354–364.
104. Deniz F, Ay SA, Salihoglu M, et al. Thyroid hormone replacement therapy improves olfaction and taste sensitivity in primary hypothyroid patients: a prospective randomised clinical trial. *Exp Clin Endocrinol Diabetes*. 2016;124(09):562–567.

105. Baskoy K, Ay SA, Altundag A, et al. Is there any effect on smell and taste functions with levothyroxine treatment in subclinical hypothyroidism? *PLoS One*. 2016;11(2):e0149979.

106. Bhatia S, Sircar SS, Ghorai BK. Taste disorder in hypo and hyperthyroidism. *Indian J Physiol Pharmacol*. 1991;35(3):152–158.

107. de Graaf C. Sensory responses, food intake and obesity. In: *Mela DJ, ed. Food, Diet and Obesity*. Woodhead Publishing; 2005:137–159.

108. Mela DJ. Eating for pleasure or just wanting to eat? Reconsidering sensory hedonic responses as a driver of obesity. *Appetite*. 2006;47(1):10–17.

109. Richardson BE, VanderWoude EA, Sudan R, Thompson JS, Leopold DA. Altered olfactory acuity in the morbidly obese. *Obes Surg*. 2004;14(7):967–969.

110. Fernández-Aranda F, Agüera Z, Fernández-García JC, et al. Smell-taste dysfunctions in extreme weight/eating conditions: analysis of hormonal and psychological interactions. *Endocrine*. 2016;51:256–267.

111. Drewnowski A. Body weight and sensory preferences for sugar and fat. *J Can Inst Food Sci Technol*. 1987;20:327–330.

112. Mela DJ, Sacchetti DA. Sensory preferences for fats: relationships with diet and body composition. *Am J Clin Nutr*. 1991;53(4):908–915.

113. Pangborn RM, Bos KEO, Stern JS. Dietary fat intake and taste responses to fat in milk by under-, normal, and overweight women. *Appetite*. 1985;6(1):25–40.

114. Warwick ZS, Schiffman SS. Sensory evaluations of fat-sucrose and fat-salt mixtures: relationship to age and weight status. *Physiol Behav*. 1990;48:633–636.

115. Salbe AD, DelParigi A, Prattley RE, Drewnowski A, Tataranni PA. Taste preferences and body weight changes in an obesity-prone population. *Am J Clin Nutr*. 2004;79(3):372–378.

116. Richardson BE, Vanderwoude EA, Sudan R, Leopold DA, Thompson JS. Gastric bypass does not influence olfactory function in obese patients. *Obes Surg*. 2012;22(2):283–286.

117. Burge JC, Schaumburg JZ, Choban PS, DiSilvestro RA, Flanbaum L. Changes in patients’ taste acuity after Roux-en-Y gastric bypass for clinically severe obesity. *J Am Diet Assoc*. 1995;95:666–670.

118. Miras AD, le Roux CW. Bariatric surgery and taste: novel mechanisms of weight loss. *Curr Opin Gastroenterol*. 2010;26(2):140–145.

119. Sauer H, Ohla K, Dammann D, et al. Changes in gustatory function and taste preference following weight loss. *J Pediatr*. 2017;182:120–126.

120. Umabiki M, Tsuzaki K, Kotani K, et al. The improvement of sweet taste sensitivity with decrease in serum leptin levels during weight loss in obese females. *Tohoku J Exp Med*. 2010;220(4):267–271.

121. Settle RG. The chemical senses in diabetes mellitus. In: *Getchell TV, Bartoshuk LM, Doty RL, Snow JB, eds. Smell and Taste and Disease*. New York: Raven Press; 1991:829–843.

122. Altundag A, Ay SA, Hira S, et al. Olfactory and gustatory functions in patients with non-complicated type 1 diabetes mellitus. *Eur Arch Otorhinolaryngol*. 2017;274(6):2621–2627.

123. Naka A, Riedl M, Luger A, Hummel T, Mueller CA. Clinical significance of smell and taste disorders in patients with diabetes mellitus. *Eur Arch Otorhinolaryngol*. 2010;267(4):547–550.

124. Abbasi AA. Diabetes: diagnostic and therapeutic significance of taste impairment. *Geriatrics*. 1981;36(12):73–78.

125. Le Floch J-P, Le Lievre G, Sadoun J, Perlemuter L, Peynegre R, Hazard J. Taste impairment and related factors in type I diabetes mellitus. *Diabetes Care*. 1989;12(3):173.

126. Le Floch J-P, Le Lievre G, Labroue M, Paul M, Peynegre R, Perlemuter L. Smell dysfunction and related factors in diabetic patients. *Diabetes Care*. 1993;16:934–937.

127. Lildholdt T, Rundcrantz H, Bende M, Larsen K. Glucocorticoid treatment for nasal polyps. The use of topical budesonide powder, intramuscular betamethasone, and surgical treatment. *Arch Otolaryngol Head Neck Surg*. 1997;123(6):595–600.

128. Ineffectiveness of zinc in treating ordinary taste and smell dysfunctions. *Nutr Rev*. 1979;37(9):283–285.

129. Hong JH, Omur-Ozbek P, Stanek BT, et al. Taste and odor abnormalities in cancer patients. *J Support Oncol*. 2009;7(2):58–65.

130. Mosel DD, Bauer RL, Lynch DP, Hwang ST. Oral complications in the treatment of cancer patients. *Oral Dis*. 2011;17(6):550–559.