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Taste and smell perception affect appetite and immunity in the elderly

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The losses in taste and smell that occur with advancing age can lead to poor appetite, inappropriate food choices, as well as decreased energy consumption. Decreased energy consumption can be associated with impaired protein and micronutrient status and may induce subclinical deficiencies that directly impact function. Most nutritional interventions in the elderly do not compensate for taste and smell losses and complaints. For example, cancer is a medical condition in which conventional nutritional interventions (that do not compensate for taste and smell losses) are ineffective. Evidence is now emerging that suggests compensation for taste and smell losses with flavor-enhanced food can improve palatability and/or intake, increase salivary flow and immunity, reduce chemosensory complaints in both healthy and sick elderly, and lessen the need for table salt.
Descriptors: aging; smell; taste; food intake; immunity
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Introduction

Taste and smell changes occur with advancing age, and this can lead to poor appetite (de Jong *et al*, 1999), inappropriate food choices (Duffy *et al*, 1995), and/or lower nutrient intake (Griep *et al*, 1996). Poor appetite in the elderly is one cause of decreased energy consumption (Morley, 1997; Morley & Thomas, 1999; Chapman & Nelson, 1994) which, in turn, impacts protein and micronutrient status and may induce subclinical deficiencies that directly impact function (Morley, 1997; Chapman & Nelson, 1994; Blumberg, 1997). Loss of appetite is especially serious in elderly patients who are critically ill and thus at high risk to develop protein-energy malnutrition as well as micronutrient deficiencies (Opper & Burakoff, 1994).

Taste and smell play a role in appetite, food choices, and nutrient intake for the following reasons. First, these chemosensory signals prepare the body to digest food by triggering salivary, gastric, pancreatic, and intestinal secretions which are termed cephalic phase responses (Giduck *et al*, 1987; Schiffman & Warwick, 1992; Teff & Engelman, 1996). Second, they enable us to detect and discriminate among foods in the face of fluctuating nutritional requirements. In fact, the activity in taste neurons is actually modified by transient physiological needs (Contreras & Frank, 1979; Jacobs *et al*, 1988; Giza *et al*, 1992, 1993). Third, they enable selection of a nutritious diet. Learned associations between a food's taste (or smell) and its post-ingestive effects (Booth, 1985; Schiffman & Warwick, 1991, 1992) enable the consumer to modulate food intake in anticipation of its nutritional consequences. Thus, taste sensations serve as an indicator of a food's nutritional value. Fourth, taste and smell signals initiate, sustain and terminate ingestion, and hence play a major role in the quantity of food that is eaten and the size of meals (Schiffman & Warwick, 1992). Fifth, taste sensations induce feelings of satiety and are primary reinforcers of eating (Schiffman, 1983; Schiffman & Warwick, 1992; Scott, 1992; Scott *et al*, 1995). Thus, chemosensory impairments can alter food choices and intake and subsequently exacerbate disease states, impair nutritional status and immunity, and produce weight loss (Schiffman, 1983, 1997).

The purpose of this paper is to review our state of knowledge of taste and smell losses in the elderly and to show how compensation for these losses can improve health and nutritional status. Chemosensory losses and complaints in cancer patients will be described as an example of a medical condition in which conventional nutritional interventions (that do not compensate for taste and smell losses or distortions) are ineffective. Finally, examples will be given in which compensation for taste and smell losses with flavor-enhanced food were found to improve palatability and/or intake, increase salivary flow and immunity, and reduce complaints about oral problems in both healthy and sick elderly (Schiffman, 1997–1999; Schiffman & Warwick, 1993; Schiffman & Miletic, 1999).

Chemosensory impairments in the elderly

Laboratory studies of taste and smell perception in the elderly indicate that there are significant chemosensory losses with age (Schiffman, 1983, 1993, 1997; Doty *et al*, 1984; Stevens *et al*, 1995; Cain & Gent, 1991; Murphy, 1993). Psychophysical tests indicate that these losses consist of: (1) elevated thresholds for taste and smell; (2) reduced intensity of suprathreshold stimuli; (3) diminished ability to discriminate among suprathreshold stimuli; (4) deficits in the ability to identify odors and tastes on the basis of taste and smell; and (5) distorted taste or smell. Medical nomenclature for these chemosensory impairments is as follows: ageusia (absence of taste), hypogeusia (diminished sensitivity of taste with elevated thresholds and reduced ability to perceive suprathreshold stimuli), dysgeusia (distortion of normal taste), anosmia (absence of smell), hyposmia (diminished sensitivity of smell and

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reduced ability to perceive suprathreshold stimuli), and dysosmia (distortion of normal smell); (Schiffman, 1997). Distorted taste and smell perception (dysgeusia and dysosmia, respectively) are not necessarily correlated with loss of sensitivity (Cowart *et al*, 1989). Hyposmia and hypogeusia tend to become noticeable around 60 y of age although they can occur earlier. Losses tend to progress more rapidly after 70 y of age (Schiffman & Warwick, 1991).

Taste impairments

Taste dysfunction in the elderly generally results from normal aging, and from certain disease states (such as cancer), medications, surgical interventions, malnutrition, and environmental exposure (see Tables 1 and 2). Over 250 drugs have been reported clinically to cause taste complaints (Schiffman, 1991; *Physicians' Desk Reference*, 1995). In most cases, the sense of taste is not totally absent (ageusia) in the elderly, but rather is reduced (hypogeusia) or distorted (dysgeusia). Patients with dysgeusia often complain about bitter/metallic side tastes not usually associated with the foods that they are eating. Ageusia can occur, however, after chemotherapy, radiation, or substantial injuries to the taste system. Elevated taste thresholds (ie reduced sensitivity) for sweet, sour, salty and bitter compounds as well as amino acids occur in healthy older individuals (Stevens *et al*, 1995; Schiffman, 1993). The degree of loss depends on the chemical structure of the tastants (substances being tasted) as well as the medical condition and pharmacological regimen of the individual (Frank *et al*, 1992; Cowart *et al*, 1994; Schiffman *et al*, 1990; Schiffman, 1994). For unmedicated healthy elderly, threshold increases for common tastes such as sucrose (sweet), NaCl (salty), quinine HCI (bitter), and citric acid (sour) are modest. However, for elderly individuals who take a moderate number of medications, greater losses in taste sensitivity at threshold levels have been found. For example, compared to young individuals, the average detection thresholds for elderly individuals with one or more medical conditions and taking an average of 3.4 medications were 11.6 times higher for sodium salts; 4.3 times higher for acids; 7.0 times higher for bitter compounds; 2.5 times higher for amino acids; 5.0 times higher for glutamate salts; and 2.7 times higher for sweeteners (Schiffman, 1993). Clinical studies of highly medicated patients in hospitals and nursing homes indicate that taste losses at the threshold level are even more severe (Schiffman & Wedral, 1996).

Like threshold studies, the majority of suprathreshold taste studies also show decrements in the elderly (see Schiffman, 1997 for review). Elderly persons perceive a broad range of tastes (including nutrients such as amino acids) as being less intense than young persons, and they have reduced ability to discriminate intensity differences between various concentrations of a tastant. Suprathreshold losses in perception of sweet and salty qualities can have health consequences for the elderly. Decrements in the suprathreshold sweet taste perception increase the possibility that persons with diabetes may consume excess sugar. Losses in suprathreshold salt (NaCl) perception makes it more difficult for hypertensive patients to comply with severe salt restriction because food is too bland.

The cause of taste changes in normal aging in the absence of disease, medications, or other medical interventions is not fully understood. Studies of anatomical changes

Table 1 Representative medications or treatments that alter taste or smell

Drugs to lower cholesterol or lipids in blood
Cholestyramine
Clofibrate
Fluvastatin sodium
Gemfibrozil
Lovastatin
Pravastatin sodium
Antihistamines
Chlorpheniramine maleate
Loratadine
Terfenadine and pseudoephedrine
Drugs to fight infectious diseases
Ampicillin
Ciprofloxacin
Clarithromycin
Ofloxacin
Streptomycin
Tetracyclines
Drugs to treat cancer
Cisplatin
Doxorubicin and methotrexate
Vincristine sulfate
Drugs for arthritis and pain
Auranofin
Colchicine
Dexamethasone
Diclofenac potassium/diclofenac sodium
Dimethyl sulfoxide
Gold
Hydrocortisone
D-penicillamine and penicillamine
Drugs for asthma and breathing problems
Albuterol sulfate
Cromolyn sodium
Flunisolide
Metaproterenol sulfate
Terbutaline sulfate
Drugs for hypertension and heart disease
Acetazolamide
Adenosine
Amiloride
Benazepril HCl and hydrochlorothiazide
Betaxolol HCl
Captopril
Clonidine
Diltiazem
Enalapril
Ethacrynic acid
Nifedipine
Propranolol
Spironolactone
Muscle relaxants and drugs for the treatment of Parkinson's disease
Baclofen
Dantrolene sodium
Levodopa
Drugs to improve mood or treat epilepsy
Amitriptyline HCl
Carbamazepine
Clomipramine HCl
Clozapine
Desipramine HCl
Doxepin HCl
Fluoxetine HCl
Imipramine
Lithium carbonate
Phenytoin
Trifluoperazine
Radiation therapy
Radiation to head
Vasodilators
Dipyridamole
Nitroglycerin patch

Table 2 Representative medical conditions that affect the senses of taste or smell

Nervous
Alzheimer's disease
Bell's palsy
Damage to chorda tympani
Epilepsy
Head trauma
Korsakoff's syndrome
Multiple sclerosis
Parkinson's disease
Tumors and lesions
Nutritional
Cancer
Chronic renal failure
Liver disease including cirrhosis
Niacin (vitamin B_3) deficiency
Vitamin B12 deficiency
Zinc deficiency
Endocrine
Adrenal cortical insufficiency
Congenital adrenal hyperplasia
Panhypopituitarism
Cushing's syndrome
Diabetes mellitus
Hypothyroidism
Kallman's syndrome
Pseudohypoparathyroidism
Turner's syndrome
Local
Allergic rhinitis, atopy, and bronchial asthma
Sinusitis and polyposis
Xerostomic conditions including Sjögren's syndrome
Viral infections
Acute viral hepatitis
Influenza-like infections

of the taste system in older individuals have been equivocal (Bradley, 1988). That is, the number of taste cells (which are clustered into buds scattered on the dorsal surface of the tongue, tongue cheek margin, base of the tongue near ducts of the sublingual glands, the soft palate, pharynx, larynx, epiglottis, uvula and first third of the esophagus) are not necessarily altered by aging. Mistretta (1984) concluded that taste losses in the elderly are due to changes in taste cell membranes (eg altered functioning of ion channels and receptors) rather than losses of taste buds. Taste cells constantly replicate with a life-span of approximately $10-10\frac{1}{2}$ days. When this process of continuous renewal is compromised by malnutrition or cancer therapy, taste sensitivity may be severely impaired.

Sensory signals from taste buds are relayed by three cranial nerves (the 7th, 9th, and 10th nerves) which transmit taste signals from taste receptor cells to the nucleus of the solitary tract (NST) in the medulla in the brain stem (Pritchard, 1991; Scott, 1992). The NST not only receives information from the gustatory system but from visceral sensory fibers originating in the esophagus, stomach, intestines, and liver as well. The taste information is relayed back to gastrointestinal organs which accounts for the cephalic phase responses described above. Thus, NST is the first processing area in which taste signals can affect ingestive and digestive activity by inducing gastric secretion as well as increased insulin and pancreatic exocrine secretions. Axons from the gustatory part of NST project to the thalamus and ultimately to the cortex. Little is known about age-related taste losses in the NST or higher neural centers.

Pungent qualities in the oral cavity (eg from carbonation or chili peppers) are transmitted by the 5th cranial nerve as well as free nerve endings of the 7th, 9th and 10th nerves (Green, 1996). Oral pungency is not a taste but rather a different sense related to nociception.

Smell perception in the elderly

Losses in smell perception in the elderly result from normal aging, certain disease states (especially Alzheimer's and Parkinson's disease), medications, viral insult, malnutrition, accumulated exposure to toxic fumes (or other environmental exposure), head trauma (see Tables 1 and 2), surgical interventions, and environmental exposure. Most research suggests that the sense of smell is even more impaired by aging than the sense of taste. Olfactory losses occur at both threshold and suprathreshold levels (Cain & Gent, 1991; Doty *et al*, 1984; Stevens & Cain, 1985). Diminished sensitivity to nasal pungency (eg CO_2 which stimulates the trigeminal nerve) also occurs in elderly individuals (Stevens *et al*, 1982).

Olfactory receptor cells are bipolar neurons that are located in the olfactory epithelium at the top of the nasal cavity (see Schiffman, 1997 for review). Olfactory cells, like taste cells, undergo continuous renewal although the average turnover time is three times longer, ie approximately 30 days. Perceptual losses in smell during aging are due in part to anatomic and physiological changes in the olfactory epithelium, the olfactory bulb and nerves (which receive input from the olfactory epithelium), and higher levels of the brain (including hippocampus and amygdaloid complex, and hypothalamus) that receive olfactory input. The anatomical projection to the hypothalamus emphasizes the importance of olfaction in eating and nutrition.

Elderly patients with cancer

Cancer is an example of a chronic medical condition in which patients are vulnerable to taste and smell disorders; and yet, nutritional interventions have not taken these sensory losses into account. Cancer disproportionately impacts the elderly (Cohen, 1998); 60% of all malignant tumors are diagnosed in persons 65 y and older, and 69% of all cancer deaths occur in this age group.

Taste and smell changes in cancer

Taste and smell changes are found in untreated patients (Ovesen *et al*, 1991; Brewin, 1980) as well as patients treated with chemotherapy (Nielsen *et al*, 1980; Lindley *et al*, 1996; Fetting *et al*, 1985), radiation (Conger, 1973), and immunotherapy (Schiffman, personal observation). Table 3 gives an overview of the taste changes that have been measured in cancer patients using a variety of psychophysical testing techniques. The data suggest that cancer and its treatment impair the ability to detect the presence of basic tastes, reduce the perceived intensity of suprathreshold concentrations of tastants, and interfere with the ability to discriminate and identify tastes and smells. Table 4 gives an overview of the food aversions, complaints, and altered preferences reported by cancer patients.

The studies in Tables 3 and 4 clearly indicate that cancer and its treatment can impair taste and smell perception. Furthermore, the data suggest that 50% or more of cancer patients may have impaired taste and smell functioning at some point during the course of their disease and treatment (eg DeWys & Walters, 1975). There appears to

Table 3 Changes in threshold, intensity, discrimination, and identification tasks (no. = number of patients)

Threshold loss	*Type of cancer*	*Effect of therapy*	no.	*Reference*
Elevated detection and recognition thresholds for NaCl (salty), sucrose (sweet), HCl (sour) and urea (bitter) prior to radiotherapy; salty, sweet, and bitter further impaired by radiotherapy	Various malignant neoplams	Radiotherapy further impaired taste loss	35	Bolze *et al* (1982)
Elevated recognition thresholds for sucrose (sweet), HCl (sour), quinine HCl (bitter) during radiotherapy; recovery by 120 days	Oropharyngeal cancers	Radiotherapy	8	Conger (1973)
Elevated detection and recognition thresholds especially for bitter and salt thresholds during radiotherapy	Head and neck	Radiotherapy	13	Mossman & Henkin (1978)
Elevated NaCl (salty) recognition thresholds	Breast and colon	Prior to treatment	48	Carson & Gormican (1977)
Elevated recognition threshold for hydrochloric acid (sour); individual differences in bitter and sweet threshold changes	Lung	Prior to therapy	30	Williams & Cohen (1978)
Elevated taste recognition thresholds for NaCl, sucrose, quinine sulfate, picric acid; thresholds returned to normal 6 weeks post-treatment	Oropharyngeal	During and after radiotherapy	1	Kalmus & Farnsworth (1959)
Thresholds for NaCl (salty), tartaric acid (sour), sucrose (sweet), and quinine (bitter) elevated by radiation and chemotherapy; recovery was not complete by 1 y	Oral squamous cell carcinoma	Radiation and chemotherapy	41	Tomita & Osaki (1990)
Elevated glucose recognition threshold	Various malignant neoplasms	During chemotherapy	36	Bruera *et al* (1984)
Significant increase in electrical taste detection threshold; no change in smell threshold	Lung, ovary, breast	Increase in untreated patients; thresholds decreased only in patients who responded to chemotherapy (after 2–3 months)	51	Ovesen *et al* (1991)
Significant decrease in recognition threshold for urea (bitter)	Gastrointestinal		30	Hall *et al* (1980)
Loss of ability to discriminate between different concentrations of salt, sweet, sour, and bitter	Melanoma	During nine courses of chemotherapy		Mulder *et al* (1983)
Significant reduction in smell identification in patients with estrogen-receptor positive breast cancer	Breast cancer	Mixed sample (treated and untreated)	46	Lehrer *et al* (1985)

be individual variability in the time course of recovery (if any) with the duration of losses ranging from several weeks to 6 months or longer (Mossman *et al*, 1982; Conger, 1973; Ophir *et al*, 1988).

The causes of altered psychophysical taste and smell measurements in cancer are not well understood but metabolic changes induced by the presence of a neoplasm as well as damage to the sensory receptors by therapies are likely involved. Radiation therapy and chemotherapy can affect the turnover of taste and smell receptors as well as alter the anatomical integrity of the taste bud. Oral complications of cancer such as infections (fungal, viral, bacterial), ulcers, drug-induced stomatitis, and dry mouth may also play a role.

There are several causes of the food aversions reported by cancer patients given in Table 4. First, impaired taste and smell alter the sensations derived from food. Second, food aversions can be learned during the course of cancer when sensory properties of foods are associated with gastrointestinal distress (eg nausea) of therapy (Andrykowski & Otis, 1990; Bernstein & Bernstein, 1981). Learned aversions and decreased food preferences can persist long after all symptoms of discomfort have subsided. Aversive conditioning has been shown in animal models to modify neural responses to taste stimuli (Chang & Scott, 1984).

Impact of taste and smell losses on nutritional status in cancer

Diminished taste sensitivity in cancer patients has been associated with inadequate food intake and/or weight loss (Williams & Cohen, 1978; Bolze *et al*, 1982; DeWys & Walters, 1975; Ames *et al*, 1993). When food is perceived as unpalatable or aversive, patients often reduce the diversity of foods consumed and fail to eat enough to meet nutritional requirements (Nielsen *et al*, 1980; Bernstein & Bernstein, 1981). Inadequate intake results in weight loss and malnutrition which can impair a patient's response to cancer therapies and increase mortality (Nielsen *et al*, 1980; Trant *et al*, 1982).

Current nutritional treatments for cancer

Nutrient intake in cancer patients undergoing treatment or with advanced cancer is generally suboptimal, and this can exacerbate immune impairments. Taste aberrations are believed to be one of the main causes of malnutrition associated with cancer and its treatment (DeWys & Walters, 1975); yet most treatment regimens for cancer have not been concerned with these sensory disturbances. The goals of nutritional intervention in cancer treatment are to support nutritional status, immune function, body composition, functional status, and quality of life (Ottery, 1995) and to prevent or attenuate cachexia during the stress of the

Table 4 Altered preferences and patient complaints (no. = number of patients)

Sensory loss	*Type of cancer*	*Effect of therapy*	no.	*Reference*
Food aversions and cravings	Various malignant neoplasms	Radiotherapy	147	Brewin (1982)
Reduced palatability of high-protein foods, cereals, sweets in patients with taste aversions	Various	Treated and untreated	111	Vickers *et al* (1981)
All food tasted nauseating, greasy or rancid; wine tasted metallic; water tasted salty	Oropharyngeal	Developed during first two weeks of radio-therapy	1	Kalmus & Farnsworth (1959)
Patients developed aversions to sweets, meats, caffeinated beverages, high fat and greasy foods during therapy	Breast and lung	Prior to and during chemotherapy	76	Mattes *et al* (1987)
Patients who reported food aversions rated food samples of chocolate, ham, pork, roast beef and chicken as less pleasant	28 types including breast, colorectal, Hodgkin's, lung, lymphoma	No difference between patients treated or untreated with chemo-therapy	133	Nielsen *et al* (1980)
Symptom of reduced appetite correlates with elevated recognition threshold for sucrose (sweet); meat aversion correlates with lowered thresholds for urea (bitter)	Various		50	DeWys & Walters (1975)
Highly varied hedonic responses to beverages containing five supra-threshold concentrations of citric acid (in lemonade), NaCl (in unsalted tomato juice), urea (in tonic water), and sucrose (in cherry drink); anorectics preferred lower sweetness levels than nonanorectics; yet sweet foods constituted a greater percentage of their daily caloric intake	Upper gastrointestinal; lung	Patients on chemotherapy had less distinct preference for any of the 5 concen-trations of sucrose particularly high levels	62	Trant *et al* (1982)
Percentage of patients reporting taste problems increased from 18% prior to radiation to over 80% during the 5th week of radiation; foods with abnormal taste included high protein foods (meat, eggs, dairy), fruits, vegetables, sweet, breads, cereal, coffee, tea	Head and neck cancer	During radiotherapy	74	Chencharick & Mossman (1983)
Complaints of metallic, bitter, or decreased taste; distorted sweet taste; changes in odor of food especially unpleasantness; increased sensitivity to odors such as perfumes and hospital odors	Breast, lung	Chemotherapy-cisplatin	44	Rhodes *et al* (1994)

oncology treatment (Mercadante, 1998). Compensating for taste and smell problems is generally not considered. Current methods for nutritional support may afford these patients a better, although not a longer life (Tchekmedyian, 1995; Ottery, 1995).

Recommendations to cancer patients generally emphasize eating a balanced and nutritious diet with adequate calories in order to: (1) prevent weight loss; (2) tolerate therapy with fewer side effects; (3) maximize physical condition to fight infection; (4) repair normal tissues damaged by chemotherapy and radiation; (5) have energy to recover quickly; and (6) feel better (Aker & Lenssen, 1988; Morra *et al*, 1992). These recommendations are supported by the fact that there are no known benefits to cancer patients from prolonged wasting, and pretreatment weight loss is a predictor of poor survival and response to therapy for cancer patients (Mercadante, 1998). Clinical data suggest that patients with an adequate dietary intake during cancer treatment are better able to cope with the side effects from chemotherapy, radiation therapy, immunotherapy, and surgery (Aker & Lenssen, 1988; Morra *et al*, 1992). However, no well-controlled prospective studies of nutrient intake using table foods have been performed to assess the outcome of 'eating a balanced nutritious diet'.

Moreover, no prospective studies of cancer patients eating flavor enhanced foods have been done. Nutritional interventions using total parenteral nutrition (TPN) and enteral nutrition in cancer treatment (which eliminate most of the pleasurable taste and smell aspects of food) are ineffective (Parkinson *et al*, 1987). A meta-analysis of randomized clinical trials of addition of TPN to standard treatment suggested that patients with metastatic cancers receiving TPN survived only 81% as long as patients who received chemotherapy without TPN (see Chlebowski, 1989). These detrimental findings may be due to several reasons including inadequacy of the formulation, failure to produce local intestinal stimulation, and deprivation of the taste and smell of foods (Mercadante, 1998). Enteral, like parenteral, products may also suffer from inadequate formulation and chemosensory problems. They often have unpleasant tastes and can cause esophageal reflux, especially in bedridden patients.

Alternative nutritional interventions

Flavor enhancement of nutrient-dense table foods has the potential to compensate for taste and smell losses in cancer patients and perhaps improve food intake. Previous studies in which the flavor of foods was intensified for frail elderly

without cancer have found improved intake, immune function, and functional status; these studies will be summarized in the next section. A recent study of flavor preferences in 13 patients currently undergoing chemotherapy (10 subjects) or radiotherapy (three subjects) for breast cancer (Schiffman, unpublished) found that they, like frail elderly without cancer, preferred flavor-enhanced foods. The breast cancer patients were asked to taste, smell, and consume two samples of a food and indicate which one they preferred. One sample was enhanced with flavor and the other was unenhanced. In all cases, the flavor-enhanced food was preferred to the food without additional flavor (see Table 5). None of the breast cancer patients had experienced nausea within 24 h of testing, and none of the patients reported an aversion to the foods that were tested.

Flavors are mixtures of odorous molecules that can be extracted or blended from natural products, or they can be synthesized based on chromatographic and mass spectrographic analysis of natural products. Flavors in some cases also contain nonvolatile compounds such as amino acid salts (eg monosodium glutamate) that induce taste stimulation. Flavors can be added to food prior to, during, or after cooking. For example, simulated beef flavor can be added to beef or beef stock to provide a more intense 'beef' sensation. Flavors are analogous to concentrated orange juice or extract of vanilla. Flavor enhancement differs from more traditional methods of increasing odor and taste sensations using spices, herbs, and salt. Spices and herbs contribute different flavors to the food rather than intensify actual food flavors.

Several cancer patients indicated that the odors of the flavor-enhanced foods reminded them of pleasant times in the past. Thus, flavor amplification can potentially reduce complaints about sensory properties of foods not only because they taste better but also because they trigger pleasant memories. Odor signals are processed in the 'limbic system' of the brain which also processes emotions and memories (see Schiffman, 1983); furthermore this portion of the brain interacts with the immune system (Schiffman & Miletic, 1999). Prospective longitudinal studies must be performed with elderly cancer patients (eg breast, lung and colorectal cancer) to determine if compensation for taste and smell losses has a sustained positive effect on food preferences and intake and improves outcome over an extended period of time.

Table 5 Preferences for flavor-enhanced and unenhanced foods among breast cancer patients

	Unenhanced (%)	*Enhanced (%)*	*Flavor used to enhance intensity*
Vegetables			
Carrots	15	85	Carrot
Green beans	8	92	Bacon
Green peas	8	92	Pea, bacon
Potatoes (mashed)	31	69	Potato, bacon
Meats			
Turkey (ground)	8	92	Bacon, beef
Chicken	23	77	Bacon, chicken
Soups (low sodium)			
Chicken	15	85	Chicken, bacon
Tomato	8	92	Bacon, tomato
Vegetable	8	92	Bacon, tomato, pea

Previous studies that have treated chemosensory losses with flavor enhancement

Addition of simulated food flavors to meats, vegetables and other nutritious foods to amplify odors to compensate for chemosensory losses has been shown previously to be helpful in an elderly population. Studies of frail elderly (without cancer) have found that amplification of the flavor levels of foods to preferred levels is associated with increases in the total number of lymphocytes (including T cells and B cells), increases in the secretion rate of salivary IgA, and improved functional status (Schiffman & Warwick, 1993; Schiffman & Wedral, 1997; Schiffman & Miletic, 1999; Schiffman, 1998). Interestingly, flavor enhancement resulted in improved immunity and functional status even when macro- and micronutrient intakes were not changed (Schiffman & Warwick, 1993). These studies indicate that flavor enhanced foods are preferred by frail and sick elderly and can improve immunity, quality of life, and functional status.

The four clinical studies described below have found that flavor enhancement of foods for the elderly can improve food palatability and acceptance, improve lymphocyte counts, increase salivary flow, or increase secretion rate of salivary immunoglobulin A (sIgA).

Study 1: flavor enhancement increases T and B cell levels in elderly retirement home residents

Schiffman and Warwick (1993) found that flavor enhancement of food for elderly retirement home residents resulted in improved immune status as determined by T and B cell levels and improved grip strength. In this study, thirty-nine elderly independent living residents at a retirement home (mean age 84.6 y) were divided into two groups. Group 1 received food that was unenhanced by flavor for the first 3 weeks, and food that was enhanced by flavor for the second 3-week period. For group 2, the order was reversed; they received enhanced food for the first 3-week period and unenhanced food for the second 3-week period. The menu plan during the 3 weeks of flavor enhancement was identical to the menu plan during the unenhanced 3-week period. Flavors were added to some but not all foods at a meal in the flavor enhanced conditon.

Six flavors were utilized throughout the study: roast beef, ham, natural bacon, prime beef, maple and cheese. The flavors contained odorous compounds but no taste compounds such as NaCl, monosodium glutamate or sweeteners. Flavors were added to vegetables (cauliflower, succotash, cabbage, peas, French cut green beans, mustard greens, Normandy vegetables, parsley cauliflower, peas and carrots, kale, spinach, stewed tomatoes, waxed beans, yellow squash, zucchini squash), gravies and sauces (mushroom gravy, prime beef brown gravy, roast beef brown gravy, roast pork gravy, Spanish sauce, tomato gravy, tomato sauce, vegetable gravy), breakfast foods (eggs, grits, maple syrup, oatmeal), and other main courses (soups, stews and macaroni cheese). These 30 foods were selected because they were nutrient dense.

Biochemical, anthropometric, and functional measures were obtained for each subject at the beginning of the study, at the end of 3 weeks, and at the end of 6 weeks. Measurements of food consumption were determined for every meal for 5 days of the week. The main findings were as follows. First, addition of flavors increased consumption of 20 out of 30 foods. However, these increases did not

shift the overall caloric intake or dietary nutrient profile. Analysis of the data indicated that they consumed the same macro- and micronutrients on the two arms of the study. This occurred because not all foods at a meal were enhanced during the 3-week experimental period; subjects simply ate less of the unenhanced food. Second, consumption of the flavor-enhanced food for three weeks was associated with improved immune function (as determined by elevated T and B lymphocyte counts) that was not attributable to altered intake of macro- and micronutrients. Third, improved grip strength in both hands was found after consumption of flavor-enhanced foods for three weeks.

This study was repeated with 4-week (rather than 3-week) food plans in which monosodium glutamate (to intensify taste) as well as flavors were added on the flavor enhanced arm of the study. Monosodium glutamate (MSG) is the sodium salt of glutamic acid. The amount of sodium in MSG needed to optimize the taste is much less than that required for NaCl. It has a meaty taste quality which is called 'umami' in Japanese. There is no analogous word to describe the taste of MSG in English. The results of this study that used MSG with flavors yielded similar results as the previous one (Schiffman, 1998).

Study 2: effect of taste and smell stimulation on secretion rate of salivary IgA in young and elderly persons

Two experiments reported by Schiffman and Miletic (1999) have found that taste and odor stimuli increase the secretion rate of salivary IgA in young (mean age = 32.4 y) and elderly (mean age = 73.2 y) individuals (Schiffman, 1998; Schiffman & Miletic, 1999). In the first experiment, three different types of drops were applied to the tongue: (1) 'flavor' drops (5% cocoa powder, 60% sugar, and 0.1% Irish cream odor); (2) sugar (60%) (sugar control); and (3) water (water control). The drops were delivered three times in 1 g doses in a 1 h period: at $t = 0$, at $t = 30$ min, and at $t = 60$ min. In the second experiment, four foods (corn, carrots, chicken broth and onion soup) were tested with and without monosodium glutamate. Each food (two solid and two liquid) was consumed three times in 6.5 g samples in a 1 h period: at $t = 0$, at $t = 30$ min, and at $t = 60$ min.

In both of the experiments, saliva was collected four times: (1) prior to chemosensory stimulation (baseline); (2) immediately after chemosensory stimulation; (3) 30 min after chemosensory stimulation; and (4) 60 min after chemosensory stimulation. The saliva was collected using the procedure described by Miletic *et al* (1996). Collections after taste and odor stimuli were made within 1 min after swallowing the drop. Salivary IgA was measured using capture ELISA and radial immune diffusion.

The results of these two experiments showed that chemosensory stimulation can improve mucosal immunity in two ways: (1) by increasing saliva production; and (2) by increasing the absolute concentrations of sIgA. In the first experiment, application of sugar (taste alone) and flavor (taste and odor combined) to the tongue was found to induce significantly higher secretion rates of sIgA than the application of water in both young and elderly subjects. Furthermore, flavor application produced significantly higher absolute concentrations of sIgA than sugar application alone. Secretion rates of sIgA in young persons were significantly higher than those in elderly persons. In the second experiment, the increase in sIgA secretion rate for the elderly subjects at 30 and 60 min for each food containing MSG was greater than that for the same food without MSG. The increases in sIgA secretion rates in these two experiments have important implications for the elderly because they often suffer from dry mouth and reduced salivary flow (and hence reduced mucosal immunity) due to normal aging, diseases, and medications they are taking.

Study 3: sensory enhancement of foods for sick elderly

Schiffman (1998) reported that addition of a combination of flavors and MSG to foods improved intake in 43 hospitalized patients. Each of the patients had clinical manifestations of malnutrition, a recent weight loss of 6% or more, and/or was below ideal weight. For each patient, all food served was measured before and after eating for two days; on one of the days the patient was served foods with added MSG and flavors, and on the other day the foods were unenhanced. The energy density of the food on each of the two days was identical. The levels of flavors and MSG added to the food were individualized based on psychophysical evaluations of each patients' taste and odor thresholds. The sodium levels were equivalent on the two days and did not exceed 2400 mg per day. The main finding was that 40 of 43 patients consumed at least 10% more calories on the day that they received flavor-enhanced food than on the unenhanced day. Furthermore, sensory enhancement over a week or more led to improved plasma protein levels (including somatomedin-C/insulin-like growth factor I, albumin, and transferrin) and T-lymphocytes in some patients.

Study 4: flavor enhancement of the entree at dinner can reduce sodium intake by 500 mg

A recent study at six retirement communities found that addition of flavors to an unsalted entree can reduce the sodium levels in a meal without compromising ratings of satisfaction. The study took place over an 8-week period. Throughout the study, two entrees (beef steak and chicken breast) were each served once a week. For the first 2 weeks, the entrees (beef or chicken) were salted with the preferred level of table salt for this population (at least 500 mg sodium). For the next 6 weeks, the entrees were flavor-enhanced by marination in sodium-free beef or chicken flavor prior to cooking; no additional table salt was added to the beef or chicken. Two vegetables which were lightly salted accompanied the entree. During the 6 weeks of flavor enhancement, the sodium content of the meal was reduced by 500 mg.

Residents were asked to rate their satisfaction with the sensory properties of the meal after eating. The results indicated that there was no difference in the degree of satisfaction between the salted version of the entree and the flavor-enhanced (sodium-free) version. These results suggest that amplification of odor can substitute for salt in the entree as long as two lightly salted vegetables accompany the meal. Hence, providing more sensory input in the form of odor can reduce the need for taste stimulation by salt. The main conclusion from this study is that addition of flavors to beef and chicken entrees can replace salt with no significant adverse effects on acceptability of flavor. Furthermore, the use of salt-free flavors could make it easier to comply with recommended daily intake of sodium (3000 mg or less).

Flavor enhancement and metabolic rate

Some but not all studies suggest that sensory stimulation from food apart from energy content increases metabolic rate (compare LeBlanc *et al*, 1984; LeBlanc & Brondel, 1985; Welle *et al*, 1981; Hill *et al*, 1985; Weststrate *et al*, 1990). For example, Henry and Emery (1986) reported that addition of very high levels of chile and mustard spices to a meal increased O_2 consumption in young adults. The metabolic rate increased by 28% for persons eating unspiced food and by 53% for persons eating spiced food. If flavors used to compensate for taste and smell losses also increase metabolic rate, this could be an obstacle to their use in treating sick elderly. In order to address this issue, the metabolic rate of four adult subjects (three females and one male) was determined before and after three meals containing the same ingredients but flavored in different ways. One meal was unflavored, a second contained ground red chile pepper, and a third meal contained bacon and onion flavors. This design allowed for a before- and after-meal comparison of metabolic rate to determine the effects of the three different meals on the diet-induced thermogenesis in each of the subjects.

The order of presentation of the three different lunch meals was randomized across subjects. The standard meal consisted of chile stew, bread with margarine spread, and a salad (lettuce leaves with salad dressing). Water was provided as a beverage. The three different flavor conditions were as follows. One meal was unflavored. In a second meal the salad dressing was flavored with crispy bacon flavor and the chili stew was flavored with Canadian bacon and sautéed onion flavor. In a third meal the salad dressing and chili stew were flavored with ground red chile pepper. The amount of spice or flavor added was individualized for each subject; it was the level preferred in pretesting and ranged from $\frac{1}{2}$ tsp to 3 tsp for each food item.

On all three test session days, subjects ate exactly the same breakfast and maintained the same light level of physical activity during the morning hours. On each test day, the subject was weighed at 11:20 a.m. At 11:30 a.m., the subject was seated in a semi-supine position in a comfortable chair for the 30-minute measurement of resting energy expenditure (REE). The mask for the Sensormatics 2900 indirect calorimeter, which measures oxygen consumed and carbon dioxide expended, was placed on the subject's face. The subject was instructed to remain seated during the REE measurement and to refrain from talking or moving around. At 12:00 p.m. (noon), the mask was removed and the subject was brought to a nearby room to consume lunch and use the toilet facilities. At 12:30 p.m., the mask was replaced, and a 2 h post-meal metabolic rate measurement was obtained using the same procedure as for the REE measurement. The mask was removed at 2:30 p.m.

Measurements of oxygen consumption were in milliliters per minute. Thirty data points, one per minute, were taken for the pre-meal REE measurement and 120 data points (one per minute) were taken for the post-meal measurement for each subject on each test day. For the purpose of analysis, data were averaged over 15 min intervals. The average oxygen consumption prior to a meal was 234.7 ml/min and after the meal was 272.9 ml/min. An analysis of variance (ANOVA) was performed to determine whether there was a significant effect of meal type (bland, bacon or chile) on the subjects' oxygen consumption data. The three meals yielded statistically equivalent data $F(2,90) = 0.15$, NS. There were no relationships between hedonic ratings of the meals and percentage increase in metabolic rate after consumption of the meals.

The main conclusion from this study is that neither the chile spice nor the bacon and onion flavors added to the test meal at preferred levels had an effect on subsequent metabolic rates for any subject. These data do not confirm the findings of Henry and Emery (1986) who reported significant elevations of metabolic rate from food flavored with chile and mustard spices. Furthermore, the findings indicate that addition of flavors to foods for the elderly will not alter caloric needs or compromise weight maintenance by elderly individuals.

Conclusion

Compensation for taste and smell losses by intensification of flavor can improve immune status and quality of life even when nutritional status per se is not the target. That is, flavor enhancement of food for the elderly and sick individuals can improve food palatability and acceptance; increase lymphocyte counts; reverse or slow functional decline, and improve overall quality of life even when macro- and micronutrient intake are not changed. Flavor enhancement also has the potential to compensate for anorexia, which is a common problem among older people because of physiological changes that are due to the aging process (Morley & Thomas, 1999).

Further studies must be performed to assess the impact of flavor enhancement of food on immune status, quality of life, and functional status in elderly individuals with different medical conditions and different types and degrees of chemosensory losses. These studies are important because the incidence of chemosensory losses and disorders will increase due to the projected growth in the absolute and relative size of the older population. By the year 2025, the number of persons aged 60 y or more is expected to reach 1.121 billion (US Senate Special Committee on Aging, 1985–1986).

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